AHRQ Healthcare Horizon Scanning System – Status Updates

Horizon Scanning Status Update

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Statement of Funding and Purpose

This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. HHSA29020100006C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

A novel intervention may not appear in this report simply because the System has not yet detected it. The list of novel interventions in the Horizon Scanning Status Update Report will change over time as new information is collected. This should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual target technology reports are developed for those that appear to be closer to diffusion into practice in the United States.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in the horizon scanning, assessing the leads or topics, or provide opinions regarding potential impact of interventions.

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None of the individuals compiling this information has any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor target technologies and innovations in health care and to create an inventory of target technologies that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It will also be a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research will be able to use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the Institute of Medicine and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is the identification and monitoring of new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is the analysis of the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. It is NOT the goal of the AHRQ Healthcare Horizon Scanning System to make predictions on the future utilization and costs of any health care technology. Rather, the reports will help to inform and guide the planning and prioritization of research resources.

This edition of the Status Update lists interventions that have been identified and are being monitored. The next edition will be published in 2 months. We welcome comments on the list, which may be sent by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to effectivehealthcare@ahrq.hhs.gov.

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Introduction

The AHRQ Healthcare Horizon Scanning System produces reports and status updates from its activities. The Status Update is a summary of data elements collected from implementation of the Horizon Scanning Identification and Monitoring Protocol. Status Updates are produced every two months, with each new report superseding the prior version. This Status Update report builds on pilot reports prepared during the first eight months of horizon scanning. It is organized by topic status and then by priority condition, with each of the priority conditions and a "cross-cutting" category presented as individual tables. The table of contents provides links directly to tables within each topic category for each priority condition. Those topics that were already in the system are presented first ("currently tracked interventions"), followed by new topics added during the two-month interval since the prior report, followed by interventions identified but archived, and finally, those interventions identified but not tracked. Within each table, we provide the Topic Title, the Potential Patient Population, the Intervention description (including the Developer/Manufacturer(s) and Phase of Development), the Potential Comparators, and Potential Health or Other Impacts.

Criteria for including topics in the Status Update are provided in detail in the protocol, which is available on the Effective Health Care Web site. Briefly, broad scanning is performed for each priority condition to detect "leads" to interventions and innovations. Sets of questions are applied to determine whether any given intervention addresses an "unmet need" such as a gap in effective ways to screen, diagnose, treat, monitor, manage, or provide or deliver care for a health condition or disease. Interventions might be lacking entirely, or existing options may be less than optimal. Leads that appear to address an unmet need are assigned to horizon scanning analysts and are assessed for grouping into potential topics. Potential topics are then described according to the "PICO" framework: potential patient Population, the Intervention, potential Comparators to the intervention, and potential Outcomes of interest for the patient population.

During a topic nomination meeting, additional criteria are applied to each topic, including questions about the potential importance of the unmet need, the likelihood of the intervention being adopted in the U.S., the innovativeness of the intervention, and the potential impact of the intervention on current treatments, sites of care, disparities in care, health care processes and infrastructure, patient and population health outcomes, understanding of the disease or condition, clinician and patient training needs and costs of care. Topics accepted during the topic nomination meeting are then entered into the System for tracking, and appear in the Status Update report as "currently tracked interventions" and "interventions added since last update."

Some of the accepted topics may also be selected during the meeting for Target Technology report development. Clinical interventions (i.e., drugs, devices, procedures) that are voted for advancing to target must be far enough along in development (typically phase III) to have some preliminary efficacy and safety data available for inclusion in the profile. Topics that are programs or care delivery innovations may be advanced to target with less data available if enough information is available to describe the care delivery innovation well, and if demonstration projects or pilot studies are underway. The horizon scanning medical librarians and analysts proceed with more in-depth and topic-specific searching for information on the topics selected for advancement.

During this process of gathering more information, it sometimes becomes apparent that an intervention does not in fact meet criteria for monitoring. Such topics are listed in the Status Update as "identified but not tracked." Once target technology reports are developed, comments are sought from up to eight experts with a variety of perspectives and areas of expertise in health care. A topic may also be archived or retired if aggregated comments from the experts suggest that an intervention is unlikely to meet an unmet need or to have impact on health outcomes or health care in the U.S. Over time, a topic may be archived because development has ceased, because it is no longer novel, or because the intervention has diffused past early adoption.

Included in this Status Update report are a total of 937 identified interventions. Of these, there are 757 interventions being tracked at the beginning of the current reporting period, 138 newly added interventions since the previous pilot report delivered in September 2011, 40 identified but archived topics, and two topics identified but not tracked. The reasons for archiving or not tracking individual topics are provided in the respective tables. As of this update, interventions related to cancer account for 30% of identified and currently monitored topics. The next most frequently identified were categorized as addressing functional limitations and disability (19%), cardiovascular diseases (12%), infectious diseases (11%), and diabetes (6%). Interventions relevant to the remaining priority conditions (arthritis, dementia, depression and other mental illness, obesity, peptic ulcer disease and dyspepsia, pregnancy and childbirth, pulmonary diseases and substance abuse) account for 22% of the total.

Section 1. Currently Tracked Interventions: 757 Interventions

Table 1. AHRQ Priority Condition: 01 Arthritis and Nontraumatic Joint Disease: 26 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Autologous mesenchymal stem cell therapy (NurOwn) for amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	NurOwn™ differentiated autologous adult stem cell therapy. The technology collects from the patient adult human mesenchymal stem cells from autologous bone marrow and processes the cells in vitro using a proprietary process in which the cells are intended to differentiate into astrocyte-like cells capable of releasing neurotrophic factors, including glial-derived neurotrophic factor; cells are then reinfused through either a single intrathecal injection into the cerebrospinal fluid or multiple intramuscular injections into biceps or triceps. BrainStorm Cell Therapeutics, New York, NY Phase I/II trial ongoing; FDA granted orphan drug status in Feb 2011; company states intention to pursue FDA regulatory approval	Riluzole Physical therapy and assistive technology (speaking tubes, motored chairs, etc.)	Slowed disease progression Improved quality of life Maintained independence and activities of daily living
Belimumab (Benlysta) for treatment of systemic lupus erythematosus	Patients in whom systemic lupus erythematosus (SLE) has been diagnosed	Belimumab (Benlysta®) is a fully human monoclonal antibody that specifically recognizes and inhibits the biological activity of B-lymphocyte stimulator (BLyS), which plays a key role in B-lymphocyte differentiation, survival, and activation. Human Genome Sciences, Inc., Rockville, MD GlaxoSmithKline, Middlesex, UK FDA approved Mar 9, 2011	Corticosteroids Antimalarial drugs Cyclophosphamide and mycophenolate Methotrexate and azathioprine Intravenous immunoglobulin	Slowed disease progression Disease remission Symptom improvement
Canakinumab (Ilaris) for treatment of acute gout	Patients in whom acute gout has been diagnosed	Canakinumab (Ilaris®) is a human monoclonal antibody targeted at interleukin-1 beta (IL-1-beta). Novartis AG, Basel, Switzerland FDA advisory committee in Jun 2011 voted 11-1 against approving canakinumab because of safety concerns, despite unanimous agreement by committee that the drug was effective; committee hoped the company would present more data in future to address safety concerns. Company received complete response letter in Aug 2011 requesting additional clinical data.	Treatment: Nonsteroidal anti-inflammatory drugs (NSAIDs) Pegloticase Steroids Prophylaxis: Febuxostat and allopurinol Probenecid	Reduced inflammation Reduced pain Improved quality of life Faster return to activities of daily living

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
C-reactive protein inhibitor (ISIS-CRPRx) for reduction of elevated C-reactive protein levels associated with rheumatoid arthritis	Patients with elevated C-reactive protein (CRP) in whom rheumatoid arthritis (RA) has been diagnosed	Elevated CRP levels have been associated with various inflammatory disorders including RAs, cardiovascular disease, and diabetes. ISIS-CRPRx is intended to directly test whether or not lowering CRP might benefit patient outcomes in patients with these disorders; ISIS-CRPRx is a first-in-class selective antisense CRP (protein found in the liver) inhibitor. In a phase I trial, the agent was administered intravenously and subcutaneously to healthy volunteers and some subjects with elevated CRPs. ISIS Pharmaceuticals, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ Phase II trial planned; studies also under consideration for patients with multiple myeloma and cardiovascular disease	No other CRP reducing agent available	Reduced CRP levels Reduced symptoms Slowed disease progression
Denosumab (Xgeva) for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	Current RA treatments attempt to reduce inflammation, but do not directly address or prevent structural bone damage observed in RA patients. Denosumab (Xgeva®) is a monoclonal antibody that targets RANKL, which is required for osteoclast development, activation, and survival (leading to bone mineral loss); may be used with methotrexate. Amgen, Inc., Thousand Oaks, CA Phase II trials ongoing; drug is approved and indicated for prevention of skeletal-related events in patients with bone metastases from solid tumors	Bisphosphonates Disease-modifying antirheumatic drugs (DMARDS): methotrexate, hydroxychloroquine, sulfasalazine NSAIDs Tocilizumab (interleukin-6 [IL-6] antagonist) Anti-tumor necrosis factor alpha (TNF alpha)	Improved RA-MRI erosion score from baseline Improved radiographic joint space narrowing score Improved bone (CTX I and PINP) and cartilage (CTX II) markers Improved bone mineral density

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Fostamatinib disodium for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	Fostamatinib disodium, previously referred to as R788, is a Syk inhibitor; reversibly blocks lymphocyte signaling involved in inflammation and tissue degradation in RA; Intended for treatment of early stage RA to reduce swelling and tissue destruction; taken orally. Rigel Pharmaceuticals, Inc., South San Francisco, CA Phase III trials ongoing	DMARDs: Methotrexate, Hydroxychloroquine, Sulfasalazine Biologic mAbs Inhibitors Anti-inflammatory agents: Glucocorticoids, NSAIDs Analgesics	Decreased inflammation Slowed disease progression Reduced pain Improved function and activities of daily living Improved quality of life
JAK 1/JAK 2 inhibitor (LY-3009104) for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	RA is a chronic inflammatory disease causing polyarthritis with frequent progression to permanent joint damage, deformity, and functional disability. Biologic therapies have become standard of care for RA that no longer responds to DMARDs; however, biologics must be administered by intramuscular, subcutaneous, or intravenous injection and are associated with increased incidence of serious infections, including tuberculosis (TB); DMARDs with improved efficacy, tolerability and convenience are needed. LY-3009104 is an oral Janus kinase 1 (JAK 1) and Janus kinase 2 (JAK 2) inhibitor; JAK 1/2 are involved in mediating the activity of many cytokines involved in RA pathogenesis; inhibiting these kinases may reduce inflammation and RA symptoms. It is administered 1 to 8 mg, once daily, or up to 2 mg, twice daily. Incyte Corp., Wilmington, DE and Eli Lilly and Co. Indianapolis, IN Phase IIb trial ongoing	Adalimumab DMARDs Etanercept Fostamatinib Infliximab Tocilizumab Tofacitinib	Improved symptom scores as measured by the American College of Rheumatology (ACR) instruments ACR 20, ACR 50, ACR 70

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
JAK 3 inhibitor (VX-509) for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	RA is a chronic inflammatory disease causing polyarthritis with frequent progression to permanent joint damage, deformity, and functional disability; biologic therapies have become standard of care for RA that no longer responds to DMARDs; however, biologics must be administered by intramuscular, subcutaneous, or intravenous injection and are associated with increased incidence of serious infections, including TB; DMARDs with improved efficacy, tolerability and convenience are needed. VX-509 is an oral JAK 3 inhibitor; JAK 3 is involved in mediating the activity of many cytokines involved in RA pathogenesis; inhibiting this kinase may reduce inflammation and RA symptoms mediated by T cells, B cells, and monocytes. It is administered 25 to 150 mg, twice daily. Vertex Pharmaceuticals, Inc., Cambridge, MA Phase II trial completed	Adalimumab DMARDs Etanercept Fostamatinib Infliximab Tocilizumab Tofacitinib	Improved symptoms scores as measured by American College of Rheumatology instruments ACR 20, ACR 50, ACR 70
KB003 for treatment of rheumatoid arthritis	Patients is whom RA has been diagnosed	RA is a chronic inflammatory disease causing polyarthritis with frequent progression to permanent joint damage, deformity, and functional disability. Biologic therapies have become standard of care for RA that no longer responds to DMARDs; however, biologics must be administered by intramuscular, subcutaneous, or intravenous injection and are associated with increased incidence of serious infections, including TB. DMARDs with improved efficacy, tolerability, and convenience are needed. KB003 is a monoclonal antibody against granulocyte-macrophage colony-stimulating factor (GM-CSF), a proinflammatory cytokine believed to be elevated in RA patients. KB003 is purported to be "humaneered" to reduce the likelihood of immune reactions that may occur after long-term use of the drug. KaloBios Pharmaceuticals, Inc., South San Francisco, CA Phase II trial ongoing	Adalimumab DMARDs Etanercept Fostamatinib Infliximab Tocilizumab Tofacitinib VX-509	Improved symptom scores (as measured by American College of Rheumatology instruments ACR 20, ACR 50, ACR 70) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
LX2931 for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	LX2931 targets lymphocytes through a novel mechanism of action that may change current treatment models and paradigms. LX2931inhibits sphingosine-1-phosphate (S1P) lyase; S1P is involved in several aspects of lymphocyte growth, migration, and activity; targeting S1P-lyase is intended to increase retention of lymphocytes in the lymphoid tissue, thereby preventing them from causing in inflammation in joints. Administered orally. Lexicon Pharmaceuticals, Inc., The Woodlands, TX Phase II trial completed	Hydroxychloroquine Methotrexate Monoclonal antibodies NSAIDs Sulfasalazine	Improved RA symptoms Reduced number of lymphocytes in circulation Improved quality of life
Mesenchymal precursor cells (NeoFuse) for treatment of degenerative disc disease	Patients in whom degenerative disc disease (DDD) of the lower back has been diagnosed	Between 15% and 40% of the population will experience DDD. Although physical therapy and medication provide a solution in most cases, spinal surgery involving either total disc replacement or spinal fusion is needed by a subset of patients. Noninvasive treatments are needed relieve the symptoms of patients who do not require surgery, would like to prevent the need for surgery, or are at risk of losing disc height following surgery. Allogeneic adult stem cells combined with hyaluronic acid (NeoFuse™) are injected into severely damaged intervertebral discs with the intention of reversing the degenerative process, stimulating regrowth of disc cartilage, and sustaining normalization of disc pathology, anatomy, and function; mesenchymal precursor cells are purported to produce the proteoglycans found in disc cartilage, so the manufacturer hypothesizes that the injection of mesenchymal stem cells into a degenerated intervertebral disc will lead to replacement of the proteoglycan of cartilage resulting in a minimally invasive, lower cost therapy for patients with moderate or severe DDD. Mesoblast, Ltd., New York, NY Phase II trials ongoing	Spinal fusion Total disc replacement	Increased activities of daily living Reduced chronic lumbar back pain Reduced use of pain medications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mesenchymal stem cells for treatment of osteoarthritis	Patients in whom osteoarthritis has been diagnosed	Other than joint replacement and symptom management, effective treatment for osteoarthritis to restore function long-term is not available; viscosupplementation provides temporary relief and improves function short-term for some patients, but long-term nonsurgical treatments are needed. Adult stem cells, platelet-rich plasma (PRP), and fat are injected into the affected site; PRP stimulates stem cell growth and the fat provides a framework and bulk for the stem cells to adhere to. Arthritis Treatment Center, Frederick, MD Small trial completed; procedure currently available to patients	Viscosupplementation Joint replacement surgery Lifestyle modification (weight loss, exercise) Pharmacologic pain management Physical therapy Alternative medicine	Reduced pain Increased range of motion Increased tissue regeneration
Methotrexate analog (CH-1504) for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	CH-1504 is an orally available, metabolically inert antifolate for potential treatment of RA; an analog of methotrexate that differs from classic antifolates because of a seemingly better safety and tolerability profile (likely due to its polyglutamylated and hydroxylated metabolites). Chelsea Therapeutics, Inc., Charlotte, NC Phase II trial completed	Methotrexate Other DMARDs	Reduced inflammation Reduced pain Delayed disease progression Improved quality of life
Monoclonal antibody (LY2127399) for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	LY2127399 is a fully human immunoglobulin G4 monoclonal antibody targeting BLyS. BLyS plays an important role in stimulating B-lymphocyte production when the human body is battling infection, but overproduction can cause production of auto-antibodies and initiate auto-immune-like disease symptoms in mice; by inhibiting the biologic activity of BLyS, LY2127399 inhibits the stimulation, proliferation, and differentiation of B cells. Intravenous and injectable formulations are under development for RA. Eli Lilly & Co., Indianapolis, IN Phase III trials ongoing	Anti-inflammatory agents Biologics DMARDs	Reduced symptoms Delayed progression of disease Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Monoclonal antibody (LY2127399) for treatment of systemic lupus erythematosus	Patients in whom SLE has been diagnosed	LY2127399 is a monoclonal antibody that acts against B-cell activating factor (BAFF), a protein related to tumor necrosis factor (TNF) that promotes survival of B cells as they exit the bone marrow and also prevents them from undergoing apoptosis (programmed cell death) later on. BAFF overexpression was found in diseased brain and BAFF; referred to as a B cell-targeted therapy. Drug is delivered by subcutaneous injection every 2 or 4 weeks and taken with standard care. Eli Lilly & Co., Indianapolis, IN Phase III trials ongoing	Standard care NSAIDs Rituximab (off-label use)	Improved SLE Responder Index Improved quality of life
Nitronaproxen (Naproxcinod) for treatment of osteoarthritis	Patients in whom osteoarthritis has been diagnosed	Effective NSAIDs with an improved safety profile are needed to prevent cardiovascular complications. Nitronaproxen is an NSAID and derivative of naproxen with a nitroxybutyl ester, making it a nitric oxide (NO) donor. Nitronaproxen is the first-in-class cyclooxygenase inhibiting NO donators (CINODs); CINODs are intended to produce analgesic efficacy similar to traditional NSAIDs, but with less gastrointestinal (GI) and cardiovascular side effects because of the local effects of NO. NicOx, Sophia Antipolis, France Phase III trials; manufacturer received FDA response letter to new drug application (NDA) requesting long-term safety data on cardiovascular effects; Jul 2011 manufacturer initiated FDA Formal Dispute Resolution Process	Celecoxib Ibuprofen Naproxen	Increased mobility Decreased pain Improved cardiovascular effects (blood pressure)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral salmon calcitonin (oral, Eligen; SMCo21) for treatment of osteoarthritis	Patients in whom osteoarthritis has been diagnosed	Treatments to slow or reverse the degradation of cartilage in patients with osteoarthritis are needed. SMCo21 is a recombinant salmon-derived calcitonin formulated in an oral tablet using Eligen® drug delivery technology made by Emisphere Technology, Inc., Cedar Knolls, NJ, which uses passive transcellular transport, to improve uptake of large molecules through biologic membranes and the GI tract; calcitonin treatment has been shown to have chondroprotective effects in vitro, including increased proteoglycan and collagen synthesis in human chondrocytes; suspected action is through activation of the calcitonin receptor; salmon calcitonin is 30 times more potent than human calcitonin. Administered 0.8 mg, orally, in clinical trials. Novartis AG, Basel, Switzerland, Nordic Bioscience, Herlev, Denmark Phase III trials completed	Autologous stem cell therapy NSAIDs Physical therapy Platelet rich plasma therapy Autologous chondrocyte implantation	Decreased CTX-I and CTX-II levels (markers of bone and cartilage degradation) Increased joint space width in the medial tibio-femoral knee joint Improved mobility Increased physical activity Decreased pain Improved quality of life
Pegloticase (Krystexxa) for treatment of chronic gout	Patients in whom acute gout has been diagnosed	Pegloticase (Krystexxa®) is a recombinant porcine-like uricase, which metabolizes uric acid to allantoin; reduces risk of precipitates, because allantoin is five to ten times more soluble than uric acid; in contrast to rasburicase, pegloticase is pegylated to increase its elimination half-life from about 8 hours to 10 to 12 days and to decrease the immunogenicity of the foreign uricase protein; intended to treat severe, treatment-refractory, chronic gout Savient Pharmaceuticals, Inc., East Brunswick, NJ FDA approved Sept 15, 2010	Treatments: NSAIDs Steroids Prophylaxis: Febuxostat and allopurinol Probenecid	Reduced inflammation Reduced pain Improved quality of life Faster return to activities of daily living

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Platelet-rich plasma therapy for treatment of knee osteoarthritis	Patients in whom knee osteoarthritis has been diagnosed	PRP therapy involves collection, separation and concentration of autologous platelets from a patient's blood, which usually takes place at a community blood bank (e.g., American Red Cross) or a hospital's own blood bank; the PRP is then re-infused in an outpatient setting at the desired anatomic site (i.e., knee); PRP contains and releases (through degranulation) at least seven different growth factors that are intended to stimulate bone healing and soft tissue healing. Orthohealing Center, Los Angeles, CA Various U.S. trials completed 2010; several ongoing	Analgesics Viscosupplementation Artificial knee replacement Lifestyle modification Physical therapy	Decreased pain Increased mobility Improved quality of life
RDEA594 for treatment of hyperuricemia and allopurinol-refractory gout	Patients in whom hyperuricemia has been diagnosed and thus are at high risk for acute gout	Only 30% to 40% of gout patients respond adequately to the currently available allopurinol. RDEA594 is a selective URAT1 transporter inhibitor; leads to uric acid excretion to reduce uric acid and crystal formation to potentially alleviate symptoms of acute gout. Ardea Biosciences, Inc., San Diego, CA Phase IIb trials ongoing	Allopurinol (gout, hyperuricemia) Febuxostat (hyperuricemia) Uricosurics (probenecid, benzbromarone and sulfinpyrazone, for hyperuricemia)	Reduced accumulation of uric acid and crystal formation Reduced acute flare-ups
Rilonacept (Arcalyst) for treatment of acute gout	Patients in whom acute gout has been diagnosed	Rilonacept (Arcalyst®) is a dimeric fusion protein consisting of the extracellular domain of human IL-1 receptor and the FC domain of human immunoglobulin G1 that binds and neutralizes IL-1; intended to decrease inflammation. Administered by subcutaneous injection. Regeneron Pharmaceuticals, Inc., Tarrytown, NY Phase III trial ongoing; submitted supplementary biologics license application (sBLA) to FDA for gout indication; FDA approved in 2008 for children with autoinflammatory cryopyrin-associated periodic syndromes in which IL-1 has a pathogenic role	Treatment: NSAIDs Pegloticase Steroids Prophylaxis: Febuxostat and allopurinol Probenecid	Reduced inflammation Reduced pain Improved quality of life Faster return to activities of daily living

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
SD-6010 (SC84250) for treatment of osteoarthritis	Patients in whom osteoarthritis has been diagnosed	NSAIDs with new mechanisms of action that can inhibit tissue destructive processes are needed for the treatment of osteoarthritis. SD-6010 (SC-84250) is an inhibitor of inducible NO synthase (iNOS), intended for the potential treatment of osteoarthritis; the iNOS pathway is activated through proinflammatory signals, and iNOS further promotes inflammation by the protein's role phagocyte-mediated oxidative cell killing (oxidative bust), which can erode cartilage in osteoarthritis patients. Administered 50 and 200 mg, orally, once per day. Pfizer, Inc., New York, NY Phase II/III trials ongoing	Celecoxib Ibuprofen Naproxen	Improved mobility Reduced pain Reduced rate of joint space narrowing
Tofacitinib (tasocitinib, CP-690,550) for treatment of rheumatoid arthritis	Patients in whom RA has been diagnosed	Tofacitinib (CP-690,550) is a selective and potent oral tyrosine kinase inhibitor that is being investigated as a targeted DMARD for treatment of RA. Tofacitinib inhibits a Janus-kinase-3 (JAK-3) signaling pathway believed to mediate several processes involved in chronic inflammatory diseases, such as antibody production by B cells, production of rheumatic factor and activation of T cells.By inhibiting the JAK-3 pathway, tofacitinib may suppress the inflammatory reactions that are the basis of RA. In recent trials, tofacitinib was administered in once daily (20 mg) or twice daily (1, 3, 5, 10 and 15 mg) doses. A targeted therapy that might reduce RA-specific inflammatory processes in the way tofacitinib purports to may provide better symptom control with fewer adverse events than other DMARDs or NSAID-activated anti-inflammatory pathways. Pfizer, Inc., New York, NY Five phase III trials completed; one ongoing; filed for approval with EMA Nov 2011; NDA filing with FDA anticipated by end of 2011 or early 2012	Anti-inflammatory agents DMARDs Monoclonal antibodies	Reduced inflammation Improved symptoms Improved activities of daily living Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
TissueGene-C allogeneic chondrocytes for treatment of knee osteoarthritis	Patients in whom grade 3 degenerative chronic osteoarthritis of the knee has been diagnosed	Current treatments require a multi-step process to harvest autologous chondrocytes from the patient, culture them, and reimplant them in the knee; this process can lead to deposit of fibrocartilage in the patient rather than the normally endogenous hyaline cartilage (microfracture surgery). Developer asserts a novel method for inserting therapeutic growth-factor gene into allogeneic chondrocyte cells, culturing and stabilizing them, and injecting them into the injured site in the knee; intended to secrete growth-factor proteins to potentially regenerate and repair tissue; TissueGene-C chondrocytes have been genetically modified to express transforming growth factor-beta; intended as a permanent repair and purported to be applicable to major (full-thickness) cartilage defects rather than just minor (partial-thickness) defects; the biologic can also be mass produced and used off the shelf. TissueGene, Inc., Rockville, MD Phase II trial ongoing	Microfracture surgery Autologous chondrocyte implantation (Carticel) Osteochondral autograft transfer Knee replacement	Decreased knee pain Improved knee function Delayed or avoided knee replacement surgery
Tissue-specific COX-2 inhibitor CG-100649 for treatment of osteoarthritis	Patients in whom osteoarthritis has been diagnosed	Effective NSAIDs with an improved safety profile are needed to prevent cardiovascular and GI complications. CG-100649 is purported to be an oral dual inhibitor of cyclooxygenase-2 (COX-2) and carbonic anhydrase (CA) in red blood cells; by interacting with CA in red blood cells CG100649 is purported to have a tissue-specific transport mechanism designed to deliver sustained levels of drug to inflamed joint tissues, while maintaining low systemic exposure to cardiovascular, GI, and renal tissue compared with traditional NSAIDs or COX-2 inhibitors. Administered 2 mg, once daily. CrystalGenomics, Seoul, South Korea Phase IIb trials ongoing	Celecoxib NSAIDS	Change in rescue medication Improved global assessment scores (patient and physician) Improved Western Ontario and McMaster Universities Osteoarthritis (WOMAC pain score and OA Index subscales

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tocilizumab (Actemra) for treatment of rheumatoid arthritis	Patients in whom moderate to severe RA has been diagnosed	Current treatments for RA generally address inflammation, but do not directly address bone resorption in patients; therapies to prevent/treat bone damage in RA patients are needed. Tocilizumab (Actemra®) is a humanized monoclonal antibody IL-6 receptor antagonist; IL-6 is involved in inflammation and is produced by osteoblasts to stimulate osteoclast activity; inhibiting IL-6 activity may reduce bone destruction associated with RA; may be used as monotherapy or in combination with methotrexate or other DMARDs. Administered as a 4 or 8 mg/kg of body weight infusion, every four weeks. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland FDA approved Jan 2010 for treatment of adults with moderate to severe active RA who have had an inadequate response to one or more TNF inhibitors; Jan 2011 clinical indication expanded to include inhibition and slowing of structural joint damage, improvement of physical function, and achievement of major clinical response in patients with moderate to severe active RA when given in combination with methotrexate	Bisphosphonates Denosumab (phase II clinical studies for RA) DMARDs: methotrexate, hydroxychloroquine, sulfasalazine NSAIDs	Decreased bone erosion Improved physical function Major clinical response (ACR 70 response for a continuous 24 week period) Narrowing of the joint space

Table 2. AHRQ Priority Condition: 02 Cancer: 205 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Abiraterone (Zytiga) for treatment of castration-resistant prostate cancer	Patients in whom metastatic prostate cancer that is nonresponsive to androgen deprivation or antiandrogen drugs has been diagnosed	Administered in combination with prednisone, abiraterone (Zytiga™) inhibits a cytochrome p450 subunit (CYPC17) responsible for a step in the androgen biosynthetic pathway; castration-resistant prostate cancer (CRPC) may escape androgen inhibition/removal through autocrine androgen signaling/upregulation of the androgen receptor; blocking the tumor cell's ability to produce testosterone and/or further reducing extra-gonadal androgen generation may inhibit tumor growth. Janssen Biotech, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ FDA approved Apr 2011	Cabazitaxel Docetaxel Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
ADXS11-001 for treatment of advanced cervical cancer	Patients in whom advanced cervical cancer has been diagnosed	Advanced cervical cancer is associated with a 5% 1-year survival rate. For patients with advanced cervical cancer, no effective therapies exist, and effective therapies on inoperable tumors are needed. ADXS11-001 is an immunotherapy comprising live, attenuated *Listeria monocytogenes* bacteria that have been engineered to express the HPV 16 E7 protein, which is believed to be crucial for cervical oncogenesis; the recombinant *Listeria* are purported to be a delivery vehicle to get E7 into antigen-presenting cells to induce cellular immunity. ADXS11-001 has been administered as 1x10^9, 3.3x10^9 or 1x10^10 cfu, intravenously, in clinical trials. Advaxis, Inc., New Brunswick, NJ Phase II trials ongoing	Cisplatin Radiotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Afatinib (BIBW 2992, Tomtovok, previously Tovok) for treatment of breast cancer	Patients in whom HER2-positive breast cancer has been diagnosed	Afatinib (BIBW 2992, Tomtovok™, previously Tovok) is a small-molecule, irreversible inhibitor of both epidermal growth factor receptor (EGFR) (Her1) and Her2 receptor tyrosine kinases; these receptor tyrosine kinases seen overexpressed in breast cancers (about 20% of patients); targeted EGFR-like receptor inhibition in these cancers has a high relative success rate. Although multiple receptor tyrosine kinases are available; Afatinib is unique in that its inhibition is irreversible. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing	Lapatinib plus capecitabine Trastuzumab plus chemotherapy (e.g., paclitaxel, docetaxel, vinorelbine, capecitabine) Trastuzumab plus lapatinib	Increased overall survival Increased progression-free survival Improved quality of life
Afatinib (BIBW 2992, Tomtovok) for treatment of head and neck cancer	Patients in whom head and neck cancer has been diagnosed	Please see above information on afatinib also. Targeted EGFR-like receptor inhibition in head and neck cancers has a high relative success rate. Although multiple receptor tyrosine kinase inhibitors are available, afatinib is unique in that its inhibition is irreversible. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase II trial ongoing; phase III trials registered, but not yet recruiting	Cetuximab (Erbitux®)	Increased overall survival Increased progression-free survival Improved quality of life
Afatinib (BIBW 2992, Tomtovok) for treatment of nonsmall cell lung cancer	Patients in whom nonsmall cell lung cancer (NSCLC) has been diagnosed	Please see above information on afatinib also. EGFR (Her1) and Her2 receptor tyrosine kinases are mutated/overexpressed in NSCLC in about 10% of patients; targeted EGFR-like receptor inhibition in these cancers has a high relative success rate. Although multiple receptor tyrosine kinase inhibitors are available; Afatinib is unique in that its inhibition is irreversible. Boehringer Ingelheim, GmbH, Ingelheim, Germany Phase II/III trials ongoing	First-line NSCLC: platinum based chemotherapy Second- and third-line NSCLC: docetaxel, pemetrexed, erlotinib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Aflibercept (Zaltrap) for treatment of metastatic castration-resistant prostate cancer	Patients in whom metastatic CRPC has been diagnosed who are undergoing first-line cytotoxic chemotherapy	Current second-line and adjunctive treatments for advanced prostate cancer have poor response rates and this patient population has poor overall prognosis. Aflibercept (Zaltrap™) is a VEGF-signaling inhibitor that contains multiple copies of the VEGFR extracellular domain designed to bind VEGF. It is an anti-angiogenic agent intended to reduce tumor vascularization, thereby inhibiting tumor growth. The drug is being tested as an adjunct to standard second-line chemotherapy with docetaxel for advanced prostate cancer. Collaboration between Regeneron, Tarrytown, NY and Sanofi-Aventis, Bridgewater, NJ Phase III trial ongoing	Abiraterone Docetaxel with prednisone Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Aflibercept (Zaltrap) for treatment of metastatic colorectal cancer	Patients with metastatic colorectal cancer (CRC) that has recurred after oxaliplatin-based chemotherapy	Current second-line and adjunctive treatments for advanced, recurrent CRC have poor response rates and this patient population has poor overall prognosis. Please also see above aflibercept (Zaltrap™) information; being tested as an adjunct to the standard chemotherapy treatment of leucovorin, irinotecan and 5-FU. Collaboration between Regeneron, Tarrytown, NY, and Sanofi-Aventis, Bridgewater, NJ Phase III trial complete; BLA submitted to FDA Nov 2011	5-FU-based therapy plus bevacizumab FOLFIRI (folinic acid [leucovorin], fluorouracil, and irinotecan) FOLFIRI plus cetuximab or panitumumab FOLFIRI plus cetuximab or panitumumab Irinotecan Irinotecan plus cetuximab	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ALD518 for treatment of cancer-treatment-related fatigue, cachexia, and anemia	Patients with cancer who have undergone treatment and are experiencing fatigue, cachexia, and anemia	Concerns over long-term adverse effects of erythropoiesis-stimulating agents and a desire to avoid blood transfusions in patients with cancer who are experiencing anemia, fatigue, and cachexia, suggest a need for alternative therapies to address these cancer-treatment-related side effects. ALD518 is an aglycosylated, humanized, immunoglobulin G1 antibody that blocks interleukin-6 (IL-6) activity; blocking the IL-6 pathway affects tumor cells' overproduction of IL-6, which is known to stimulate inflammation-related activity that produces conditions such as fatigue, cachexia, and anemia. ALD518 is administered as a single intravenous infusion; its median elimination half-life of 25 days suggests a long duration of action. Alder Biopharmaceuticals, Inc., Bothell, WA Phase II trial completed Dec 2010; no additional development as of Nov 2011; also under study for rheumatoid arthritis	Blood transfusion Erythropoiesis-stimulating agents: Recombinant erythropoietins (Epogen and Procrit) and related protein darbepoetin alfa (Aranesp)	Improved quality of life Avoidance of transfusions for anemia Increased lean body mass Increased hemoglobin Reduced fatigue Reduced inflammation
Allogeneic DNA immunotherapy (Allovectin-7) for advanced melanoma	Patients in whom stage III or IV recurrent metastatic melanoma has been diagnosed	Advanced melanoma is associated with a poor prognosis. New effective treatments with acceptable safety profile are needed. Allovectin-7® is a DNA-based immunotherapeutic composed of a lipid encapsulated plasmid expressing HLA-B7 and beta2 microglobulin (required to generate a functional MHC I molecule); designed to stimulate innate and adaptive immune responses against local and distant tumors; expression of tumor antigens in the context of the MHC I molecule HLA-B7 generates an allogeneic response against tumors; lipid/DNA complexes have adjuvant activity for the vaccine. It is given as an intratumoral infusion on outpatient basis. Vical, San Diego, CA Phase III trials ongoing; FDA granted orphan drug and fast track status for invasive and metastatic melanoma	Dacarbazine or Interferon Ipilimumab Personalized vaccination (in clinical development) Proleukin (interleukin-2 [IL-2]) Temozolomide Therapeutic vaccines (in clinical development) Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ALN-VSP/RNAi for treatment of secondary liver metastases	Patients with liver metastases from advanced solid tumors	Metastases to the liver from solid tumors in other parts of the body are difficult to treat and are associated with a poor prognosis despite available treatment options. ALN-VSP is an infused RNAi therapeutic that targets two genes involved in the disease pathway of liver cancer: kinesin spindle protein (KSP), which is involved in cancer cell proliferation, and vascular endothelial growth factor (VEGF) is involved in the growth of new blood vessels that feed tumors. Alnylam Pharmaceuticals, Cambridge, MA Phase I trial completed	Chemotherapy Intrahepatic microspheres/drug-eluting beads Radiation therapy Immunotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Anaplastic lymphoma kinase inhibitor (crizotinib, Xalkori) for treatment of nonsmall cell lung cancer	Patients with NSCLC that harbors a genetic rearrangement that leads to constitutive activation ALK	ALK is an oncogenic tyrosine kinase that was identified in gene fusions that caused activation of ALK in lymphoblastoma; crizotinib (Xalkori®) inhibits ALK (and Met kinase) activity; in tumors that are driven by constitutive ALK activity, may reduce tumor growth/survival. Pfizer, Inc., New York, NY FDA approved Aug 2011 for treatment of locally advanced or metastatic NSCLC that is ALK-positive as detected by an FDA-approved test.	First-line chemotherapy: Pemetrexed plus cisplatin Second-line chemotherapy: Docetaxel plus pemetrexed Erlotinib (Tarceva)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Androgen receptor antagonist (MDV3100) for treatment of castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	Most prostate cancer tumors are dependent on androgen signaling for growth and survival; multiple androgen signaling inhibitors are available (e.g., bicalutamide, abiraterone); however, many prostate cancers do not respond to these therapies or develop resistance. MDV3100 is an androgen receptor antagonist that is purported to inhibit androgen signaling at three levels: by blocking testosterone binding to the androgen receptor; by inhibiting nuclear translocation of the activated androgen receptor; and by inhibiting DNA binding of activated androgen receptor; by more completely inhibiting androgen signaling, MDV3100 may overcome limitations of current antiandrogen therapies. MDV3100 is an oral drug being tested in both chemotherapy-naive patients and patients who have previously been treated with docetaxel. MDV-3100 is administered daily at a dose of 160 mg. Medivation, Inc., San Francisco, CA Phase III trial in patients previously treated with docetaxel was stopped early due to clear benefit in MDV-3100 arm; NDA submission expected to be filed in 2012; phase III trial in pre-docetaxel setting ongoing.	Chemotherapy-naive CRPC: Docetaxel Abiraterone plus prednisone Sipuleucel-T Pretreated CRPC: Abiraterone plus prednisone Cabazitaxel	Increased overall survival Increased progression-free survival Improved quality of life
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of advanced hepatocellular carcinoma	Patients in whom advanced hepatocellular carcinoma has been diagnosed; no prior systemic chemotherapy	Patients with advanced liver cancer have a poor prognosis and more effective treatments are needed. AMG 386 is a peptibody that binds to the signaling molecules angiopoietin 1 and angiopoietin 2 and consists of a peptide specific for angiopoietin 1/2 fused to the Fc region of a human antibody; intended to block the activation of the TIE2 receptor by angiopoietin 1/2; the angiopoietin/TIE2 pathway acts in parallel with the VEGF/vascular endothelial growth factor receptor (VEGFR) pathway to promote angiogenesis; the drug represents a novel first-in-class neutralizing inhibitor of angiopoietin 1/2. In clinical trials for hepatocellular carcinoma, AMG 386 is being administered in combination with the multikinase inhibitors sorafenib or sunitinib to patients who may have been previously treated with locoregional therapy or systemic cytokine-based therapy Amgen, Inc., Thousand Oaks, CA Phase II trial ongoing	Sorafenib Sunitinib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of HER-2 negative breast cancer	Patients with metastatic or unresectable locally recurrent HER-2 negative breast cancer; no prior systemic chemotherapy	Please see above AMG 386 description. In a clinical trial for breast cancer treatment, AMG 386 is being administered in combination with the microtubule stabilizer paclitaxel plus or minus the VEGF inhibitor bevacizumab. Amgen, Inc., Thousand Oaks, CA Phase II trial ongoing	Paclitaxel monotherapy Paclitaxel plus bevacizumab	Increased overall survival Increased progression-free survival Improved quality of life
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of metastatic colorectal cancer	Patients with metastatic CRC who have had one prior chemotherapy regimen	Patients with metastatic CRC have a poor prognosis and more effective treatment options are needed. Please see above information on AMG 386. In clinical trials for metastatic CRC, AMG 386 is being administered in combination with the cytotoxic chemotherapy regimen FOLFIRI. Amgen, Inc., Thousand Oaks, CA Phase II trials ongoing	FOLFIRI FOLFIRI plus cetuximab Irinotecan Irinotecan plus cetuximab	Increased overall survival Increased progression-free survival Improved quality of life
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of metastatic gastrointestinal cancer	Patients in whom metastatic gastric, gastroesophageal junction, or distal esophageal adenocarcinoma has been diagnosed; no prior chemotherapy	Patients with metastatic gastrointestinal (GI) cancer have a poor prognosis and more effective treatments are needed. Please see above information on AMG 386. In clinical trials for gastric cancer, AMG 386 is being administered in combination with cisplatin and capecitabine. Amgen, Inc., Thousand Oaks, CA Phase II trial results reported mid-2011 for this indication were negative; development status uncertain	Cisplatin plus capecitabine	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of ovarian, peritoneal, and fallopian tube cancers	Patients in whom epithelial ovarian, primary peritoneal, or fallopian tube cancer has been diagnosed that is partially platinum sensitive or resistant	Patients with treatment-resistant ovarian, peritoneal, or fallopian tube cancer have a poor prognosis and more effective treatments are needed. Please see above information on AMG 386. In clinical trials for ovarian cancer, AMG 386 is being administered in combination with pegylated liposomal doxorubicin or paclitaxel. Amgen, Inc., Thousand Oaks, CA Phase III trials ongoing	Docetaxel Etoposide Gemcitabine Liposomal doxorubicin Paclitaxel Topotecan	Increased overall survival Increased progression-free survival Improved quality of life
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of persistent or recurrent endometrial cancer	Patients with persistent or recurrent endometrial cancer that has not responded to prior chemotherapy	Please see above information on AMG 386. In the trial just starting patients are receiving AMG 386 intravenously on days 1, 8, 15, and 21; courses will repeat every 28 days if disease has not progressed and side effects are tolerable. Amgen, Inc., Thousand Oaks, CA Phase II trial ongoing	Cisplatin/doxorubicin Cisplatin/doxorubicin/paclitaxel Ifosfamide/paclitaxel Carboplatin/paclitaxel Cisplatin Carboplatin Doxorubicin or liposomal doxorubicin Paclitaxel Hormonal therapy	Increased overall survival Increased progression-free survival Improved quality of life
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of recurrent glioblastoma multiforme	Patients in whom recurrent glioblastoma multiforme has been diagnosed	Patients with glioblastoma multiforme have a poor prognosis and more effective treatments are needed. Please see above information on AMG 386. In the clinical trial for glioblastoma, AMG 386 is being administered intravenously in combination with the VEGF inhibitor bevacizumab. Amgen, Inc., Thousand Oaks, CA Phase II trial ongoing	Bevacizumab monotherapy Cyclophosphamide Nitrosurea Platinum-based cytotoxic chemotherapy Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Angiopoietin 1/2 neutralizing peptibody (AMG 386) for treatment of renal cell carcinoma	Patients in whom advanced clear cell carcinoma of the kidney has been diagnosed; no prior systemic chemotherapy.	Please see above information on AMG 386. In clinical trials for renal cell carcinoma (RCC), AMG 386 is being administered in combination with the VEGFR inhibitor sorafenib. Amgen, Inc., Thousand Oaks, CA Phase II trial results reported mid-2011were negative; further development uncertain	Sorafenib	Increased overall survival Increased progression-free survival Improved quality of life
Anti-angiogenic multikinase inhibitor pazopanib (Votrient) for treatment of soft tissue sarcomas	Patients in whom advanced soft tissue sarcoma (excluding gastrointestinal stromal tumors [GIST] and liposarcomas) has been diagnosed and who have undergone prior systemic chemotherapy	Doxorubicin is currently the only FDA-approved treatment for soft tissue sarcomas (excluding GIST and liposarcomas) and no consensus treatment exists for patients who have progressed on doxorubicin chemotherapy. Pazopanib (Votrient™) is a multikinase inhibitor that has activity against multiple receptor tyrosine kinases (VEGFR1, VEGFR2, VEGFR3, platelet-derived growth factor receptor [PDGFR], c-kit) and has the potential to inhibit tumor angiogenesis and growth; although other multikinase inhibitors (e.g., sorafenib, sunitinib) have been used off-label to treat soft tissue sarcoma, no such compound has been approved by FDA. GlaxoSmithKline, Middlesex, UK Phase III trial complete; new drug application (NDA) has been submitted to FDA; pazopanib approved by FDA for treatment of RCC in 2009, and is marketed as Votrient	No consensus second-line treatment for soft tissue sarcoma Placebo Ridaforolimus (submitted to FDA) Sorafenib (off label) Sunitinib (off label)	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Antibody-drug conjugate (ASG-5ME) for treatment of castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	ASG-5ME is an antibody-drug conjugate. The antibody portion is a fully human antibody specific for SLC44A4 (solute carrier antigen family member), which is expressed by a large portion of tumors of epithelial origin. This antibody is linked to a potent antineoplastic drug, monomethyl auristatin E (MMAE, vedotin), via a linker that can be cleaved by cathepsin upon cellular uptake, releasing the drug. MMAE (a tubulin polymerization inhibitor) is too toxic for global delivery, but would be inactive in the uncleaved configuration. Agensys, an affiliate of Astellas Pharma, Deerfield, IL Seattle Genetics, Inc., Bothell, WA Phase I trial ongoing	Abiraterone Cabazitaxel Docetaxel	Increased overall survival Increased progression-free survival Improved quality of life
Antibody-drug conjugate (ASG-5ME) for treatment of late-stage pancreatic cancer	Patients in whom late-stage pancreatic cancer has been diagnosed	Please see above information on ASG-5ME. Agensys, an affiliate of Astellas Pharma, Deerfield, IL Seattle Genetics, Inc., Bothell, WA Phase I trial ongoing	Chemotherapy with gemcitabine or gemcitabine and erlotinib	Increased overall survival Increased progression-free survival Improved quality of life
Anti-CTLA-4 monoclonal antibody (ipilimumab, Yervoy) for treatment of advanced nonsmall cell lung cancer	Patients with recurrent or metastatic NSCLC who have not received previous systemic therapy	Only about 25% of patients with advanced NSCLC respond to standard first-line therapies such as carboplatin/paclitaxel. Ipilimumab (Yervoy™) is a first-in-class targeted anti-cytotoxic T lymphocyte antigen 4 therapy; it is intended to block activation of cytotoxic T lymphocyte antigen 4, which could lead to increased antitumor cytotoxic activity (reduce immune tolerance to tumor cells). As first-line NSCLC treatment in trials, ipilimumab is being administered in combination with carboplatin and paclitaxel. Bristol Myers Squibb, New York, NY Phase III trial ongoing	Bevacizumab Carboplatin/paclitaxel Carboplatin/pemetrexed Cisplatin/pemetrexed Erlotinib Crizotinib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anti-CTLA-4 monoclonal antibody (ipilimumab, Yervoy) for treatment of metastatic hormone-refractory prostate cancer	Patients in whom metastatic chemotherapy-naïve or docetaxel-treated CRPC has been diagnosed	Men with progressive metastatic, CRPC have a poor prognosis and few treatment options. Please see above information on ipilimumab. Bristol Myers Squibb, New York, NY Phase III trial ongoing	Abiraterone Cabazitaxel Docetaxel Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Anti-CTLA-4 monoclonal antibody (ipilimumab, Yervoy) for treatment of metastatic melanoma	Patients in whom metastatic melanoma has been diagnosed	Few effective treatments exist for metastatic melanoma, particularly for patients in whom B-RAF mutation-negative melanoma has been diagnosed. Please see above information on ipilimumab. Bristol Myers Squibb, New York, NY FDA approved Mar 2011	Dacarbazine High-dose interleukin-2 Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anti-insulin-like growth factor receptor monoclonal antibody (ganitumab) for treatment of metastatic pancreatic cancer	Patients in whom metastatic pancreatic cancer has been diagnosed	Only about 5% of patients with pancreatic cancers respond to the current standard of care (gemcitabine chemotherapy), and the prognosis for these patients is very poor. Insulin-like growth factor receptor type I (IGF-1R) has been implicated in cell growth and cell survival; therefore, targeted inhibition of IGF-1R is a potential therapeutic cancer intervention; ganitumab (AMG 479) is a humanized monoclonal antibody specific for IGF-1R. In current clinical trials for pancreatic cancer it is being administered intravenously in combination with the cytotoxic agent gemcitabine. Amgen, Inc., Thousand Oaks, CA Phase III trial ongoing	Gemcitabine Gemcitabine plus erlotinib Gemcitabine plus cisplatin or oxaliplatin Gemcitabine plus a fluoropyrimidine	Increased overall survival Increased progression-free survival Improved quality of life
Anti-Met monoclonal antibody (onartuzumab, MetMAb) for treatment of advanced nonsmall cell lung cancer	Patients with advanced (stage IIIb/IV) NSCLC that has progressed after first-line systemic chemotherapy	Patients with advanced/metastatic NSCLC that has progressed following first-line therapy have poor prognosis and few treatment options. Met (also known as Hepatocyte Growth Factor Receptor) is a receptor tyrosine kinase that regulates cell growth and survival. Met has been implicated in the development of tumor resistance to EGFR inhibition. Onartuzumab (MetMAb) blocks ligand-mediated activation of the Met receptor tyrosine kinase and is being studied in combination with the EGFR inhibitor erlotinib in treatment of NSCLC. F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trial completed; phase III trial registered, but not yet recruiting.	Docetaxel Erlotinib monotherapy Pemetrexed Tivantinib (c-Met kinase inhibitor in development)	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anti-PD-1 monoclonal antibody (CT-011) for treatment of diffuse large B-cell lymphoma	Patients in whom diffuse large B-cell lymphoma (DLBCL) has been diagnosed and who have undergone an autologous stem cell transplantation	While high-dose chemotherapy followed by autologous stem cell transplant is curative in a subset of DLBCL patients, a significant proportion of patients have recurrent disease following this treatment. CT-011 is a monoclonal antibody specific for PD-1, which is a negative regulator of the immune response that may be involved in immune tolerance of various cancers. CureTech, Ltd., Yavne, Israel Teva Pharmaceutical Industries, Ltd., Petach Tikva, Israel, is investing in the research Phase II trial complete; CT-011 is also being studied for treatment of CRC and melanoma	No consensus treatment option for patients post-autologous stem cell transplant	Increased progression-free survival Increased overall survival Improved quality of life
Anti-prostate-specific membrane antigen antibody drug conjugate for treatment of metastatic castration-resistant prostate cancer	Patients with metastatic CRPC that has progressed on treatment with docetaxel	Current median overall survival for patients with docetaxel-resistant CRPC is only about 15 months. Prostate-specific membrane antigen (PSMA) is an antigen expressed on the surface of prostate cancer cells. PSMA-antibody drug conjugate is a conjugate between a PSMA-specific antibody and a highly cytotoxic drug (MMAE); the linker connecting the drug to the antibody ensures that the drug is only released upon endocytosis into a target cell, which is mediated by the binding of the antibody portion of the drug to PSMA. Progenics Pharmaceuticals, Inc., Tarrytown, NY Phase I trial complete	Abiraterone Cabazitaxel	Increased progression-free survival Increased overall survival Improved quality of life (e.g., palliation of pain associated with metastases)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Assay (PROGENSA PCA3) for detection of prostate cancer	Patients undergoing digital rectal examinations for prostate cancer screening	The assay is a urine test that is performed after a digital rectal examination; detects a non-protein coding messenger RNA, prostate cancer antigen 3, that is highly overexpressed in the "vast majority" of prostate cancers; being developed as a test kit. Gen-Probe, Inc., San Diego, CA CE marked since 2006; FDA accepted premarket approval (PMA) application Apr 2011; postponed Oct 2011 decision date; decision expected first quarter 2012	Digital rectal examination alone Prostate-specific antigen blood test screening	Improved sensitivity and specificity Improved predictive values Avoided unnecessary followup (i.e., biopsy)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Autologous vascularized lymph node transfer for mastectomy-associated lymphedema	Patients who have undergone mastectomy	During mastectomy, lymph nodes under the arm closest to the affected breast are removed, which often leads to chronic swelling and soreness in the arm (lymphedema); lymphedema develops within 5 years in up to 40% of women who have undergone breast cancer surgery in the U.S.; it is considered generally incurable and can severely restrict activity. Autologous vascularized lymph node transfer is a microsurgical procedure to treat lymphedema; the excised lymph nodes are replaced with healthy nodes transplanted from the femoral region of the patient; the transplanted lymph nodes connect with lymph vessels improving waste filtration and drainage in the arm. Prior to implantation of the nodes, scar tissue may be excised to remove blockage of lymph vessels. Service de Chirurgie Thoracique, Hôpital Européen Georges Pompidou, Paris, France Procedure rarely done in U.S.; a randomized trial is beginning	Physical therapy Compression garments	Ability to stop physiotherapy Decrease, or disappearance of lymphedema assessed by isotopic lymphangiography Improved skin elasticity Improved mobility Resolution of pain
Axitinib therapy for treatment-resistant metastatic renal cell carcinoma	Patients previously treated for metastatic RCC	Axitinib is an oral and selective inhibitor of VEGFR1, VEGRF2 and VEGFR3, which appear to have roles in tumor growth, vascular angiogenesis, and metastatic progression of cancer (the spread of tumors). Pfizer, Inc., New York, NY Phase III trials ongoing; new drug application submitted to FDA and accepted for standard review in Jun 2011	Sorafenib Tivozanib (in development)	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bavituximab for treatment of advanced breast cancer	Patients in whom advanced breast cancer has been diagnosed	Breast cancer remains a leading cause of cancer deaths in women, suggesting the need for new therapies with novel mechanisms of action. Bavituximab is a monoclonal antibody directed against phosphatidylserine (PS) exposed on the surface of cancer cells; PS expression is believed to be immunosuppressive; bavituximab is thought to bind to PS and block the immunosuppressive signals to improve immune responses to the tumor; also, as chemotherapy increases the exposure of PS on tumor blood vessels, bavituximab combined with chemotherapy may hold potential for synergistic therapeutic effects. Administered intravenously, 6 mg/kg of body weight for up to six 28-day cycles, in combination therapy with carboplatin and paclitaxel. Peregrine Pharmaceuticals Inc., Tustin, CA Phase II trials completed; investigator-sponsored phase I trial ongoing	Docetaxel Paclitaxel Paclitaxel plus carboplatin	Increased overall survival Increased progression-free survival Improved quality of life
Bavituximab for treatment of advanced nonsmall cell lung cancer	Patients in whom locally advanced or metastatic NSCLC has been diagnosed	Advanced NSCLC has a poor prognosis with few therapeutic options. Please see above information on Bavituximab. Administered intravenously 3 mg/kg, weekly, in combination with carboplatin and paclitaxel in trials for first-line treatment of NSCLC and in combination with docetaxel in the second-line treatment of NSCLC.. Peregrine Pharmaceuticals Inc., Tustin, CA Phase II trials ongoing	Carboplatin Docetaxel Erlotinib Paclitaxel Pemetrexed	Increased overall survival Increased progression-free survival Improved quality of life
Bavituximab for treatment of advanced pancreatic cancer	Patients in whom advanced pancreatic cancer has been diagnosed	Advanced pancreatic cancer has a poor prognosis with few therapeutic options. Please see above information on Bavituximab. Administered 3 mg/kg, weekly, in combination with gemcitabine in trials for pancreatic cancer. Peregrine Pharmaceuticals, Inc., Tustin, CA Phase II trials ongoing	Gemcitabine	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bavituximab for treatment of hepatocellular carcinoma	Patients in whom hepatocellular carcinoma has been diagnosed	Advanced liver cancer has a poor prognosis with few therapeutic options; new therapies with novel mechanisms of action are needed. Please see above information on Bavituximab. Administered intravenously in various dose regimens of 0.3 to 6 mg/kg, weekly, for 8 or 12 weeks in clinical trials as a monotherapy and combination therapy with sorafenib. Peregrine Pharmaceuticals, Inc., Tustin, CA Phase I/II trials ongoing	Doxorubicin Sorafenib	Increased overall survival Increased progression-free survival Improved quality of life
Bcl-2 family inhibitor (navitoclax) for treatment of chronic lymphocytic leukemia	Patients in whom chronic lymphocytic leukemia (CLL) has been diagnosed; may either be treatment naïve or have relapsed or refractory disease	Patients in whom CLL has been diagnosed often exhibit disease control with current therapies; however, these therapies are not curative, and in many patients, the disease will eventually progress. Inhibition of apoptosis is a hallmark of CLL as well as other cancers; the prevention of apoptosis may in part be due to the activity of a family of proteins related to Bcl-2, which are often overexpressed in cancer. Navitoclax (ABT-263) is a small-molecule inhibitor of multiple Bcl-2 family members (Bcl-2, Bcl-xl, Bcl-w); it is being tested as a first-line therapy for CLL in combination with the anti-CD20 monoclonal antibody rituximab. Administered orally. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland, in collaboration with Abbott Laboratories, Abbott Park, IL Phase II trial ongoing	Various chometherapy regimens such as: Alemtuzumab Bendamustine and rituximab Chlorambucil with or without prednisone Cladribine Cyclophosphamide and prednisone with or without rituximab Fludarabine, cyclophosphamide, and rituximab Rituximab	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bevacizumab (Avastin) for treatment of ovarian cancer	Patients in whom advanced or recurrent ovarian cancer has been diagnosed	Ovarian cancer is the second deadliest cancer after pancreatic cancer; no new first-line treatment options have been made available in the past decade; new treatment options are needed. Bevacizumab (Avastin®) is a monoclonal antibody on the market for several other indications; intended to bind VEGF and prevent the interaction of VEGF with its receptors (Flt-1 and KDR) on the surface of endothelial cells. By preventing the interaction of VEGF with its receptors, bevacizumab prevents the proliferation of endothelial cells and the formation of new blood vessels needed to nourish growing tumors. Administered 15 mg/kg, intravenously, every 3 weeks and intended to be used with platinum-based chemotherapy. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trial complete	Paclitaxel plus carboplatin	Increased overall survival Increased progression free survival Improved quality of life
Bispecific T-cell-engager (BiTE) anti-CD19 antibody (blinatumomab) for treatment of acute lymphoblastic leukemia	Patients in whom relapsed/refractory Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL) has been diagnosed and patients in whom minimal residual disease-positive ALL has been diagnosed	No new treatments for Philadelphia chromosome-negative relapsed/refractory ALL have been developed in 30 years; 5-year survival for this patient population is only 7%. Blinatumomab is the most advanced molecule from a novel class of antibody-based compounds intended to link tumor cells to cytotoxic T cells; the molecule consists of two separate antibody antigen binding domains: (1) specific for CD19, an antigen expressed by the immature lymphocytes expanded in ALL and (2) specific for CD3 a molecule expressed on the surface of cytotoxic T cells; blinatumomab is purported to lead to tumor apoptosis by bridging an interaction between tumor cells and T cells. Micromet, Inc., Rockville, MD Phase II trial ongoing in relapsed/refractory ALL (preliminary results reported); one phase II trial completed in minimal residual disease-positive ALL; one phase II trial ongoing; FDA granted orphan drug status	Relapsed/Refractory ALL: anthracyclines (doxorubicin, daunorubicin) asparaginase cyclophosphamide cytarabine (ara-C) epipodophyllotoxins (etoposide, teniposide) vincristine MRD-positive ALL: No current standard of care	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Biophotonic cervical screening system (Luviva Advanced Cervical Scan) for detection of cervical disease in adolescent females	Females aged 16 to 21 years who are sexually active	Luviva™ consists of a base unit and a single-patient-use calibration disposable scanner; uses biophotonic technology (hyperspectral imaging spectroscopy) to identify biochemical and morphologic changes at the cellular level associated with cervical cancer and precancer painless and minimally invasive; gives screening results immediately. Guided Therapeutics, Inc., Norcross, GA PMA application under FDA review; in Nov 2011 FDA stated that no FDA panel review was necessary prior to making a decision; decision anticipated Jan 2012	Biopsy Colposcopy HPV DNA test Pap test	Earlier detection of cervical disease Improved screening and follow-up compliance Reduced unnecessary referrals to biopsy and colposcopy
Blocking radiation exposure of limb-draining lymph nodes for prevention of lymphedema	Patients in whom early-stage breast cancer has been diagnosed and who are undergoing postsurgical adjuvant radiation therapy	Lymphedema is a chronic condition that, depending on the treatment regimen, affects between 5% and 50% of women who have undergone primary treatment for breast cancer. Whole breast irradiation, which may also target lymph nodes in the axilla, is a significant risk factor for developing lymphedema. This increased risk might be mitigated by selectively blocking from exposure to radiation critical lymph nodes that drain the limb. In a recent clinical trial, limb-draining lymph nodes were identified by single-photon emission computed tomography and computed tomography (SPECT-CT) and an intensity-modulated radiation therapy plan was designed to limit exposure of these nodes; in this trial, patients were limited to those with early stage breast cancer with negative sentinel lymph node biopsy or only micrometastases to sentinel lymph nodes. Mayo Clinic, Rochester, MN Unphased small trial ongoing	Standard external beam radiation therapy	Decreased rate of lymphedema Decreased radiation dose to critical lymph nodes Equivalent cancer-related progression-free survival Equivalent cancer-related overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BLP25 liposome therapeutic vaccine (Stimuvax) for advanced nonsmall cell lung cancer	Patients in whom advanced NSCLC has been diagnosed	Advanced NSCLC has a poor prognosis and often responds poorly to current chemotherapeutic regimens; new treatment strategies with novel mechanisms of action are needed. Stimuvax® is a therapeutic vaccine composed of a 25-amino acid sequence of the MUC-1 protein, which is frequently expressed in NSCLC cells, encapsulated in a liposomal formulation; the vaccine is thought to work by stimulating anti-MUC-1 T cell responses. It is administered after a single intravenous infusion of 300 mg/m^2 of cyclophosphamide 3 days prior to the first immunization; then the vaccine is administered in 8 consecutive weekly subcutaneous injections (1,000 mcg Stimuvax); the vaccine is then administered at 6-week intervals beginning at week 14 until antitumor responses are observed. Merck KGaA, Darmstadt, Germany Oncothyreon, Seattle, WA Phase III trials restarted in 2011 after being halted for about a year	Bevacizumab Cetuximab Cisplatin Docetaxel Erlotinib Gefitinib Gemcitabine Irinotecan Paclitaxel Pemetrexed Vinorelbine	Increased overall survival Increased progression-free survival Improved quality of life
BRAF kinase inhibitor (dabrafenib) for treatment of metastatic melanoma	Patients in whom metastatic melanoma characterized as having activated BRAF mutations has been diagnosed	Dabrafenib (GSK2118436) is an activated BRAF kinase inhibitor. The developer describes it as "a highly potent and selective ATP competitive BRAF inhibitor with >100-fold selectivity for mutant (mut) BRAF… It displays dose-dependent inhibition of MEK and ERK phosphorylation in mut BRAF cell lines and tumor regression in xenograft models." GlaxoSmithKline, Middlesex, UK Phase III trials ongoing for melanoma; phase I and II trials ongoing for other solid tumors	High dose IL-2 Dacarbazine (DTIC-Dome) Ipilimumab Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BRAF kinase inhibitor vemurafenib (Zelboraf) for treatment of metastatic melanoma	Patients in whom metastatic melanoma with activated BRAF mutations has been diagnosed	Vemurafenib (Zelboraf®) is an activated BRAF kinase inhibitor. F. Hoffmann-La Roche Ltd., Basel, Switzerland Roche Molecular Systems, Inc., Pleasanton, CA (test) First BRAF in class to be approved; FDA approved Aug 2011 for treatment of unresectable or metastatic melanoma with BRAFV600E mutation as detected by the test approved at the same time: cobas® 4800 BRAF V600 mutation automated molecular assay designed to detect presence of BRAF gene mutation.	High dose IL-2 Dacarbazine (DTIC-Dome) Ipilimumab	Increased overall survival Increased progression-free survival Improved quality of life
BRCA1 testing to personalize chemotherapy for advanced gastric cancer	Patients in whom gastric cancer is diagnosed and who may receive chemotherapy with 5-fluorouracil, oxaliplatin, docetaxel (FLOT)	Tumors bearing *BRCA1* mutations are not responsive to taxane treatments (e.g., docetaxel). Therefore, patients identified as having a *BRCA1* mutation might respond to a simplified regimen of 5-fluorouracil and oxaliplatin (FLO) as well as they would respond to the standard regimen incorporating docetaxel. Personalizing the chemotherapy regimen could potentially reduce side effects associated with docetaxel in eligible patients. Phase II/III trials ongoing in China *BRCA1* testing is widely available, but has not been widely used in the U.S. for personalizing chemotherapy regimens for gastric cancer	Chemotherapy regimen without *BRCA1* testing to inform course of treatment	Reduced side effects from therapy (e.g., anemia, fluid retention, peripheral neuropathy, nausea, diarrhea, mouth sores, hair loss, fatigue/weakness, changes to the fingernails/toenails) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Brentuximab vedotin (Adcetris) for treatment of recurrent/refractory anaplastic large cell lymphoma	Patients in whom recurrent and/or chemotherapy-refractory systemic CD30-positive anaplastic large cell lymphoma (ALCL) has been diagnosed	Brentuximab vedotin (Adcetris™, SGN-35 or cAC10-vcMMAE) is a monoclonal antibody-drug conjugate; monoclonal antibody portion of the drug recognizes the CD30 antigen present on some ALCLs; drug portion is the highly cytotoxic MMAE, which inhibits mitosis by blocking tubulin polymerization. For two indications: (1) the treatment of patients with Hodgkin's lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates, and (2) the treatment of patients with systemic ALCL after failure of at least one prior multi-agent chemotherapy regimen. Seattle Genetics, Inc., Bothell, WA FDA approved Aug 19, 2011 for treatment of systemic ALCL after failure of at least one prior multi-agent chemotherapy regimen.	Autologous stem cell transplantation Allogeneic stem cell transplantation	Increased overall survival Increased progression-free survival Improved quality of life
Brentuximab vedotin (Adcetris) for treatment of recurrent/refractory Hodgkin's lymphoma	Patients in whom recurrent and or radiation/chemo-therapy-refractory Hodgkin's lymphoma has been diagnosed	Hodgkin's lymphoma is a CD30-positive hematologic malignancy with limited salvage therapy options. Please see above information on brentuximab vedotin (SGN-35 or cAC10-vcMMAE). Seattle Genetics, Inc., Bothell, WA FDA approved Aug 19, 2011 for treatment of patients with Hodgkin's lymphoma after failure of ASCT or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates.	Standard of care	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cabozantinib (XL 184) for treatment of advanced medullary thyroid cancer	Patients in whom unresectable, locally advanced, or metastatic medullary thyroid cancer has been diagnosed	No treatments exist for advanced thyroid cancer that target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Cabozantinib is an oral, small-molecule, receptor tyrosine kinase inhibitor that targets MET and VEGFR2; MET plays key roles in proliferation, migration, invasion and angiogenesis; overexpression of the hepatocyte growth factor (HGF) ligand of MET and activation of the MET pathway supports tumors; VEGFR-2 and MET allow tumors to overcome hypoxia and stimulate angiogenesis; VEGF and MET also appear to stimulate osteoclasts and osteoblasts, thus showing potential for treating bone metastasis; selective anti-VEGF therapies do not inhibit MET, which may be responsible for tumor evasiveness and drug resistance in patients who receive VEGF tyrosine kinase inhibitors, making MET/VEGF co-inhibition an emerging target in cancer therapy. Administered 25 and 100 mg once daily. Exelixis, San Francisco, CA Phase III trial reported as meeting primary endpoint in Oct 2011; NDA submission to FDA expected some time in 2012; FDA granted orphan drug status for follicular, medullary, and anaplastic thyroid carcinoma	Radiotherapy Sorafenib Sunitinib Vandetanib	Increased overall survival Increased progression-free survival Improved quality of life
Cabozantinib (XL 184) for treatment of advanced or recurrent breast cancer	Patients in whom advanced or recurrent breast cancer has been diagnosed	Few treatment options exist for advanced breast cancer and none of them target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Please see additional information above. Administered 100 mg, once daily, in breast cancer trials. Exelixis, San Francisco, CA Phase II trials ongoing	Cyclophosphamide Doxorubicin Paclitaxel	Increased overall survival Increased progression-free survival Improved quality of life Reduced bone metastasis

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cabozantinib (XL 184) for treatment of advanced or recurrent hepatocellular carcinoma	Patients in whom advanced or recurrent hepatocellular carcinoma has been diagnosed	Few treatment options exist for advanced hepatocellular carcinoma and none of them target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Please see additional information on cabozantinib above. Administered 100 mg, once daily, in trials. Exelixis, San Francisco, CA Phase II trials ongoing	Chemotherapy Radiation Sorafenib	Increased overall survival Increased progression-free survival Improved quality of life Reduced bone metastasis
Cabozantinib (XL 184) for treatment of advanced or recurrent melanoma	Patients in whom advanced or recurrent melanoma has been diagnosed	Few treatment options exist for advanced melanoma and none of them target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Please see additional information in first entry on cabozantinib above. Administered 100 mg, once daily, in trials. Exelixis, San Francisco, CA Phase II trials ongoing	BCG (bacillus Calmette Guérin) injection Carboplatin Cisplatin Dacarbazine Interferon-alpha (INFa) Imiquimod IL-2 Paclitaxel Radiation therapy Surgery Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life
Cabozantinib (XL 184) for treatment of advanced or recurrent nonsmall cell lung cancer	Patients in whom advanced, recurrent, or metastatic NSCLC has been diagnosed	Few treatment options exist for advanced NSCLC, and none of them target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Please see additional information in first entry on cabozantinib above. Administered 100 mg, once daily, in trials. Exelixis, San Francisco, CA Phase II trials ongoing	Bevacizumab Cetuximab Cisplatin Docetaxel Erlotinib Gemcitabine Paclitaxel Pemetrexed Radiotherapy Surgery Vinorelbine	Increased overall survival Increased progression-free survival Improved quality of life Reduced bone metastasis

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cabozantinib (XL 184) for treatment of advanced or recurrent primary ovarian peritoneal or fallopian tube cancer	Patients in whom advanced or recurrent ovarian, primary peritoneal, or fallopian tube carcinoma has been diagnosed	Few treatment options exist for advanced or recurrent primary ovarian peritoneal or fallopian tube cancer, and none of them target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Please see additional information in first entry on cabozantinib above. Administered 100 mg, once daily, in trials. Exelixis, San Francisco, CA Phase II trials ongoing	Bevacizumab (Avastin) Chemotherapy Radiation Sorafenib Sunitinib Surgery (debulking)	Increased overall survival Increased progression-free survival Improved quality of life Reduced bone metastasis
Cabozantinib (XL 184) for treatment of castration-resistant prostate cancer	Patients in whom CRPC (may include bone metastasis) has been diagnosed	No treatments for CRPC are available that target MET, which may be responsible for prostate cancer drug resistance in patients treated with current RTK inhibitors. Please see additional information in first entry on cabozantinib above. Administered 100 mg, once daily, in trials. Exelixis, San Francisco, CA Phase II trials ongoing; phase III trials being initiated	Abiraterone Cabazitaxel Docetaxel Radium-223 (in development)	Increased overall survival Increased progression-free survival Improved quality of life Reduced bone metastasis Reduced bone pain
Cabozantinib (XL 184) for treatment of recurrent or progressive glioblastoma multiforme	Patients in whom recurrent or progressive glioblastoma multiforme has been diagnosed	No treatments for glioblastoma multiforme target MET, which may be responsible for drug resistance in patients treated with current RTK inhibitors. Please see additional information in first entry on cabozantinib above. Administered in 25 or 100 mg doses, once daily, in trials. Exelixis, San Francisco, CA Phase II trials ongoing	Anti-angiogenic therapy Chemotherapy Corticosteroids Personalized vaccination (in clinical development) Radiation Radiosurgery Surgery	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PI3 kinase delta isoform inhibitor (GS-1101) for treatment of chronic or small lymphocytic leukemia	Patients in whom CLL or small lymphocytic leukemia have been diagnosed	GS-1101 (formerly CAL-101) inhibits the activity of a novel target: PI3K delta, which is a kinase that promotes cell survival, cell division, and cell growth; delta isoform of Class I PI3K is only expressed in the blood; targeted inhibition could treat blood-based cancers without side effects on nonblood tissues Gilead, San Dimas, CA Phase II trial ongoing; under study in combination with rituximab	Fludarabine with cyclophosphamide Fludarabine with rituximab Fludarabine, cyclophosphamide, and rituximab Cyclophosphamide, doxorubicin, vincristine and prednisolone Rituximab	Improved overall survival Improved progression-free survival Improved quality of life
Carfilzomib for treatment of multiple myeloma	Patients in whom recurrent or treatment-refractory multiple myeloma has been diagnosed	Multiple myeloma patients typically respond to current therapy only 11% of the time and typically survive for only 6 to 10 months after diagnosis, so effective treatments are needed. Carfilzomib is a small-molecule inhibitor of the proteasome; the proteasome is responsible for the degradation of cellular proteins, and inhibition of the proteasome can lead to accumulation of unwanted proteins, cell cycle arrest, and apoptosis. Onyx Pharmaceuticals, Emeryville, CA Phase III trial ongoing; FDA granted fast track status; Onyx submitted NDA in Sept 2011	Combination therapies: Cytotoxic chemotherapies (bendamustine, cyclophosphamide, doxorubicin, melphalan, vincristine) Immunomodulatory drugs (lenalidomide, thalidomide) Proteasome inhibitors (bortezomib) Steroids (dexamethasone, prednisone)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CD40 agonist (CP-870,893) for treatment of pancreatic cancer	Patients in whom unresectable pancreatic cancer has been diagnosed	The 5-year survival rate for patients in whom pancreatic cancer has been diagnosed is only about 5%; therefore, novel therapies for this condition are needed. CP-870,893 is an intravenously administered monoclonal antibody that functions as a CD40 agonist and is intended to stimulate a patient's immune response, potentially eliminating the tumor. While CP-870,893 was originally intended to activate T cells, preliminary data indicate that the therapy may actually lead to macrophage activation, which leads to the destruction of supporting tumor stroma; in current clinical trials, CP-870,893 is being administered in combination with the standard of care chemotherapy drug gemcitabine. Pfizer, Inc., New York, NY, in collaboration with University of Pennsylvania, Philadelphia, PA Phase I trial complete; second phase I trial ongoing	Gemcitabine monotherapy Gemcitabine plus erlotinib	Increased progression-free survival Increased overall survival Improved quality of life
CD56-specific antibody-drug conjugate (IMGN901) for treatment of multiple myeloma	Patients in whom CD56-positive relapsed or relapsed/refractory multiple myeloma has been diagnosed	Patients in whom relapsed multiple myeloma has been diagnosed have few treatment options and median survival of less than 1 year. IMGN901 is a novel antibody-drug conjugate that links the highly cytotoxic agent mertansine to a monoclonal antibody specific for CD56, a cell surface marker expressed on multiple cancer types including multiple myeloma; in current clinical trials, IMGN901 is being administered as an adjunct to a conventional cytotoxic chemotherapy regimen of lenalidomide and dexamethasone. ImmunoGen, Inc., Waltham, MA Phase I trial ongoing; FDA granted orphan drug status	Lenalidomide plus dexamethasone	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CD56-specific antibody-drug conjugate (IMGN901) for treatment of small cell lung cancer	Patients in whom advanced small cell lung cancer (SCLC) has been diagnosed; may be chemotherapy naïve or have received previous systemic chemotherapy treatment	The 5-year survival rate for patients in whom small cell lung cancer is diagnosed is only about 15%. IMGN901 is a novel antibody-drug conjugate that links the highly cytotoxic agent mertansine to a monoclonal antibody specific for CD56, a cell surface marker expressed on multiple cancer types including small cell lung cancer. In current clinical trials, IMGN901 is being administered as an adjunct to a conventional cytotoxic chemotherapy regimen (carboplatin plus etoposide). ImmunoGen, Inc., Waltham, MA Phase I/II trial ongoing	Carboplatin plus etoposide	Increased progression-free survival Increased overall survival Improved quality of life
Chimeric antigen receptor gene therapy for treatment of chronic lymphocytic leukemia	Patients in whom recurrent CLL has been diagnosed	While CLL can typically be controlled for many years with current chemotherapy options, these treatments are not curative and disease typically recurs. One treatment option currently under study is the use of chimeric antigen receptor (CAR) gene therapy to genetically modify autologous T lymphocytes to promote T-cell activation, T-cell proliferation, and immune memory; in a recently reported study, a lentiviral vector was used to transfect autologous T cells with a CAR transgene that consisted of four parts: (1) an extracellular domain consisting of an antibody variable chain specific for CD19 (a cell surface marker expressed by CLLs); (2) a hinge region; (3) a costimulatory domain (in this case a portion of CD137); and (4) CD3-zeta (a signal transduction component of the T-cell receptor); binding of the extracellular domain of this recombinant protein to CD19 on target cells induces the activation of the pathways typically downstream of major histocompatibility complex activation and CD137 stimulation, activating a persistent immune response against CD19. University of Pennsylvania, Philadelphia, PA Case studies reported	Allogeneic stem cell transplant	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
C-met kinase inhibitor (tivantinib) for treatment of hepatocellular carcinoma	Patients with unresectable hepatocellular carcinoma that has failed to respond to one prior therapy	In patients who cannot be cured by surgical removal of the tumor, survival rates for hepatocellular carcinoma are very low (~5%) with median survival after diagnosis of only ~6 months. No effective second-line therapy is available for this type of cancer. Tivantinib (ARQ 197) is a small-molecule inhibitor of the c-met receptor tyrosine kinase; c-met has been implicated in a number of tumor-associated biologic processes (e.g., cell dissociation, cell migration, inhibition of apoptosis, cell proliferation). There is no currently available c-met inhibitor. ArQule, Inc., Woburn, MA Phase II trial ongoing	Placebo	Increased overall survival Increased progression-free survival Improved quality of life
C-met kinase inhibitor (tivantinib) for treatment of locally advanced or metastatic gastric cancer	Patients with locally advanced or metastatic gastric cancer that has progressed after prior first-line chemotherapy	No effective treatment is available for this patient population whose prognosis is poor. Please see above information on tivantinib (ARQ 197). ArQule, Inc., Woburn, MA Phase II trial ongoing	Capecitabine Irinotecan Oxaliplatin	Increased overall survival Increased progression-free survival Improved quality of life
C-met kinase inhibitor (tivantinib) for treatment of metastatic colorectal cancer	Patients with metastatic CRC with wild-type KRAS who have received prior systemic chemotherapy	While many treatment options are available for metastatic CRC, 5-year survival rates are only ~25%, and more effective treatment is needed. Please see above information on tivantinib (ARQ 197). For this indication, tivantinib is being administered in combination with the topoisomerase inhibitor irinotecan and the anti-EGFR antibody cetuximab. ArQule, Inc., Woburn, MA Phase I/II trial ongoing	Irinotecan plus cetuximab CapeOX Cetuximab monotherapy FOLFIRI FOLFIRI plus cetuximab FOLFOX Irinotecan plus or minus oxaliplatin Panitumumab	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
C-met kinase inhibitor (tivantinib) for treatment of microphthalmia transcription factor-associated tumors	Patients diagnosed with locally advanced or metastatic microphthalmia transcription factor (MiT) tumors, including clear cell sarcoma, alveolar soft part sarcoma, and translocation-associated RCC	Tivantinib (ARQ 197) is a small-molecule inhibitor of the c-met receptor tyrosine kinase; c-met has been implicated in a number of tumor-associated biological processes (e.g., cell dissociation, cell migration, inhibition of apoptosis, cell proliferation); in particular, research has shown that MiT tumors often upregulate c-met, and MiT tumors are typically resistant to current treatments and are typically fatal if not fully resectable. ArQule, Inc. (developer),Woburn, MA Daiichi Sankyo (performing testing), Tokyo, Japan Phase II trial complete	MiT tumors are resistant to existing therapies.	Increased overall survival Increased progression-free survival Improved quality of life
C-met kinase inhibitor (tivantinib) for treatment of nonsmall cell lung cancer	Patients in whom advanced NSCLC has progressed or recurred after chemotherapy	Patients with advanced NSCLC that has progressed after chemotherapy have a poor prognosis and few treatment options. Tivantinib (ARQ 197) is a c-met kinase inhibitor; c-met is a receptor tyrosine kinase that has been implicated in the development of tumor resistance to EGFR inhibition. No c-met inhibitor is currently available. Tivantinib is being studied in combination with the EGFR inhibitor erlotinib in treatment of NSCLC. ArQule, Inc. (developer), Woburn, MA Daiichi Sankyo (performing testing), Tokyo, Japan Phase III trials ongoing	Second line comparators: Erlotinib monotherapy Docetaxel Pemetrexed Third-line comparator: Erlotinib monotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
C-met kinase inhibitor (tivantinib) for treatment of relapsed or refractory germ cell tumors	Patients in whom germ cell tumors (e.g., testicular seminomas, testicular nonseminomas) have recurred after platinum-based chemotherapy	Although complete remission rate for germ cell tumors is high (85% to 90%) using current chemotherapy regimens, patients whose disease is refractory to standard chemotherapy have a cure rate of only ~25% with high-dose chemotherapy and stem cell transplantation. Tivantinib (ARQ 197) is a small-molecule inhibitor of the c-met receptor tyrosine kinase; c-met has been implicated in a number of tumor-associated biologic processes (e.g., cell dissociation, cell migration, inhibition of apoptosis, cell proliferation). No c-met inhibitor is currently available. ArQule, Inc. (developer), Woburn, MA Daiichi Sankyo (performing testing), Tokyo, Japan Phase II trial ongoing	Various chemotherapy regimens, including: Vinblastine/mesna/ ifosfamide/cisplatin Paclitaxel/ifosfamide/ mesna/cisplatin High-dose chemotherapy plus autologous stem cell rescue	Increased overall survival Increased progression-free survival Improved quality of life
C-met kinase inhibitor (tivantinib) for treatment of unresectable pancreatic cancer	Patients in whom unresectable locally advanced or metastatic pancreatic cancer has been diagnosed	Patients with advanced pancreatic cancer have a poor prognosis and effective treatments are lacking; 5-year survival rate is approximately 5%. Please see above information on ARQ 197. ArQule, Inc., Woburn, MA Phase II trial ongoing	Gemcitabine Gemcitabine plus erlotinib Gemcitabine plus cisplatin or oxaliplatin Gemcitabine plus a fluoropyrimidine	Increased overall survival Increased progression-free survival Improved quality of life
COLD-PCR amplification for detection of small quantities of mutated DNA	Populations undergoing screening for cancer	Co-amplification at Lower Denaturing Temperature (COLD-PCR) is an amplification step that can be used before traditional laboratory screening methods (Sanger sequencing, TaqMan PCR, HPLC, etc.). Small amounts of mutant DNA can be amplified selectively from a background of high concentration wild-type DNA, such as exists in cancer-derived DNA from patient plasma samples. Dana-Farber Cancer Institute, Boston, MA Transgenomic, Omaha, NE Firm has completed “development studies.”	Various methods including: Sequencing RFLP analysis MALDI-TOF analysis Denaturing HPLC/Surveyor Ligation-mediated PCR Peptide nucleic acid (PNA)3-locked nucleic acids Antiprimer quenching real-time PCR	Earlier detection of cancer presence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Combined digital breast tomography and diffuse optical tomography for breast cancer diagnosis	Patients who are undergoing followup diagnostic imaging for breast cancer after a suspicious result on mammography screening	Diffuse optical tomography uses laser technology coupled with optical equipment software to detect hemoglobin, angiogenesis, and increased metabolism. Several optical imaging systems are on the market; digital breast tomography uses x-ray images to create three-dimensional reconstructions of breast tissue; researchers hypothesize that using sequential optical/radiographic imaging would improve detection of breast cancer and improve discrimination between benign and cancerous lesions based on differential metabolic activities observed in these tissues. Multiple manufacturers Early phase trials	Standard mammography Digital breast tomography alone Diffuse optical tomography alone Computed tomography Magnetic resonance imaging Ultrasound	Increased sensitivity, leading to earlier detection and improved outcomes Increased specificity, leading to a reduced number of biopsy procedures and their attendant stress
Trastuzumab emtansine for treatment of breast cancer	Patients in whom metastatic HER-2-positive breast cancer has been diagnosed	Trastuzumab emtansine (formerly trastuzumab-DM1) is a combination of a HER-2-specific antibody (trastuzumab, Herceptin) and a cytotoxic microtubule inhibitor (DM1, mertansine). This combination is intended to enable preferential delivery of a highly cytotoxic agent to cells expressing HER-2 to produce the same (or better) results as HER-2 inhibition plus chemotherapy, but with reduced side effects. ImmunoGen, Inc. (developer), Waltham, MA F. Hoffmann-La Roche Ltd. (testing), Basel, Switzerland Phase III trials ongoing; regulatory filing anticipated in 2012	Lapatinib-based chemotherapy regimens Trastuzumab-based chemotherapy regimens	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Computer-assisted system (Sedasys) for automated propofol sedation during gastrointestinal endoscopy procedures	Patients who are undergoing propofol-induced sedation during colonoscopy or upper GI procedures	The Sedasys® system integrates physiologic patient monitoring (oxygen saturation, respiratory rate, heart rate, blood pressure, end-tidal carbon dioxide and patient responsiveness) with personalized drug delivery (system automatically responds to signs of over-sedation) for delivery of propofol. The system is intended to enable non-anesthesiologists (i.e., other physicians or nurses) to administer sedation for endoscopic GI procedures. Ethicon Endo-Surgery, Inc. (A Johnson and Johnson company), Cincinnati, OH PMA rejected by FDA Oct 2010; Ethicon appealed and in Mar 2011 FDA agreed to a second review by the Medical Devices Dispute Resolution Panel, which is scheduled to meet mid-Dec 2011	Propofol sedation administered and monitored by anesthesiologist	Successful and safe propofol sedation without need for an anesthesiologist
Cordycepin (OVI-123) for treatment of refractory acute lymphoblastic leukemia	Patients in whom refractory ALL has been diagnosed	Many patients with ALL are successfully treated, however patients with refractory disease (often adults) have few options and disease progresses quickly. Cordycepin is an adenosine nucleoside analog that is purported to have activity against terminal deoxynucleotidyl transferase (TdT)-positive cells; expression of TdT is one of the hallmarks of ALL; although the mechanism of action for cordycepin remains largely unknown, cordycepin is believed to induce apoptosis in leukemia cells. Administered intravenously on days 1, 2, and 3 of a 21 day cycle. OncoVista Innovative Therapies, Inc., San Antonio, TX Phase I/II trial initiated, but currently on hold due to limited capital resources; firm intends to reinitiate trial in first quarter of 2012; FDA granted orphan drug status for ALL	Allogeneic bone marrow transplant Asparaginase Chemotherapy Dasatinib Imatinib Nilotinib Nelarabine Radiation Steroids	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Concomitant colorectal cancer screening and annual influenza vaccination (FLU-FOBT) program	Patients recommended for routine CRC screening (i.e., between 50 and 75 years of age) who are receiving influenza vaccinations	While CRC screening methods are widely available and known to be effective in reducing morbidity and mortality from CRC, compliance with the recommended screening guidelines is low. In the FLU-FOBT program, nurses in community clinics provide patients seeking annual influenza vaccinations with fecal occult blood tests for CRC screening. University of California-San Francisco, San Francisco, CA Large randomized control trials completed	Primary care physician recommended CRC screening	Increased rate of compliance with CRC screening guidelines Reduced morbidity from CRC Reduced mortality from CRC Reduced costs of care through earlier intervention Reduced health disparities
Cotara (131 iodine-chTNT-1/B-linked MAb) for treatment of glioblastoma multiforme	Patients in whom glioblastoma multiforme has been diagnosed	Glioblastoma multiforme is the most common and most deadly form of brain cancer; complete surgical resection is generally not possible and the prognosis is poor; more effective adjuvant therapies are needed. Cotara consists of a monoclonal antibody linked to a radioactive isotope, iodine 131, which is intended to bind to the DNA histone complex that is exposed in dead and dying cells at the center of solid tumors; intended to target dying cells at the center of tumors, delivering its radioactive payload there to minimize radiation to healthy surrounding tissue. Administered as a single interstitial infusion over approximately 25 hours at a dose of 2.5 mCi/cc. Peregrine Pharmaceuticals, Inc., Tustin, CA Phase II trials completed	Personalized therapeutic vaccines (investigational) Radiotherapy Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CP-4126 (CO-101) for treatment of advanced pancreatic cancer	Patients in whom advanced pancreatic cancer has been diagnosed	CP-4126 is a lipid-conjugated version of the anticancer agent gemcitabine (nucleoside analog); gemcitabine is a standard chemotherapeutic treatment for pancreatic cancer; however, many pancreatic cancers do not readily take up gemcitabine (possibly because they express low levels of the main gemcitabine transporter). The lipid conjugation purports to overcome this problem by allowing the nucleoside to cross the lipid bilayer without having to use the transporter. Clavis Pharma ASA, Oslo, Norway Clovis Oncology, Boulder, CO Phase II trial ongoing	Gemcitabine	Increased overall survival Increased progression-free survival Improved quality of life
Custirsen (OGX-011) for treatment of metastatic castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	Custirsen (OGX-011) is an antisense RNA molecule designed to reduce expression of clusterin, a cell survival protein. Custirsen is an injected agent intended as an adjunct to chemotherapy. OncoGenex Pharmaceuticals, Inc., Bothell, WA Teva Pharmaceutical Industries Ltd., Jerusalem, Israel Phase III trials (SATURN and SYNERGY) ongoing under FDA special protocol assessment; FDA granted fast track status	Standard chemotherapy Abiraterone Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Custirsen (OGX-011) for treatment of advanced nonsmall cell lung cancer	Patients in whom NSCLC has been diagnosed	Custirsen (OGX-011) is an antisense RNA molecule intended for treatment of advanced, unresectable NSCLC as an adjunct to chemotherapy. Given by injection. OncoGenex Pharmaceuticals, Inc., Bothell, WA Teva Pharmaceutical Industries Ltd., Jerusalem, Israel Phase II trials completed; phase III trials being planned	Conventional chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CYT387 small-molecule inhibitor of JK1 and JK2 for treatment of myelofibrosis	Patients in whom myelofibrosis has been diagnosed	CYT387 is an inhibitor of Janus kinase 1 (JAK 1) and Janus kinase 2 (JAK 2); hypothesis is that constitutively active JAK 2 protein drives myelofibrosis pathology in some cases; inhibiting this causative protein factor of the disease state could reverse disease course. YM Biosciences, Mississauga, Ontario, Canada Phase I/II trials ongoing	Ruxolitinib	Increased overall survival Increased progression-free survival Improved quality of life (reduced spleen enlargement, bone pain, easy bruising, fatigue)
CYT997 vascular disrupting agent for treatment of various cancers	Patients in whom one of several types of cancer has been diagnosed	CYT997 is a tubulin polymerization inhibitor. This disrupts the cell cycle by interfering with proper formation of the mitotic spindle, leading to arrest at the G2/M phase of the cell cycle. Like most other microtubule disrupting molecules, CYT997 has demonstrated the ability to cause vascular disruption in preliminary studies. Drug can be delivered orally or intravenously. Cytopia Research Pty Ltd., later acquired by YM BioSciences, Mississauga, Ontario, Canada Phase II trial ongoing for glioblastoma multiforme	Other microtubule polymerization inhibitors (vinblastine) Other microtubule inhibitors/binders (e.g., taxol)	Increased overall survival Increased progression-free survival Improved quality of life
Cytokine cocktail (Multikine) immune therapy for head and neck cancer	Patients in whom head and neck cancer has been diagnosed	Multikine is a mix of immune stimulators (tumor necrosis factor [TNF], interleukin-1, other cytokines); intended to be delivered before conventional treatment (surgery, radiotherapy, chemotherapy); manufacturer believes this is when the immune system is best able to mount an immune response. Cytokine mixture delivered directly to the tumor and nearby lymph nodes five times a week for 3 weeks. CEL-SCI Corp., Vienna, VA Phase III trial ongoing	Surgical resection Radiation therapy with adjuvant chemotherapy (cisplatin)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Denosumab (Xgeva) for prevention of cancer-related bone fractures and pain	Patients in whom bone metastases have been diagnosed	Denosumab (Xgeva®) is a monoclonal antibody that targets RANKL, which is involved in cancer-related bone destruction. Denosumab is intended to prevent skeletal-related events, including bone fractures and pain from cancer treatment; Xgeva denosumab is a higher dose of Prolia denosumab used for osteoporosis. Amgen, Inc., Thousand Oaks, CA FDA approved Nov 2010 to help prevent fractures and slow bone disease in patients with solid tumors	Pamidronic acid Zoledronic acid	Delayed skeletal related events Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
EGFRvIII-directed immunotherapy rindopepimut for treatment of glioblastoma multiforme	Patients in whom glioblastoma multiforme has been newly diagnosed and who have undergone primary resection of the bulk tumor	Glioblastoma multiforme typically recurs within 6 months; a splice variant of the EGFR that is found predominantly on cancerous tissues, EGFRvIII represents a potential target antigen for anti-cancer therapy. Rindopepimut (CDX-110) is a peptide based vaccine designed to be specific for the EGFRvIII variant; in current clinical trials, rindopepimut is being administered in combination with the immune stimulation granulocyte macrophage colony-stimulating factor (GM-CSF) and standard maintenance chemotherapy (temozolomide). Celldex Therapeutics, Inc., Needham, MA Phase II trials completed	Temozolomide alone	Increased progression-free survival Increased overall survival Improved quality of life
Electrical impedance scanner (SciBase III Electrical Impedance Spectrometer) for melanoma diagnosis	Patients in whom a suspicious skin lesion that may be melanoma has been identified	Distinguishing melanoma from nonmelanotic skin lesions is difficult and requires a significant amount of training. The SciBase III Electrical Impedance Spectrometer uses differences in electrical impedance between melanotic tissue and other tissue types to detect melanoma in an automated fashion; the system consists of an impedance spectrometer and a disposable probe that has microscopic electrode spikes that penetrate the skin. SciBase AB, Stockholm, Sweden Pivotal trial ongoing (1,200 lesions); FDA premarket approval (PMA) submission planned for 2012	Dermatologist diagnosis MelaFind multispectral dermascope (in development)	Increased specificity and sensitivity for melanoma Improved positive and negative predictive values Reduction in unnecessary biopsies

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Endocervicoscopy (office-based) for diagnosis of high-grade cervical lesions	Patients in whom abnormal high grade cervical cytology has been diagnosed and who have undergone unsatisfactory colposcopy, and who wish to preserve their fertility	Procedures to minimize the invasiveness and complications associated with treating high grade cervical lesions with unsatisfactory or negative colposcopy are needed, especially for women desiring to preserve fertility. Endocervicoscopy is the endoscopic evaluation of the endocervical mucosa, after application of acetic acid 5%, performed with an office continuous-flow hysteroscope; endocervicoscopy may be used to obtain a more precise localization of lesions and minimize the depth of cone excisions, which may result in more conservative treatment and preservation of fertility in patients. University of Naples Federico II, Naples, Italy Trial completed (95 patients; phase unstated)	Blind curettage of the endocervix	Reduced adverse events/complications Reduced pain Reduced recovery time Sparing of fertility
EndoVe electrical field generator to improve chemotherapy uptake	Patients undergoing chemotherapy for solid localized tumors	EndoVe endoscopic device applies a local electrical field to the tumor; hypothesized to increase the rate at which cells take up chemotherapeutic agents. Would allow use of lower doses of chemotherapeutic agents. Mercy Hospital, Cork, Ireland Phase I trial ongoing for rectal cancer	Conventional chemotherapy administration	Increased overall survival Increased progression-free survival Improved quality of life Reduced chemotherapy dose, potentially reducing side effects Lower costs associated with lower doses of chemotherapy

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Enkephalin (NTDDS NP2) gene therapy for chronic cancer pain	Patients experiencing intractable pain stemming from metastatic disease	Opioids are the mainstay of treatment for chronic severe cancer pain, but are associated with many undesired side effects and are potentially addictive. Enkephalin gene therapy is a nerve targeting drug delivery system (NTDDS) that is a herpes virus-based gene therapy delivery vector; it encodes the natural opioid peptide, enkephalin, which is intended to lead to expression of enkephalin in peripheral nerves, thereby interrupting pain signals to the central nervous system (CNS) to treat chronic cancer pain; it has potential to have significantly reduced side effects relative to systemic opioids because of its targeted nature. Diamyd Medical AB, Stockholm, Sweden Phase II trial ongoing	Oral and intravenous opioid pain medications	Reduced cancer-related pain Reduced side effects from pain medication Improved quality of life
Ex vivo expanded cord blood as allogeneic bone marrow transplant for treatment of hematologic malignancies	Patients with hematologic malignancy who need a bone marrow transplant and for whom no suitable matched donor is available	Perfectly matched bone marrow donors are not available for all patients who could benefit from transplantation because of the difficulty in identifying perfectly matched donors. While an exact match is needed for adult marrow transplants to avoid complications from graft versus host disease (GVHD), cord blood causes significantly less GVHD; however, the number of stem cells in cord blood is not large enough to provide complete bone marrow engraftment. The manufacturer is using an off-the-shelf preparation of mesenchymal precursor cells to expand cord blood stem cells ex vivo to improve engraftment rates upon introduction to the host. Because an imperfect match may be tolerated when using cord blood as the donor source, it may provide a suitable treatment option for many patients. Mesoblast, Ltd., New York, NY Pilot studies completed by MD Anderson Cancer Center, Houston, TX; phase III trial protocol approved by FDA to begin	Pooled unexpanded cord blood transplant Unexpanded cord blood transplant	Improved bone marrow engraftment rate Improved rate of neutrophil recovery Improved rate of platelet recovery

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gene-mediated cytotoxic immunotherapy for malignant glioma	Patients in whom malignant glioma has been diagnosed	Median survival of patients diagnosed with malignant glioma is only about 15 months and current treatments are often unsuccessful. Gene-mediated cytotoxic immunotherapy (GMCI) purports to lead to direct tumor cytotoxicity as well as a protective immune response; treatment consists of an adenovirus vector that contains a herpes simplex virus (HSV) thymidine kinase gene (Adv-tk); following injection of the virus into the tumor site, the patient is administered the anti-HSV drug valacyclovir, which is activated by the tk transgene and produces an active drug that kills rapidly dividing cells; this in turn leads to local cytotoxicity through local release of activated valacyclovir and the release of tumor antigens that may be taken up by dendritic cells (DC) and produce a systemic immune response. In treatment of malignant glioma GMCI is being administered in combination with radiation therapy and surgical resection. Advantagene, Inc., Auburndale, MA Phase II trial ongoing	Radiation therapy Surgical resection Chemotherapy Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gene-mediated cytotoxic immunotherapy for pancreatic adenocarcinoma	Patients in whom pancreatic adenocarcinoma has been diagnosed	Patients in whom pancreatic cancer has been diagnosed have a 5-year survival rate of only 5%; therefore, novel treatments for pancreatic cancer are needed. GMCI is being tested for prevention of recurrence following conventional therapy; GMCI purports to lead to direct tumor cytotoxicity as well as a protective immune response; treatment consists of an adenovirus vector that contains a HSV thymidine kinase gene (Adv-tk); following injection of the virus into the tumor site, the patient receives the anti-HSV drug valacyclovir, which is activated by the tk transgene and produces an active drug that kills rapidly dividing cells; this in turn leads to local cytotoxicity through local release of activated valacyclovir and the release of tumor antigens that may be taken up by DC and produce a systemic immune response. In treatment of pancreatic cancer GCMI is being administered in combination with radiation therapy in locally advanced disease and in combination with surgical resection in surgically resectable disease. Advantagene, Inc., Auburndale, MA Phase I trial ongoing	Surgical resection Radiation therapy Chemotherapy Chemoradiation therapy Gemcitabine	Increased overall survival Increased progression-free survival Improved quality of life
Genetic test (Cologuard) for colorectal cancer screening	All patients undergoing routine CRC screening	Genetic test (Cologuard™) screens DNA for gene mutations commonly found in CRCs; four-gene plus one biomarker test performed on stool samples. This test is the next generation of the ColoSure which looked at only one gene. Exact Sciences Corp., Madison, WI Clinical trial ongoing (phase unstated)	Colonoscopy Computed tomographic colonography Fecal Occult Blood Testing	Improved sensitivity and specificity for precancerous lesions and CRC Improved positive and negative predictive values Reduced unnecessary followup for screening

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Genetic test (Insight) for identifying ALK-activating gene fusions/mutations in patients with cancer	Patients with cancer types driven by underlying activated ALK mutations	Genetic test to identify mutations in the *ALK* gene. Test would allow identification of patients for whom ALK inhibitory pharmaceuticals in development might be appropriate. Insight Genetics, Nashville, TN Early phase development; available as research-use-only product	Immunohistochemistry Variant-specific PCR Fluorescence in situ hybridization to identify chromosomal translocations/deletions leading to ALK fusions.	Informed targeted therapy for cancer patients Increased overall survival Increased progression-free survival Improved quality of life
Genetic test (Methylated Septin 9 Plasma DNA Test) for screening for colorectal cancer	All patients undergoing routine CRC screening	Genetic test (Methylated Septin 9 Plasma DNA Test; RealTime mS9 Colorectal Cancer Test) screens DNA from plasma samples for a specific methylated version of the septin 9 gene that is commonly found in CRC. Epigenomics AG (developer), Berlin, Germany Abbott Laboratories (licensee), Abbott Park, IL First-generation test kit (Epi proColon) available in Europe; second-generation test kit (Epi proColon 2.0) anticipated to be available in Europe in 2011; Epigenomics intends to file PMA application with FDA by end of 2011.	Colonoscopy Computed tomographic colonography Fecal DNA test	Increased sensitivity and specificity Increased predictive values Avoided unnecessary follow-up procedures Improved compliance with colorectal screening Earlier intervention for identified cancer
GSK1572932A vaccine for treatment of MAGE-A3 nonsmall cell lung cancer	Patients in whom NSCLC has been diagnosed that expresses the MAGE-A3 biomarker	MAGE-A3 is an antigen that is expressed by a variety of tumor cells, in particular about 20% of NSCLCs. GSK1572932A is a MAGE-A3 peptide vaccine that is intended to be given to patients who have tumors that express the MAGE-A3 marker as an adjuvant to conventional chemotherapy. GlaxoSmithKline, Middlesex, UK Phase III trial ongoing	Surgery Chemotherapy Radiation therapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
GM-CT-01 (Davanat) for treatment of advanced colorectal cancer	Patients in whom advanced CRC has been diagnosed	When CRC is detected early, it can be effectively treated; however, advanced stages of CRC are associated with poor prognosis and require improved treatment options. GM-CT-01 (Davanat®) is a polysaccharide polymer (galactose and mannose) designed to target and inhibit galectin receptors found on the surface of tumor cells. Galectins promote tumor cell survival, angiogenesis, metastasis, and immune evasion. Davanat is administered with standard chemotherapeutic regimens and is intended to improve the safety, efficacy, and delivery of these agents. Galectin Pharmaceuticals, Inc., Newton, MA Phase II trials completed	5-Fluorouracil Bevacizumab Cetuximab Irinotecan Leucovorin Personalized vaccination Reolysin	Increased overall survival Increased progression-free survival Improved quality of life
Hemopurifier blood filter (HER2osome) to remove infectious agents and immunosuppressive proteins from circulation	Patients in whom certain infectious diseases or cancer has been diagnosed	The Hemopurifier disposable cartridge is intended for use with conventional dialysis machines or other blood circulatory pumps; intended to provide immunotherapy to cancer patients by removing immunosuppressive proteins from circulation. Hemopurifier claims to capture tumor-secreted exosomes "known to kill off the immune cells of those afflicted with cancer." The selective filtration device contains affinity agents that tightly bind to high-mannose structures unique to the surface of exosomes produced by cancer; these cancer particles are immobilized in approximately 2,800 porous hollow fibers within the filter and selectively removed from the circulatory system. Also intended for use as countermeasure against bioterror and pandemic threats and to reduce viral load in hepatitis C Aethlon Medical, Inc., San Diego, CA Early phase trial ongoing under FDA investigational device exemption (IDE); company requested meeting with FDA in May 2011 to expand IDE trial indication to include hepatitis C viral load reduction	Treatment without filtration	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
HER2-dimerization inhibitor (pertuzumab) for treatment of metastatic breast cancer	Patients in whom metastatic HER2-positive breast cancer has been diagnosed and who are receiving first-line trastuzumab and docetaxel	No curative treatment for patients in whom metastatic breast cancer has been diagnosed has been identified and patients with HER2-positive breast cancer receiving trastuzumab-based chemotherapy have median survival times of only about 3 years. Trastuzumab is an FDA-approved monoclonal antibody specific for Her2 that is purported to function by causing a reduction in the level of HER2 protein at the cell surface and by inhibiting proteolytic cleavage and release of the extracellular domain of HER2; pertuzumab is a novel HER2-specific monoclonal antibody that binds to a different site on the Her2 extracellular domain; pertuzumab is purported to function by inhibiting the heterodimerization of HER2 with other HER receptors, which is required for HER2 activation; originally tested as a monotherapy with limited benefit, pertuzumab is currently undergoing studies in combination with trastuzumab to ascertain whether a more comprehensive inhibition of HER2 activity can improve outcomes in patients diagnosed with metastatic breast cancer. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trials ongoing; phase III trial in previously untreated metastatic breast cancer met primary endpoint Jul 2011; NDA submission to FDA expected late 2011/early 2012	Trastuzumab plus capecitabine Trastuzumab plus docetaxel Trastuzumab plus paclitaxel plus or minus carboplatin Trastuzumab plus vinorelbine	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Histamine dihydrochloride (Ceplene) for treatment of acute myeloid leukemia	Patients in whom acute myeloid leukemia (AML) has been diagnosed and who are in remission following consolidation chemotherapy	While many patients in whom AML has been diagnosed will achieve remission following induction and consolidation chemotherapy, the majority of these patients will experience disease recurrence. Ceplene® is being studied as a maintenance therapy to prevent disease recurrence in this setting; Ceplene is purported to act as an immune stimulant, which may activate a T-cell response against leukemia cells; in clinical trials, it is being administered as an adjunct to the cytokine IL-2. Ceplene is administered as a subcutaneous injection. EpiCept Corp., Tarrytown, NY Phase III trial completed; NDA submitted to FDA late 2010 and rejected; EpiCept is currently working with FDA to generate a special protocol assessment for a new phase III Ceplene trial; Ceplene is approved for use in European Union	No consensus treatment exists for postremission patients.	Decrease in relapse rate Increased overall survival Improved quality of life
Histone deacetylase inhibitor (SB939) for treatment of recurrent or metastatic prostate cancer	Patients in whom recurrent or metastatic prostate cancer (hormone refractory prostate cancer) has been diagnosed	A broad spectrum histone deacetylase inhibitor (SB939). Intended to work against class I, II, III, and IV histone deacetylases; mechanism of tumor inhibition by histone deacetylase inhibitors unclear, but may be caused by DNA repair inhibition or modification of cell cycle proteins. S*BIO Pte Ltd., Singapore Phase II trials ongoing	Abiraterone Docetaxel Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Hologic Selenia 3D tomosynthesis system for mammography	Women undergoing routine mammography to screen for breast cancer	Three-dimensional imaging intended to show inner architecture of breast, free from distortion caused by tissue shadowing or density. Hologic, Inc., Bedford, MA FDA approved for marketing Mar 3, 2011	Standard 2D digital mammography	Increased sensitivity and specificity Increased predictive values Reduced unnecessary follow-up procedures

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
HyperAcute-Pancreas (algenpantucel-L) immunotherapy for pancreatic cancer	Patients in whom surgically resectable (stage I or stage II) adenocarcinoma of the pancreas has been diagnosed	Patients in whom pancreatic cancer has been diagnosed have a 5-year survival rate of approximately 5%. Algenpantucel-L immunotherapy is a treatment intended to stimulate an immune response against the patient's pancreatic cancer cells. The therapy consists of two allogeneic pancreatic cancer cell lines that have been genetically engineered to express the enzyme alpha (1,3) galactosyl transferase, which marks the cells with a nonhuman carbohydrate that elicits a strong antibody immune response. Antibody binding to the cell lines leads to complement-mediated cell lysis, potentially leading to the uptake of pancreatic cancer antigens and a systemic immune response against the patient's cancer. In current clinical trials, HyperAcute®-Pancreas is being administered by injection in combination with standard of care postoperative chemotherapy. NewLink Genetics Corp., Ames, IA Phase III trial ongoing under special protocol assessment with FDA; FDA granted fast-track and orphan drug status	Standard chemotherapy alone (gemcitabine plus or minus 5-fluorouracil)	Increased overall survival Increased progression-free survival Improved quality of life
Hypofractionated external beam whole-breast radiotherapy for treatment of early stage breast cancer	Patients in whom early stage (I and II) breast cancer has been diagnosed	Accelerated whole breast irradiation therapy; treatment delivers typical radiation therapy dose in shorter course of therapy (7 to 10 fractions rather than 25 fractions). Clinical trials are testing dose regimens for effectiveness and long-term safety	Standard external beam radiotherapy Breast brachytherapy Accelerated partial breast radiotherapy	Reduced number of fractions Reduced treatment time Increased treatment completion rates Similarly effective overall survival rates to standard radiation

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Immunomodulator (Imprime PGG) for treatment of advanced colorectal cancer	Patients in whom advanced CRC has been diagnosed	Many patients with late-stage CRC are unable to tolerate or do not benefit from current chemotherapeutic regimens; new therapies to treat advanced CRC are needed. Imprime PGG® is a novel beta glucan immunomodulator purported to induce an antitumor response through binding and stimulating neutrophils, which typically play a major role in innate immune responses, but not antitumor responses; Imprime PGG is purported to work synergistically with monoclonal antibody therapy such as cetuximab. Administered 4 mg/kg injection, weekly, in each treatment cycle. Biothera, Eagan, MN Phase III trial ongoing	Cetuximab monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Immunotherapy (Arcelis) for treatment of renal cell carcinoma	Patients in whom RCC has been diagnosed	Arcelis™ (formerly AGS-003) is a personalized RNA-loaded dendritic cell immunotherapy in which DC from the patient are removed and loaded with messenger RNA isolated from the patient's tumor, then readministered to the patient. AGS-003 given in combination with sunitinib. Argos Therapeutics, Inc., Durham, NC Phase III trial planned	INFa IL-2 Monoclonal antibodies Surgery	Increased overall survival Increased progression-free survival Improved quality of life
Immunotherapy (BioSante vaccine) for prevention of acute myeloid leukemia	Patients who have achieved complete remission of acute myelogenous leukemia following intensive chemotherapy	An immunotherapy technology that uses cell lines derived from the target tissue (leukocytes) that express GM-CSF, is an immune stimulator intended to destroy the tumor; a non-patient-specific immune modulator. BioSante Pharmaceuticals, Inc., Lincolnshire, IL Phase II trials completed; FDA gave orphan drug designation; development seems stalled as of Nov 2011, but still listed in company's pipeline	Repeated cycles of intensive cytarabine-based consolidation chemotherapy Autologous stem cell transplantation Allogeneic stem cell transplantation	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Immunotherapy (BioSante vaccine) for chronic myeloid leukemia recurrence	Patients who have undergone successful initial treatment for chronic myelogenous leukemia (CML)	An immunotherapy technology that uses cell lines derived from the target tissue (in this case leukocytes) that express GM-CSF, which is an immune stimulator intended to destroy the tumors; a non-patient-specific immune modulator. BioSante Pharmaceuticals, Inc., Lincolnshire, IL Phase II trials completed for preventing recurrence after successful treatment with Gleevec (imatinib); FDA gave orphan drug status; development seems stalled as of Nov 2011, but still listed in company's pipeline	Gleevec alone	Increased overall survival Increased progression-free survival Improved quality of life
Immunotherapy (BioSante vaccine) for treatment of castration-resistant prostate cancer	Patients in whom metastatic CRPC has been diagnosed	An immunotherapy technology that uses cell lines derived from the target tissue (in this case prostate cancer cells) that express GM-CSF, which is an immune stimulator; a non-patient-specific immune modulator. BioSante Pharmaceuticals, Inc., Lincolnshire, IL Phase II trial slated to begin late 2010; development seems stalled as of Nov 2011, but still listed in company's pipeline	Chemotherapy regimens (e.g., docetaxel) Provenge immunotherapy	Increased overall survival Increased progression-free survival Improved quality of life
JAK 1/2 inhibitor (ruxolitinib, Jakafi) for treatment of myelofibrosis	Patients in whom myelofibrosis (primary myelofibrosis, post-polycythemia vera myelofibrosis, or post essential thrombocythemia myelofibrosis) has been diagnosed	Janus kinase (JAK) inhibitor (INCB018424, ruxolitinib, Jakafi™) that inhibits kinase activity of both JAK 2 and JAK 1; half of myelofibrosis cases bear an activating mutation in JAK 2; therefore, its inhibition is a key target. Incyte Corp., Wilmington, DE in collaboration with Novartis AG, Basel, Switzerland. FDA approved Nov 2011	None Off-label treatments are only palliative	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Injected hydrogel (SpaceOAR) to protect healthy tissue during radiation therapy	Patients undergoing radiation therapy treatment for cancers that are adjacent to delicate healthy structures (e.g., prostate cancer)	SpaceOAR™ system (spacing organs at risk) is a hydrogel injected as a liquid that forms a solid in the body and is intended for use during radiation therapy to distance organs at risk of collateral radiation damage from the targeted tumor (e.g., displace the rectum from the prostate). Augmenix, Inc., Waltham, MA Phase trial in U.S. not stated; approved for marketing in Europe; Varian Medical Systems, Inc., invested in Augmenix with option to buy company	Radiation therapy without normal-tissue spacer	Reduced radiation-associated side effects to healthy tissue
Integrated positron emission tomography and magnetic resonance imaging system (Biograph mMR) for diagnosis and monitoring of cancer	Patients in whom cancer has been diagnosed	Imaging exams that combine positron emission tomography with magnetic resonance imaging (Biograph™ mMR) to provide simultaneous acquisition of morphologic, functional, and metabolic imaging data; intended to take 30 minutes to perform the exam, compared with 60 minutes or more for sequential positron emission tomography with magnetic resonance imaging exams. Siemens Healthcare, Malvern, PA Received FDA 510(k) clearance Jun 2011	Stand-alone magnetic resonance imaging and positron emission tomography exams	Improved imaging Improved patient throughput Increased patient satisfaction

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Interleukin-12 gene therapy (EGEN-001) for recurrent or persistent ovarian cancer	Patients in whom recurrent or persistent ovarian or fallopian tube cancer has been diagnosed; must have received at least one round of treatment with a platinum-based cytotoxic chemotherapy regimen	Patients in whom advanced ovarian cancer has been diagnosed often have recurrent disease and poor prognosis. EGEN-001 is a novel gene therapy intended to induce the expression of IL-12 in tumor cells; IL-12 expression is purported to lead to three antitumor activities: (1) activation/proliferation of natural killer (NK) cells, leading to an innate immune response against the tumor; (2) maturation/proliferation of T lymphocytes, leading to an adaptive immune response against the tumor; and (3) activation of NK cells and T lymphocytes leading to upregulation of interferon-gamma (INFg), which has antiangiogenic properties. EGEN-001 is administered by intraperitoneal catheter to the local tumor microenvironment. EGEN, Inc., Huntsville, AL Phase II trial ongoing; FDA granted orphan drug status	Carboplatin Carboplatin/docetaxel Carboplatin/gemcitabine Carboplatin/liposomal doxorubicin Carboplatin/paclitaxel Cisplatin Cisplatin/gemcitabine Docetaxel Etoposide Gemcitabine Liposomal doxorubicin Paclitaxel Topotecan	Increased progression-free survival Increased overall survival Improved quality of life
Kinase inhibitor (ENMD-2076) for platinum-based treatment-resistant ovarian cancer	Patients in whom ovarian cancer has been diagnosed	ENMD-2076 is a kinase inhibitor that targets aurora A (cell cycle progression) and angiogenic kinases VEGFR, Flt-3, FGFR3 (tumor vascularization). EntreMed, Inc., Rockville, MD Phase II trial ongoing	Carboplatin Carboplatin/docetaxel Carboplatin/gemcitabine Carboplatin/liposomal doxorubicin Carboplatin/paclitaxel Cisplatin Cisplatin/gemcitabine Docetaxel Etoposide Gemcitabine Liposomal doxorubicin Paclitaxel Topotecan	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Lansoprazole (PrevOnco) for treatment of advanced unresectable hepatocellular carcinoma	Patients in whom advanced unresectable hepatocellular carcinoma has been diagnosed	PrevOnco™ incorporates lansoprazole, a proton-pump inhibitor (commonly marketed anti-ulcer compound); incorporates proprietary NexACT drug delivery technology, which is designed to reduce by seven times the dose needed. Has shown strong anti-cancer activity in mice bearing human liver tumors; taken orally. Apricus Biosciences, Inc., San Diego, CA Phase III trial special protocol assessment under discussion with FDA; FDA granted orphan drug status	Doxorubicin Nexavar	Increased overall survival Increased progression-free survival Improved quality of life
Lenalidomide for treatment of castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	Angiogenesis and a suboptimal antitumor immune response are important pathways involved in CRPC pathogenesis and progression; new prostate cancer treatments that are antiangiogenic and immunomodulatory are needed. Lenalidomide is a derivative of thalidomide; the mechanism of action has not been fully characterized yet; lenalidomide is purported to possess immunomodulatory, antiangiogenic, and antineoplastic properties; it has delayed tumor growth in some animal hematopoietic tumor models, including multiple myeloma; lenalidomide inhibits secretion of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF alpha), from peripheral blood mononuclear cells; lenalidomide also inhibited expression of cyclooxygenase-2 (COX-2), but not COX-1 in vitro. Administered orally, 25 mg, daily, on days 1 through 14 of every 28-day cycle. Celgene, Summit, NJ Phase III trial ongoing	Abiraterone Cabazitaxel Docetaxel Sipuleucel-T Thalidomide	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Levonorgestrel-release intrauterine device (Mirena) for uterus-sparing treatment of endometrial hyperplasia and early endometrial carcinoma	Females with endometrial hyperplasia or stage 1A endometrial cancer who wish to preserve fertility	Intrauterine device (Mirena®) is a levonorgestrel (a progestogen)-release intrauterine device, plus gonadotropin-releasing hormone; has shown some efficacy against endometrial cancer and precancers in preliminary studies. Bayer AG, Leverkusen, Germany Multiple trials ongoing	Radical hysterectomy	Preserved fertility with similar clinical outcome to surgery

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Liver chemosaturation drug/device combination (melphalan-Chemosat) for treatment of melanoma metastases to the liver	Patients with ocular or cutaneous melanoma that has metastasized to the liver	Liver cancer is largely refractory to standard systemic chemotherapy; while targeted chemotherapy delivery options are available for treatment of liver cancer (e.g., hepatic artery delivered chemotherapy, trans-arterial chemoembolization), systemic side effects preclude the use of maximum chemotherapy doses. The Chemosat® system is a delivery method that introduces a chemotherapy drug (melphalan) through the hepatic artery and removes the drug by filtering blood exiting the liver through the venous system; in this way, high doses of chemotherapy can be delivered while sparing the patient systemic side effects; adjunctive therapy to treat the primary melanoma and nonhepatic metastases may also be administered. Delcath Systems, New York, NY Phase III trial completed; FDA returned NDA in Feb 2011 asking for further safety data; pre-NDA meeting to be held with FDA in Jan 2012; CE marked in Europe for liver cancer	Hepatic artery-delivered chemotherapy Trans-arterial chemoembolization	Increased overall survival Increased progression-free survival Improved quality of life
MarginProbe System for intraoperative identification of positive margins during breast cancer lumpectomy	Patients undergoing breast lumpectomy	Successful breast lumpectomy requires that the margins of a resected tumor be free of cancerous tissue; however, with current standard of care, up to 30% of patients undergo a second lumpectomy because cancer-positive margins are identified by pathology results several days after the initial operation. The MarginProbe system enables intraoperative identification of cancer-positive margins in excised tissues thereby allowing the surgeon to resect additional tissue during the same surgical procedure; the MarginProbe system uses radiofrequency spectroscopy to discern differences in the electromagnetic signature of cancerous cells relative to normal tissue. Dune Medical Devices, Inc., Framingham, MA Pivotal trial completed; PMA submitted; FDA has granted expedited review; system is available in Europe	No currently marketed comparator in the U.S.	Reduced number of re-excision surgeries performed Improved rate of complete surgical resection (e.g., no positive margin)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
MEK inhibitor (trametinib) for treatment of advanced melanoma with activating *B-RAF* mutation	Patients with stage IIIc or stage IV malignant cutaneous melanoma that harbors an activating *B-RAF* mutation	Patients with metastatic melanoma have a poor prognosis with current treatments yielding a 5-year survival rate of less than 10%. Melanomas harboring activating B-RAF mutations are driven in part by activation of the MAPK/ERK pathway of which MEK is a member; trametinib (GSK1120212) is an inhibitor of MEK 1 and MEK 2, which may have antineoplastic activity in tumors dependent on MAPK/ERK pathway activation. GlaxoSmithKline, Middlesex, UK Phase III trial in combination with standard chemotherapy; phase II trial in patients previously treated with the *B-RAF* inhibitor dabrafenib; phase II trial in combination with the *B-RAF* inhibitor dabrafenib	High dose IL-2 Dacarbazine (DTIC-Dome) Ipilimumab Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life
MEK inhibitor (trametinib) for treatment of pancreatic cancer	Patients in whom metastatic pancreatic cancer has been diagnosed	Only about 5% of patients with pancreatic cancers respond to the current standard of care (gemcitabine chemotherapy), and the prognosis for these patients is very poor. The survival and proliferation of many cancers is maintained in part by activation of the MAPK/ERK pathway of which MEK is a member; trametinib (GSK1120212) is an inhibitor of MEK 1 and MEK 2, which may have antineoplastic activity in tumors dependent on MAPK/ERK pathway activation; in the current clinical trial, trametinib is being administered in combination with gemcitabine. GlaxoSmithKline, Middlesex, UK Phase II trial ongoing	Gemcitabine alone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mobile telemedicine for cervical screening	Patients in rural areas in need of routine cervical screening	Females living in rural areas face barriers to access to cervical screening; options to improve rates of routine screening are needed. Visual inspection of the cervix with application of 4% acetic acid (VIA) is an inexpensive alternative to cytology-based screening; in remote, resource-limited areas, photographic inspection with acetic acid (PIA) can be performed by a clinician, who sends photographic images of a patient's cervix treated with 4% acetic acid and taken using a mobile phone; images are transmitted by MMS to a regional medical center for evaluation by a trained health care practitioner for signs of disease. Department of Dermatology, University of Pennsylvania, Philadelphia, PA Pilot study conducted in Gaborone, Botswana	Pap screening Visual inspection of the cervix with application of 4% acetic acid	Reduced cost of care Increased rate of cervical cancer screening Reduced rates of cervical disease Increased screening adherence
Modified HER2/neu peptide (AE37) therapeutic vaccine to prevent recurrent breast cancer	Patients with HER2/neu expression who have completed treatment of lymph-node-positive breast cancer or high-risk lymph-node-negative breast cancer with no evidence of remaining disease	Despite numerous first-line treatment options for breast cancer, many women experience disease recurrence; therefore, there is a need for a treatment that could kill residual tumor cells missed by first-line treatments or destroy recurrent disease. AE37 is a modified peptide vaccine directed against the Her2/neu receptor, which is overexpressed in about 30% of breast cancers; the peptide can be displayed by major histocompatibility complex (MHC) class II and, therefore, could activate helper T cells, which could improve establishment of long-term immunity; the peptide has been modified with a four-amino acid sequence called the li-Key, which may improve class II MHC presentation by enabling the AE37 peptide to displace antigens from class II MHC and present the HER2/neu derived peptide. Antigen Express, Inc., Worchester, MA Phase II trial ongoing	Trastuzumab	Improved overall survival Improved progression free survival Reduced breast cancer recurrence Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
mTOR inhibitor (everolimus, Afinitor) for treatment of estrogen-receptor-positive breast cancer	Patients with metastatic estrogen-receptor-positive breast cancer that has progressed after first-line hormone therapy	For patients whose breast cancer progresses following treatment with first-line antiestrogen therapy, followup antiaromatase therapy may delay progression; however, not all patients respond. Everolimus (Afinitor®) is a small-molecule inhibitor of the protein mTOR (mammalian target of rapamycin), which is a central regulator of cell growth. Inhibition of mTOR by everolimus has been demonstrated to be effective in the treatment of multiple cancer types (e.g., RCC, astrocytoma); however, its use in breast cancer treatment has not yet been approved. In the current clinical trial, everolimus is being administered in combination with the second-line hormone therapy exemestane. Novartis AG, Basel, Switzerland Phase III trial ongoing	Exemestane monotherapy	Increased progression-free survival Increased overall survival Improved quality of life
mTOR inhibitor (ridaforolimus) for treatment of soft tissue and bone sarcomas	Patients with metastatic soft tissue and bone sarcomas who have previously had a positive response to systemic chemotherapy	While many soft tissue and bone sarcomas initially respond to chemotherapy, most cancers develop resistance and recur. Ridaforolimus is a small-molecule inhibitor of the protein mTOR, which plays a central role in the regulation of cell growth; while various mTOR inhibitors have been approved for cancer indications in the U.S., no mTOR inhibitor has been approved for treatment of soft tissue and bone sarcomas. ARIAD Pharmaceuticals, Inc., Cambridge, MA, in collaboration with Merck & Co., Inc., Whitehouse Station, NJ Phase III trial ongoing; NDA submitted to FDA and accepted for standard review in Oct 2011	No currently approved therapy in the maintenance therapy setting.	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mucin-1 therapeutic cancer vaccine (CVac) for ovarian cancer	Patients in whom ovarian cancer has been diagnosed and who are in first or second remission after cytoreduction and chemotherapy	No maintenance therapies are currently approved to preserve remission in ovarian cancer treatment. CVac is an autologous dendritic cell-based vaccine that is primed with mucin-1 (a tumor antigen) coupled to mannan (a sugar derivative that acts as an immune stimulant). The vaccine is intended to induce an immune response to ovarian cancer cells, preventing or slowing recurrence. Prima BioMed, Ltd., Melbourne, Australia Phase II trial ongoing; phase II/III trial planned for 2012	Bevacizumab Paclitaxel	Increased progression-free survival Increased of overall survival Improved quality of life
MUC1-targeted therapeutic vaccine (TG4010) for nonsmall cell lung cancer	Patients in whom chemotherapy-naive NSCLC has been diagnosed and who are MUC1-positive	Only about 25% of patients with NSCLC respond to standard first-line therapies such as carboplatin/paclitaxel. TG4010 is a therapeutic cancer vaccine administered by subcutaneous injection; it comprises a viral vector encoding both a tumor antigen (MUC1) and an immune stimulant (IL-2); about 60% of NSCLC tumors express MUC1; patients' tumors must be MUC1-positive and patients must have normal levels of natural killer cells at the time of treatment initiation. In current clinical trials, TG4010 is being administered in combination with standard of care cytotoxic chemotherapy. Transgene AG, Cedex, France Phase IIb/III trial scheduled to initiate recruitment Dec 2011; FDA granted fast track status	Paclitaxel/carboplatin MAGE-A3 therapeutic vaccine (in development)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Multispectral dermascope (MelaFind) to identify melanoma in suspect lesions	Patients in whom pigmented skin lesions are present requiring diagnosis	Computer-controlled multispectral dermascope (MelaFind®) uses light to image skin through a thin layer of liquid (alcohol or oil) to try to make lesion structures visible under the skin surface; a digital camera inside the probe captures images and differentiates pigmented skin lesions to try to determine melanoma risk using algorithms. MELA Sciences, Inc., Irvington, NY FDA approved Nov 2011"for use on clinically atypical cutaneous pigmented lesions with one or more clinical or historical characteristics of melanoma, excluding those with a clinical diagnosis of melanoma or likely melanoma. MelaFind is designed to be used when a dermatologist chooses to obtain additional information for a decision to biopsy. MelaFind should NOT be used to confirm a clinical diagnosis of melanoma." CE marked Sep 6, 2011	Human observation of skin lesions (dermascope) Biopsy	Increased specificity and sensitivity Reduced number of biopsies performed on suspect lesions Earlier detection of suspect lesions Increased overall survival Improved quality of life
Necitumumab for treatment of advanced nonsmall cell lung cancer	Patients in whom advanced squamous NSCLC has been diagnosed	Advanced NSCLC has a high mortality rate and patients have a poor prognosis; new therapies that can improve survival are needed. Necitumumab is a monoclonal antibody antagonist directed against the EGFR protein, which may downregulate tumor activity; necitumumab may competitively inhibit the binding of EGF and other ligands, such as transforming growth factor-alpha, and block activation of receptor-associated kinases, resulting in inhibition of cell growth and induction of apoptosis; necitumumab may also mediate antibody-dependent cellular cytotoxicity; may be administered as an 800 mg intravenous infusion on days 1 and 8 of every 3-week cycle; may be used in combination with gemcitabine-cisplatin. The drug is in a similar class as cetuximab, which is used for treatment of many cancers but is not labeled for treatment of NSCLC. Eli Lilly & Co., Indianapolis, IN Bristol-Myers Squibb Co., Princeton, NJ Phase III trial ongoing	Cetuximab (used off-label; not indicated for NSCLC) Erlotinib Panitumumab	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label human papillomavirus vaccination (Gardasil and Cervarix) to prevent head and neck cancer	Persons engaging in oral sexual activity and kissing	Oncogenic HPV strains can cause cervical and anal cancer, as well as other cancers including head and neck cancer; between 1984 and 1989, only 16% of oropharyngeal cancers were linked to HPV; between 2000 and 2004, HPV was responsible for 75% of oropharyngeal cancers; if current trends continue, oropharyngeal cancer in men will surpass incidence of cervical cancer in 2025. Both commercially available human papillomavirus (HPV) vaccines (Gardasil®, Cervarix®) contain virus-like particles for oncogenic HPV types 16 and 18 which are responsible for the majority of HPV associated cancers; HPV vaccines may be used off-label for the prevention of head and neck cancers due to HPV 16 or 18 despite the current lack of data, and no apparent attempt to generate data on this indication by vaccine manufacturers. Gardasil, Merck & Co., Inc., Whitehouse Station, NJ; Cervarix, GlaxoSmithKline, plc, Middlesex, UK Both vaccines FDA approved for prevention of cervical cancer	Abstinence No vaccination Safer sex-practices Selective choice of partners	Reduced incidence of head and neck cancers Reduced incidence of head and neck precancers
Off-label metformin for treatment of breast cancer	Patients in whom breast cancer has been diagnosed.	Retrospective studies of diabetic patients taking metformin and preclinical studies of in vitro cell lines and in vivo cancer models have demonstrated that metformin may have anti-neoplastic properties. Metformin may exert its effects through activation of AMPK, which functions to limit downstream components of the mTOR pathway. In addition, metformin's actions in reducing circulating insulin levels may be antineoplastic due to the potential growth stimulating activity of insulin. Metformin is being studied in multiple breast cancer settings and could represent a novel treatment with a relatively low side effect profile. Phase II trials ongoing in neo-adjuvant setting; phase III trial ongoing in adjuvant setting to prevent recurrence; phase I/II trials ongoing in metastatic disease	Various hormone therapies Various chemotherapy regimens	Increased overall survival Increased progression-free survival Improved patient quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label rosuvastatin to prevent colon cancer recurrence	Patients who have had a stage I or II colon cancer surgically resected	Patients who undergo curative resection of stage I or II colon cancers have a 50% recurrence rate within the first 3 years after surgery, making a chemopreventive agent for this patient population highly sought. Retrospective studies of clinical trials assessing the use of statins for cardiovascular applications suggested that patients treated with statins had a reduced incidence of precancerous colon polyps; therefore, rosuvastatin is believed to have potential as a chemopreventive agent for colon cancer. Under study by National Surgical Adjuvant Breast and Bowel Project, Pittsburg, PA, and the National Cancer Institute, Bethesda, MD Phase III trial ongoing	There is no commonly used chemopreventive agent for CRC Compounds currently under investigation include: Aspirin Calcium supplements Curcumin Nonsteroidal antiinflammatory drugs (NSAID)s Omega-3 fatty acids	Reduced recurrence rate of adenomatous polyps Increased overall survival
Off-label zoledronic acid (Zometa) as first-line treatment of multiple myeloma	Patients in whom multiple myeloma has been diagnosed	Zoledronic acid is a bisphosphonate used to prevent skeletal fractures in cancer patients, including those in whom multiple myeloma is diagnosed; recent studies suggest that Zometa® has also improved overall survival rates in patients with multiple myeloma, which may support off-label use. Novartis AG, Basel, Switzerland Postmarket trial (NCT00432458) underway independently (of manufacturer)	Chemotherapy Hematopoietic stem-cell transplantation Medicines: Alendronate Etidronate Oral clodronate (trial comparator) Pamidronate Other bisphosphonates	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label zoledronic acid (Zometa) for treatment of breast cancer	Postmenopausal women in whom stage II/III breast cancer has been diagnosed and who have undergone surgery and/or surgical resection	Zoledronic acid (Zometa®) is a bisphosphonate used to prevent skeletal fractures in cancer patients at risk for fracture from bone metastases; recent studies suggest that the drug may also treat the primary cancer, improve overall survival, and reduce cancer recurrence rates in women with low estrogen levels (e.g., post-menopausal patients). Given that the drug is commercially available, its off-label use for this may be an option exercised by oncologists. Novartis AG, Basel, Switzerland Two phase III trials completed. One trial (ABCSG-12) reported positive results; however, a second (AZURE) trial observed a benefit only in post-menopausal women. Based on AZURE trial resultsl, Novartis decided not to pursue expanded label for zoledronic acid; however, physicians may prescribe off-label; additional phase III trials of zoledronic acid for breast cancer are ongoing	Chemotherapy Hormone therapy	Increased overall survival Increased progression-free survival Improved quality of life
Oncolytic reovirus (Reolysin) therapy for advanced *KRAS* mutant colorectal cancer	Patients in whom advanced or metastatic *KRAS* mutant CRC has been diagnosed	Oncolytic reovirus (Reolysin®) intended to treat various cancers and cell proliferative disorders, including CRC; Reolysin replicates specifically in cells that have activated RAS; 50% of CRCs are believed to have activated RAS. Given in combination with FOLFIRI. Oncolytics Biotech, Inc., Calgary, Alberta, Canada Phase I trial ongoing	Surgery Chemotherapy Radiation	Increased overall survival Increased progression-free survival Improved quality of life
Oncolytic reovirus (Reolysin) therapy for advanced pancreatic cancer	Patients in whom advanced pancreatic cancer has been diagnosed	Oncolytic reovirus (Reolysin) intended to treat various cancers and cell proliferative disorders, including pancreatic cancer for which no effective options are available. Reolysin replicates specifically in cells that have activated RAS; Activated RAS is seen in 90% of pancreatic cancers. Administered intravenously in combination with gemcitabine. Oncolytics Biotech, Inc., Calgary, Alberta, Canada Phase II trials ongoing	Surgery Other chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oncolytic reovirus (Reolysin) therapy for platinum-resistant head and neck cancer	Patients in whom platinum-resistant head and neck cancer has been diagnosed	Reolysin is an oncolytic reovirus being developed to treat various cancer and cell proliferative disorders; replicates specifically in cells that have activated RAS, which may play a role in more than two thirds of all cancers; administered in combination with paclitaxel and carboplatin. Oncolytics Biotech, Inc., Calgary, Alberta, Canada Phase III trial ongoing	Surgery Radiation Chemotherapy Targeted therapy	Increased overall survival Increased progression-free survival Improved quality of life
Oncolytic reovirus (Reolysin) therapy for recurrent malignant gliomas	Patients in whom recurrent malignant gliomas (brain or spinal cord tumors) have been diagnosed	Oncolytic reovirus (Reolysin) intended to treat various cancers and cell proliferative disorders, including brain cancer; replicates specifically in cells that have activated RAS. Activating mutations of RAS are believed to play a role in more than half of brain tumors. Administered in combination with FOLFIRI. Oncolytics Biotech, Inc., Calgary, Alberta, Canada Phase I/II trial complete	Surgery Radiation Chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Oncolytic reovirus (Reolysin) therapy for recurrent or persistent ovarian cancer	Patients in whom recurrent or persistent ovarian, fallopian tube, or primary peritoneal cancer has been diagnosed	Reolysin is a formulation of oncolytic reovirus being developed for the treatment of various cancers and cell proliferative disorders; has been shown to replicate specifically in cells that have activated RAS; activating mutations of RAS and its upstream elements may play a role in more than two thirds of all human cancers, including most metastatic disease. Oncolytics Biotech, Inc., Calgary, Alberta, Canada Phase II trial ongoing	Radiation Chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oncolytic reovirus (Reolysin) therapy for refractory solid tumors in children	Pediatric patients in whom relapsed or refractory solid tumor has been diagnosed	Reolysin is a formulation of oncolytic reovirus being developed for treatment of various cancers and cell proliferative disorders. It has been shown to replicate specifically in cells that have activated RAS. Activating mutations of the RAS and its upstream elements may play a role in more than two-thirds of all human cancers, including most metastatic disease. Currently being examined in combination with cyclophosphamide in pediatric patients with relapsed or refractory solid tumors. Oncolytics Biotech Inc., Calgary, Alberta, Canada Phase I trial ongoing	Surgery Chemotherapy Radiation	Increased overall survival Increased progression-free survival Improved quality of life
Oncolytic virus (JX-594) for treatment of nonresectable hepatocellular carcinoma	Patients in whom nonresectable hepatocellular carcinoma has been diagnosed	Less than 20% of liver cancer can be treated surgically and effective treatments are needed for the nonsurgical patients. JX-594 is a genetically modified vaccinia virus with two genetic modifications: (1) the viral thymidine kinase gene is deleted, so the virus is dependent on host thymidine kinase for replication; sufficient levels are found in tumor cells; (2) a gene encoding colony-stimulating factor is added. It is proposed to marshal an immune response to infected cells; vaccinia virus also has natural tropism to tumor cells; therapeutic effects are mediated by immune response and by tumor cell/tumor vasculature cell lysis caused by the viral life cycle. Jennerex, Inc., San Francisco, CA Phase II trials ongoing	Sorafenib Transcatheter arterial chemoembolization (cisplatin, doxorubicin)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
OncoVex (GM-CSF) for treatment of advanced melanoma	Patients in whom advanced melanoma has been diagnosed	Patients with advanced melanoma have a poor prognosis and few treatment options, suggesting a need for novel treatment options. OncoVex (GM-CSF) is an oncolytic virus; the virus is purported to replicate only in tumor cells; OncoVex is engineered to lyse tumors cells and express tumor-specific antigens and GM-CSF, which help to generate tumor specific immune responses for additional benefit. Administered up to 4 mL of 10^8 pfu/mL/per intratumoral injection in trials. Amgen, Inc., Thousand Oaks, CA Phase III trial ongoing	Dacarbazine or INF Personalized vaccination (in clinical development) Proleukin (IL-2) Temozolomide Therapeutic vaccines (in clinical development)	Increased overall survival Increased progression-free survival Improved quality of life
Orteronel (TAK 700) for treatment of castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	Many prostate tumors remain dependent on androgens for growth and survival; new treatments that can disrupt the production of bioactive androgens may provide effective tumor therapy. Orteronel (TAK 700) is a steroid 17-alpha-hydroxylase inhibitor; this enzyme is involved in the formation of dehydroepiandrosterone (DHEA) and androstenedione, which may ultimately be metabolized into testosterone; testosterone is required for the growth of many prostate tumors; orteronel may be used in chemotherapy-naive patients or after docetaxel, in combination with prednisone. Millennium Pharmaceuticals, Inc., Cambridge, MA Phase III trials ongoing	Abiraterone Cabazitaxel Docetaxel Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Ovarian scanning (HistoScanning) for diagnosis of ovarian masses	Patients with a suspicious ovarian mass	HistoScanning™ captures transvaginal sonographic images and analyzes them to try to determine whether the mass is benign or malignant. Advanced Medical Diagnostics, sa/nv, Waterloo, Belgium Early phase trials ongoing	Visual analysis of mass morphology Doppler transvaginal sonography Exploratory surgery	Increased sensitivity and specificity More accurate referral for follow up Avoid unnecessary diagnostic follow up and unnecessary treatment

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Partial wave spectroscopy for lung cancer screening	Patients at high risk of developing lung cancer (e.g., smokers, ex-smokers)	Partial wave spectroscopy is proposed as a new microscopy technique that is intended to increase the resolution of detection down to "nanoscale." It is purported to enable detection of subtle changes in cellular architecture in noncancerous tissue located at a distance from cancerous lesion (known as *field carcinogenesis*). Northwestern University, Chicago, IL Preliminary validation study completed on 135 smokers	No screening equivalent currently available Other tests for lung cancer screening Chest radiograph Sputum cytology Computed tomography	Increased sensitivity and specificity Increased predictive value Avoid unnecessary testing Earlier intervention and treatment Increased overall survival
Pegylated arginine deiminase (ADI-PEG 20) for treatment of hepatocellular carcinoma	Patients with advanced hepatocellular carcinoma (HCC) whose disease has failed to respond to one prior course of systemic therapy	For patients who cannot be cured by surgical removal of the tumor, survival rates for HCC are very low (about 5%), with median survival after diagnosis of only about 6 months. ADI-PEG 20 is a pegylated preparation of arginine deiminase, which acts by depleting the essential amino acid arginine from the bloodstream; research has demonstrated that the cells of many tumor types are unable to autonomously synthesize arginine and, therefore, tumor cells are preferentially affected by the loss of arginine supply in the blood. It is administered through intramuscular injection on outpatient basis. Polaris Pharma, San Diego, CA Phase III trial initiated under FDA special protocol assessment; FDA granted orphan drug status	Placebo Regorafenib (in development)	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-cytokine complex (NGR-hTNF) for treatment of advanced nonsmall cell lung cancer	Patients in whom advanced or recurrent NSCLC has been diagnosed	NGR-hTNF is a peptide-cytokine complex; the NGR peptide binds preferentially to tumor vasculature, and TNF can induce an immune cell reaction/apoptosis. Being tested in combination with conventional chemotherapy regimens. MolMed, S.p.A., Milan, Italy Phase II trial ongoing	Standard chemotherapy regimens: Cisplatin/gemcitabine, cisplatin/pemetrexed	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Peptide-cytokine complex (NGR-hTNF) for treatment of advanced or metastatic hepatocellular carcinoma	Patients in whom advanced or metastatic hepatocellular carcinoma has been diagnosed	NGR-hTNF is a peptide-cytokine complex; the NGR peptide binds preferentially to tumor vasculature, and TNF can induce an immune cell reaction/apoptosis. MolMed, S.p.A., Milan, Italy Phase II trial completed	Chemoembolization Standard systemic chemotherapy: Sorafenib Gemcitabine/oxaliplatin	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-cytokine complex (NGR-hTNF) for treatment of malignant pleural mesothelioma	Patients in whom malignant pleural mesothelioma has been diagnosed who have undergone treatment with pemetrexed and cisplatin	NGR-hTNF is a peptide-cytokine complex; NGR peptide binds preferentially to tumor vasculature and TNF may induce an immune cell reaction/apoptosis thereby destroying tumors. MolMed, S.p.A., Milan, Italy Phase III trial ongoing in second-line setting; phase II trial ongoing in first-line setting	Pemetrexed plus cisplatin as first-line treatment Single-agent chemotherapy as a second-line treatment (e.g., doxorubicin, gemcitabine, vinorelbine)	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-cytokine complex (NGR-hTNF) for treatment of metastatic colorectal cancer	Patients in whom metastatic CRC has been diagnosed that has not responded to standard treatment	NGR-hTNF is a peptide-cytokine complex; the NGR peptide binds preferentially to tumor vasculature, and TNF can induce an immune cell reaction/apoptosis. Being tested in combination with oxaliplatin-based chemotherapy. MolMed, S.p.A., Milan, Italy Phase II trial completed	Standard chemotherapy: Oxaliplatin/capecitabine	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-cytokine complex (NGR-hTNF) for treatment of metastatic ovarian cancer	Patients in whom metastatic ovarian cancer has been diagnosed that is refractory to platinum-based chemotherapy	NGR-hTNF is a peptide-cytokine complex; the NGR peptide binds preferentially to tumor vasculature, and TNF can induce an immune cell reaction/apoptosis. Being tested in combination with doxorubicin. MolMed, S.p.A., Milan, Italy Phase II trial ongoing	Standard second-line chemotherapies, including: docetaxel, doxorubicin, etoposide, gemcitabine, tamoxifen, topotecan	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Peptide-cytokine complex (NGR-hTNF) for treatment of metastatic small cell lung cancer	Patients in whom metastatic small cell lung cancer has been diagnosed that is refractory to standard chemotherapy	NGR-hTNF is a peptide-cytokine complex; the NGR peptide binds preferentially to tumor vasculature, and TNF can induce an immune cell reaction/apoptosis. Being tested in combination with doxorubicin. MolMed, S.p.A., Milan, Italy Phase II trial complete	Doxorubicin monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-cytokine complex (NGR-hTNF) for treatment of soft tissue sarcomas	Patients in whom locally advanced or metastatic soft tissue sarcoma has been diagnosed	NGR-hTNF is a peptide-cytokine complex; the NGR peptide binds preferentially to tumor vasculature, and TNF can induce an immune cell reaction/apoptosis. Being tested as monotherapy or in combination with doxorubicin. MolMed, S.p.A., Milan, Italy Phase II trial ongoing	Doxorubicin monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Perifosine (KRX-0401) for treatment of chronic lymphocytic leukemia	Patients in whom CLL has been diagnosed	Many patients with CLL do not achieve an initial treatment response, and most patients eventually relapse, demonstrating the need for new and effective treatments. Perifosine (KRX-0401) is an oral anticancer agent that inhibits Akt activation in the PI3K pathway by interfering with the membranes of cancer cells, through disruption of "lipid rafts"; other key signal transduction pathways can also be affected, including JNK, limiting cell growth and proliferation; perifosine may be administered 50 mg, orally, twice a day, for a maximum of six 28-day cycles as a single oral agent and in combination with novel therapies Keryx Biopharmaceuticals, Inc., New York, NY Phase II trial ongoing	Chemotherapy Prednisolone Rituximab	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Perifosine (KRX-0401) for treatment of multiple myeloma	Patients in whom multiple myeloma has been diagnosed	Perifosine (KRX-0401) anticancer agent inhibits Akt activation in the PI3K pathway; also affects other key signal transduction pathways, including JNK; intended for treatment of several tumor types. Administered as a single oral agent and in combination with novel therapies. Keryx Biopharmaceuticals, Inc., New York, NY Phase III trials ongoing for multiple myeloma under FDA special protocol assessment	Steroids Chemotherapy Thalidomide Stem cell transplants Newer drugs, such as lenalidomide and bortezomib	Increased overall survival Increased progression-free survival Improved quality of life
Perifosine (KRX-0401) for treatment of refractory advanced colorectal cancer	Patients in whom advanced chemotherapy-resistant CRC has been diagnosed	Perifosine (KRX-0401) is an anticancer agent that inhibits Akt activation in the PI3K pathway and affects other key signal transduction pathways, including JNK; intended as monotherapy and in combination with novel therapies; taken orally Keryx Biopharmaceuticals, Inc., New York, NY Phase III trial ongoing under FDA special protocol assessment	Surgery Chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Poly ADP-ribose polymerase inhibitor (iniparib) for treatment of metastatic nonsmall cell lung cancer	Patients in whom treatment-naive stage IV metastatic NSCLC has been diagnosed	The 5-year survival rate for patients with stage IV NSCLC is less than 10% and effective treatments are needed. Iniparib is intended to inhibit poly ADP-ribose polymerase (PARP) activity in a DNA repair pathway. No PARP inhibitors are currently on the market. It has been observed that cancers are often deficient in a second arm of the DNA repair pathway, and loss of both types of DNA repair is hypothesized to result in cancer cell lethality in response to DNA damage. Iniparib is being administered in combination with a DNA damage inducing chemotherapy regimen (gemcitabine, carboplatin). BiPar Sciences, San Francisco, CA Sanofi-Aventis, Bridgewater, NJ Phase III trial ongoing	Cytotoxic chemotherapy (e.g., gemcitabine, carboplatin) alone. PARP Inhibitors in development: AG014699 CEP9722 MK 4827 Olaparib Veliparib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Poly ADP-ribose polymerase inhibitor (iniparib) for treatment of metastatic triple-negative breast cancer	Women in whom triple-negative (estrogen receptor negative, progesterone receptor negative, HER-2 amplification negative) metastatic breast cancer has been diagnosed	There is no standard effective therapy for metastatic triple-negative breast cancer and patients with this condition have a median survival of approximately 1 year. Iniparib is intended to inhibit PARP activity in a DNA repair pathway. No PARP inhibitors are currently on the market. It has been observed that triple-negative breast cancer is often deficient in a second arm of the DNA repair pathway, and loss of both types of DNA repair is hypothesized to result in cancer cell lethality in response to DNA damage. Iniparib is administered in combination with a DNA damage-inducing chemotherapy regimen (gemcitabine, carboplatin). BiPar Sciences, San Francisco, CA Sanofi-Aventis, Paris, France Phase III trial is ongoing; however, in Jan 2011, it was announced that the trial missed its primary endpoint.	Cytotoxic chemotherapy (gemcitabine, carboplatin) alone. Other PARP inhibitors in development: AG014699, CEP9722, MK 4827, Olaparib, Veliparib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Poly ADP-ribose polymerase inhibitor (olaparib) for treatment of ovarian cancer	Patients in whom ovarian cancer has been diagnosed	Patients in whom advanced ovarian cancer has been diagnosed often have recurrent disease and poor prognosis. Olaparib is a novel orally administered, small-molecule drug intended to inhibit PARP, which functions in a DNA repair pathway; no PARP inhibitors are currently on the market. It has been observed that cancers are often deficient in a second DNA repair pathway, and loss of both types of DNA repair is hypothesized to result in cancer cell lethality in response to DNA damage. Olaparib is being tested in clinical trials in combination with carboplatin and paclitaxel in the first-line setting and as a monotherapy in the recurrent disease setting. AstraZeneca, London, UK Phase II trials ongoing; one phase II trial complete	First-line comparators: Carboplatin/paclitaxel Recurrent disease comparators include: Bevacizumab Carboplatin with docetaxel or gemcitabine or liposomal doxorubicin Cisplatin Cisplatin/gemcitabine Docetaxel Etoposide Gemcitabine Paclitaxel Topotecan	Increased progression-free survival Increased overall survival Improved quality of life
Ponatinib for treatment of chronic myelogenous leukemia or Philadelphia-chromosome-positive acute lymphoblastic leukemia	Patients in whom CML or Philadelphia-chromosome-positive ALL has been diagnosed	Patients with treatment-refractory CML or ALL generally have a poor prognosis, rapidly progressing disease, and few treatment options, so new therapies are needed. The translocation leading to the Philadelphia chromosome mutation is a hallmark of CML and activates several proteins and enzymes that accelerate cell division and destabilize the genome; some ALL cells also carry this mutation (more frequently in adults, who are harder to treat); ponatinib is a next-generation BCR-ABL tyrosine kinase inhibitor rationally designed to be effective against common mutations conferring resistance to current BCR-ABL tyrosine kinase inhibitors. Administered 45 mg, orally, once daily. Ariad Pharmaceuticals, Inc., Cambridge, MA Phase II trials ongoing; FDA granted orphan drug status for CML and Philadelphia chromosome-positive ALL	Dasatinib Imatinib Nilotinib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Positron emission tomography imaging agent (F18-ML10, EarliTest) for assessing tumor response to treatment	Patients undergoing treatment for solid tumors	The availability novel diagnostic tools that could allow detection of tumor response early during treatment could allow earlier modification of ineffective treatments. EarliTest™ is a positron emission tomography imaging agent (F18-ML10) that specifically labels cells undergoing apoptosis, a process of apoptosis that is often the result of anticancer treatments. By directly monitoring the cellular outcome of therapy, the product is purported to give an earlier indication of whether a therapy is having an antitumor effect. Aposense, Ltd., Petach Tikva, Israel Phase II trials ongoing	Circulating Tumor Cell detection Fluorodeoxyglucose CT imaging MRI imaging PET imaging	Correlation between EarliTest result and tumor response Correlation between EarliTest result and improved patient outcomes (e.g., progression-free survival, overall survival)
Prophage series G-200 therapeutic vaccine for gliomas	Patients diagnosed with primary or recurrent brain and CNS cancers (gliomas)	Prophage (vitespen and HSPPC-96) is a cancer vaccine that is derived from antigens displayed by the patient's individual tumor. A tumor sample is collected and sent to the laboratory, where workers coimmunoprecipitate the antigens with heat shock protein GP96. These antigens are delivered in weekly/biweekly injections in an attempt to stimulate an immune response against residual cancer cells. Under development for both adults and pediatric patients. Agenus, Inc., Lexington, MA Phase II trials ongoing adults; phase I trial planned for pediatric brain cancers; FDA granted orphan drug status	Current surgery (radiation)/chemotherapy treatments for glioblastoma multiforme.	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ProstVac immune therapy for castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	Men with progressive metastatic, CRPC often have a poor prognosis and currently have few treatment options. No currently available viral vector vaccine is available. ProstVac® is a prime-boost immune therapy strategy using fowlpox and vaccinia viral vectors encoding prostate specific antigen and three immune costimulatory molecules; the patient's immune system is primed using the vaccinia virus followed by multiple fowlpox vector boosts. Given in one prime step and then weekly injections to generate an immune response. BN ImmunoTherapeutics, Mountain View, CA Phase III trial initiated but not yet recruiting patients	Abiraterone Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Radiofrequency ablation of liposomal-encapsulated doxorubicin (ThermoDox) for treatment of hepatocellular carcinoma	Patients in whom hepatocellular carcinoma has been diagnosed	ThermoDox™ is a heat-labile liposomal encapsulation of the chemotherapeutic agent doxorubicin to induce local hyperthermia (39.5 ^{o} to 42^{o} C) when radiofrequency energy is applied to release the agent. Celsion Corp., New York, NY Phase III trial ongoing; National Cancer Institute recommended phase III trial as priority for hepatocellular carcinoma; interim analysis anticipated by end of 2011; granted orphan drug status by FDA in Mar 2009	Radiofrequency tumor ablation alone Transcatheter arterial chemoembolization (directed chemotherapy delivery) Surgical resection	Decreased need for liver transplantation Reduced side effects Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Radium-223 (Alpharadin) for treatment of bone metastases associated with solid tumors	Patients in whom bone metastases associated with advanced hormone-refractory metastatic prostate cancer have been diagnosed	Bone metastases occur in late stages of the majority of solid tumors and are associated with significant morbidity and mortality; however, few treatments specifically targeting bone metastases are available. Alpharadin® is a preparation of radium-223, an alpha-particle-emitting isotope that has a natural affinity for bone; Alpharadin purportedly accumulates in the bone where it preferentially attacks tumors rather than bone marrow because of the short distance over which alpha particles are cytotoxic. Alpharadin is administered in multiple intravenous doses. Algeta ASA, Oslo, Norway, in collaboration with Bayer HealthCare Pharmaceuticals, Wayne, NJ Phase III trial complete; NDA submission to FDA expected in 2012	Standard therapy with and without alpharadin Standard therapy plus denosumab or cabozantinib (in development)	Increased progression-free survival Increased overall survival Increased rate of alkaline phosphatase normalization Reduced pain from bone metastases Improved quality of life
Regorafenib multikinase inhibitor for treatment of gastrointestinal stromal tumors	Patients in whom advanced/metastatic GIST has been diagnosed that progressed following treatment with imatinib and sunitinib	Patients whose disease progresses after imatinib and sunitinib therapy have few treatment options and poor prognosis with approximate progression-free survival and overall survival times of 100 days and 300 days, respectively. Regorafenib is an inhibitor of multiple tyrosine kinases, including the pro-angiogenic kinases VEGFR2 and TIE-2 (as well as RAF, RET, and KIT); inhibition of both primary angiogenic kinase pathways is a novel combination in multikinase inhibitor drugs (e.g., imatinib, sunitinib). Bayer AG, Leverkusen, Germany Phase II and phaseIII trials ongoing; In Feb 2011, FDA granted orphan drug status for GIST	Sorafenib Nilotinib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Regorafenib multikinase inhibitor for treatment of hepatocellular carcinoma	Patients with unresectable hepatocellular carcinoma that has progressed after treatment with the multikinase inhibitor sorafenib	In patients who cannot be cured by surgical removal of the tumor, survival rates for hepatocellular carcinoma are very low (~5%) with median survival after diagnosis of only ~6 months. No second-line therapy is currently available after sorafenib. Regorafenib is an inhibitor of multiple tyrosine kinases, including the pro-angiogenic kinases VEGFR2 and TIE-2 (as well as RAF, RET, and KIT); inhibition of both primary angiogenic kinase pathways is a novel combination in multikinase inhibitor drugs (e.g., imatinib, sunitinib). Bayer AG, Leverkusen, Germany Phase II trial ongoing	Placebo	Increased overall survival Increased progression-free survival Improved quality of life
Regorafenib multikinase inhibitor for treatment of metastatic colorectal cancer	Patients diagnosed with metastatic CRC as both a first-line treatment in combination with standard cytotoxic chemotherapy (FOLFOX) and as a salvage treatment after all available treatments have been tried	Many treatment options are available for first-line treatment of metastatic CRC, but 5-year survival rates are only ~25%. No multikinase inhibitors have been approved for use in metastatic CRC. Regorafenib is an inhibitor of multiple tyrosine kinases, including the pro-angiogenic kinases VEGFR2 and TIE-2 (as well as RAF, RET, and KIT); inhibition of both primary angiogenic kinase pathways is a novel combination in multikinase inhibitor drugs (e.g., imatinib, sunitinib). Bayer AG, Leverkusen, Germany Phase III trial for salvage therapy was reported as having met its primary endpoint in Oct 2011; FDA has granted regorafenib fast-track status for this indication; phase II trial for first-line therapy ongoing	first line therapy comparators include: FOLFOX alone FOLFOX plus targeted therapy (e.g., bevacizumab, cetuximab, panitumumab) Other cytotoxic chemotherapy regimens plus or minus targeted therapy (e.g., CapeOX, FOLFIRI, 5-FU/leucovorin, capecitabine, FOLFOXIRI)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Regorafenib multikinase inhibitor for treatment of renal cell carcinoma	Patients in whom metastatic or unresectable RCC has been diagnosed	No curative treatments are currently available for unresectable/metastatic RCC, and this drug represents a new treatment option with a novel multikinase inhibitory profile. Regorafenib inhibits multiple tyrosine kinases, including the pro-angiogenic kinases VEGFR2 and TIE-2 (as well as RAF, RET, and KIT); inhibition of both primary angiogenic kinase pathways is a novel combination in multikinase inhibitor drugs (e.g., imatinib, sunitinib). Bayer AG, Leverkusen, Germany Phase II trial ongoing	Sunitinib Temsirolimus Bevacizumab plus or minus INF Pazopanib High-dose IL-2 Sorafenib	Increased overall survival Increased progression-free survival Improved quality of life
Saracatinib (AZD0530) for treatment of platinum-resistant ovarian cancer	Patients in whom platinum-resistant ovarian cancer has been diagnosed	Saracatinib (AZD0530) a 5-, 7-substituted anilinoquinazoline with antiinvasive and antitumor activities is a dual-specific inhibitor of Src and Abl, which are protein tyrosine kinases affecting cell motility, migration, adhesion, invasion, proliferation, differentiation, and survival; taken orally. AstraZeneca, London, UK Phase II/III trial ongoing	Surgery Chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life
SNS01-T for treatment-refractory multiple myeloma	Patients in whom treatment-refractory multiple myeloma has been diagnosed	SNS01-T is a novel therapeutic intended to sensitize cancer cells to apoptotic signals via targeting eukaryotic translation initiation Factor 5A1; 5A1 functions as a shuttle protein, selectively translocating mRNA from the nucleus to cytosolic ribosomes for translation; preclinical studies have shown that Factor 5A1 kills cancer cells through the expression of p53, caspases, tumor necrosis factor receptor 1 and the INFg receptor and the negative regulation of bcl-2 and telomerase Senesco Technologies, Inc., New Brunswick, NJ Phase I/II trial ongoing; FDA granted orphan drug status	Autologous stem cell transplant Bisphosphonates Bortezomib Chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Survivin peptide vaccine (DPX-Survivac) to prevent recurrence of ovarian cancer	Patients in whom stage IIc-IV ovarian cancer has been diagnosed who have undergone successful debulking surgery and treatment with carboplatin/ paclitaxel	Patients in whom ovarian cancer has been diagnosed often relapse following successful initial treatment of their disease; therefore, maintenance therapies that prolong the time to recurrence or prevent recurrence are needed. DPX-Survivac is a novel peptide vaccine that consists of survivin peptides in a lipid-based depot formulation (DepoVax™). Survivin is a tumor-associated antigen that has been shown to be overexpressed in multiple cancers including ovarian cancer. In clinical trials, DPX-Survivac is being administered in three injected doses in combination with or without a low dose of cyclophosphamide (intended to act as an immune stimulant). Immunovaccine, Inc., Halifax, Nova Scotia, Canada Phase I/II trial ongoing	Bevacizumab Paclitaxel	Increased recurrence-free survival Increased overall survival Improved quality of life
Talactoferrin alfa for treatment of nonsmall cell lung cancer	Patients in whom NSCLC has been diagnosed who are undergoing first-line chemotherapy; patients with treatment-resistant NSCLC	Talactoferrin alfa is a derivative of lactoferrin, a modulator of the immune response, and is intended to stimulate the immune system in an effort to destroy the tumor. Talactoferrin alfa is currently under study in the first-line setting in combination with carboplatin and paclitaxel and under study in the third-line setting as a monotherapy. Agennix AG, Heidelberg, Germany Phase III trials ongoing	First-line comparator: carboplatin and paclitaxel alone Third-line comparator: standard of care	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tasquinimod for treatment of castration-resistant prostate cancer	Patients in whom CRPC has been diagnosed	Advanced prostate tumors can become resistant to androgen-deprivation therapy; new treatments with novel mechanisms of action are needed to limit the growth of advanced CRPC. Tasquinimod is a novel oral antiangiogenic compound that is intended to restrict blood flow to prostate tumors thus inhibiting growth; tasquinimod which may also exert antitumor effects. Administered 0.25, 0.5, or 1 mg/day. Active Biotech, AB, Lund, Sweden Phase III trials ongoing	Abiraterone MDV-3100 (in development) Orteronel (in development) Sipuleucel-T Thalidomide (in development)	Improved overall survival Improved progression-free survival Improved quality of life
Telomerase inhibitor (imetelstat) for treatment of nonsmall cell lung cancer	Patients in whom advanced/metastatic NSCLC has been diagnosed and whose disease has not progressed after treatment with platinum-based cytotoxic chemotherapy with or without the addition of biologic therapy with bevacizumab	Patients in whom advanced/metastatic NSCLC has been diagnosed have poor prognosis and disease often recurs or progresses following initial treatment. One cause of disease recurrence may be the existence of "cancer stem cells," which are typically refractory to cytotoxic chemotherapy and have the potential to regenerate tumors following cessation of cytotoxic chemotherapy. One hallmark of cancer stem cells is the expression of an enzyme called telomerase that is essential for maintaining the fidelity of chromosome termini (telomeres), which typically degrade after repeated cell divisions. Imetelstat is an oligonucleotide that binds the active site of telomerase, inhibiting its activity. Imetelstat is currently under study as a maintenance therapy following a successful cytotoxic chemotherapy regimen and may be administered in combination with the antiangiogenic monoclonal antibody bevacizumab. Geron Corp., Menlo Park, CA Phase II trial ongoing	Observation Bevacizumab	Increased progression-free survival Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tengion neo-urinary conduit for postcystectomy urinary diversion	Patients who have undergone a cystectomy (bladder removal), usually as treatment for bladder cancer	Tengion Neo-Urinary Conduit™ obtains a fat-cell sample from the patient prior to cystectomy and in the laboratory, a biodegradable scaffold is used to grow a smooth muscle tube from the fat cell sample. The tube is used to divert urine from the ureters to the outside the body after bladder removal. Tengion, Inc., East Norriton, PA Phase I trial ongoing	Ileal conduit urinary diversion (uses a portion of the intestine as the urinary conduit) Studer's Ileal neobladder (uses a portion of the intestine to form a bladder-like pouch that is controlled by abdominal muscles)	Successful routing of urine outside the body without disrupting the GI tract
Tesetaxel (oral taxane) for treatment of advanced cancers	Patients in whom advanced gastric cancer, melanoma, prostate cancer, breast cancer, or bladder cancer has been diagnosed	Current microtubule stabilizing taxanes (e.g., docetaxel, paclitaxel) are administered by intravenous infusion and have been associated with infusion site reactions. Tesetaxel would be the first orally administered taxane; other oral taxanes are in development but not as far along. In addition, preclinical studies suggested that tesetaxel could evade a common mechanism by which cancer cells develop taxane resistance and, therefore, could potentially be used to treat taxane-resistant cancers. Genta, Inc., Berkeley Heights, NJ Phase II trials ongoing	Conventional (injected) taxanes (paclitaxel, docetaxel)	Reduced taxane-administration-related adverse events Increased overall survival Increased progression-free survival Improved quality of life
Therapeutic dendritic cell vaccine (ICT-107) for glioblastoma multiforme	Patients in whom glioblastoma multiforme has been diagnosed	Glioblastoma multiforme is difficult to treat, with few effective options. New therapies that can improve survival and slow disease progression are needed. Personalized dendritic cell vaccine (ICT-107) is a dendritic cell-based therapeutic vaccine targeting multiple autologous tumor associated antigens including AIM2, HER-2, gp-100, MAGE-1, TRP-2, and IL-13Ra2 for the potential intradermal treatment of glioblastoma. ImmunoCellular Therapeutics Ltd., Los Angeles, CA Phase II trial ongoing; FDA granted orphan drug status in 2010	Anti-angiogenic therapy Chemotherapy Corticosteroids Radiation therapy Radiosurgery Surgery	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Therapeutic vaccine (BiovaxID) for treatment of indolent follicular non-Hodgkin's lymphoma	Patients in whom indolent follicular non-Hodgkin's lymphoma (NHL) has been diagnosed	Personalized cancer vaccine (BiovaxID™) works by producing B-cell hybridomas from the patient's cancer cells. Cancer-specific antibody idiotype is amplified, isolated, and conjugated to an immunostimulant; then readministered with GM-CSF in attempt to induce anti-idiotypic response to the lymphoma tumor. Biovest International, Inc., Tampa, FL Phase III trial complete; FDA granted orphan drug status	Other chemotherapy Other monoclonal antibodies Immunotherapy Radiation therapy Combination therapy Hematopoietic stem cell transplantation	Increased overall survival Increased progression-free survival Improved quality of life
Therapeutic vaccine (BiovaxID) for treatment of mantle cell lymphoma	Patients in whom mantle cell lymphoma has been diagnosed	Personalized cancer vaccine (BiovaxID) works by producing B-cell hybridomas from patient's cancer cells; cancer-specific antibody idiotype is amplified, isolated, and conjugated to an immunostimulant, then readministered with GM-CSF, in an effort to induce anti-idiotypic response to the lymphoma/tumor. Biovest International, Inc., Tampa, FL Phase II trial complete; FDA granted orphan drug status	Chemotherapy Radiation Lymphocyte transplantation Monoclonal antibodies Radioimmunotherapy (ibritumomab and tositumomab)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Therapeutic vaccine IMA901 for renal cell carcinoma	Patients in whom renal metastatic and/or locally advanced RCC has been diagnosed	RCC is typically highly resistant to conventional chemotherapy/radiation therapy; therefore, there are few treatment options for RCC patients. IMA901 is a rationally designed therapeutic cancer vaccine comprised of 10 different tumor-associated peptides that are found to be highly overexpressed in the majority of patients who have RCC; immunization is intended to induce cellular immune responses against renal tumors; IMA901 is purported to have a stable, off-the-shelf formulation. Administered intradermally with GM-CSF and sunitinib as a first-line therapy. Immatics Biotechnologies GmbH, Tübingen, Germany Phase III trial ongoing	Sunitinib	Increased overall survival Increased progression-free survival Improved quality of life
Therapeutic vaccine tertomotide (GV-1001) for pancreatic cancer	Patients in whom pancreatic cancer has been diagnosed	Advanced pancreatic cancer has a 5-year survival rate of approximately 5% with few therapeutic options. Tertomotide (GV-1001) is a therapeutic peptide vaccine against telomerase, a protein responsible for adding telomeres, noncoding DNA at the ends of chromosomes, which help to determine the life span of cells; overexpression of telomerase can lead to immortalization of cells and oncogenesis; tertomotide is purported to induce cellular immune responses against telomerase. Tertomotide is administered intradermally in combination with GM-CSF on days 1, 3, and 5 in week 1, once weekly in weeks 2, 3, 4 and 6, and then once a month in the absence of disease progression or unacceptable toxicity; patients may also be concurrently treated with gemcitabine. KAEL-GemVax Co., Ltd., Seoul, South Korea Phase III trial ongoing (data expected second half of 2012)	Gemcitabine Oncolytic virus therapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Therapeutic vaccine (TVAX) for recurrent glioma	Patients in whom recurrent stage IV glioma has been diagnosed	A personalized vaccine (TVAX) consisting of irradiated cancer cells derived from the patient and administered with GM-CSF; "precursor killer T-cells" are generated after the first administration of the vaccine; then vaccine-induced killer T-cells are collected from the patient's blood for additional priming at the manufacturer's laboratory and reinfused intravenously into the patient's bloodstream. TVAX Biomedical, LLC, Lenexa, KS Phase II trial ongoing; phase III trial in astrocytoma FDA approved to begin.	Chemotherapy Radiation Surgery	Increased overall survival Increased progression-free survival Improved quality of life
Therapeutic whole-cell tumor vaccine (OncoVAX) for colorectal cancer	Patients in whom stage II CRC has been diagnosed who will undergo surgical resection of the primary tumor	OncoVAX® is a whole-cell tumor vaccine. Tumor cells are isolated from the resected tumor, irradiated to prevent tumorigenicity upon reintroduction; patient receives in three weekly injections; administered in conjunction with bacillus Calmette-Guérin (adjuvant). Vaccinogen, Inc., Frederick, MD Phase IIIa trial in CRC completed; phase IIIb trial planned; potential introduction in the U.S. market in 2013 to 2014	No current CRC therapeutic vaccines on the market Chemotherapy following surgical resection	Increased overall survival Increased progression-free survival Improved quality of life
Tivozanib (AV-951) for treatment of advanced or metastatic breast cancer	Patients in whom advanced or metastatic breast cancer has been diagnosed that is refractory to standard chemotherapy	Tivozanib is a small-molecule inhibitor of VEGFR1, VEGFR2, VEGFR3; inhibition of these receptors blocks angiogenesis. Being studied in combination with paclitaxel. Administered orally. AVEO Pharmaceuticals, Inc., Cambridge, MA Phase I/II trial complete	Paclitaxel alone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tivozanib (AV-951) for treatment of metastatic nonsmall cell lung cancer	Patients in whom recurrent advanced or metastatic NSCLC has been diagnosed that is refractory to standard chemotherapy	Tivozanib is a quinoline-urea-derived vascular endothelial growth factor receptor (VEGFR) inhibitor that inhibits several tyrosine kinases. It is being investigated for the treatment of NSCLC. The theoretical basis for VEGFR inhibitors in the treatment of solid tumors lies in the fact that VEGF is a key mediator of normal and tumor-induced angiogenesis, or the proliferation and survival of endothelial cells, and vascular permeability. When VEGFRs are activated by vascular endothelial growth factor (VEGF), endothelial cells migrate and proliferate, resulting in the formation of new tumor vasculature. If the VEGF pathway is disrupted, a tumor can no longer trigger the development of its own blood supply, thereby impeding the tumor's growth and dissemination. Given in oral formulation, dosed in cycles of once daily for several weeks, followed by 1 week off treatment. AVEO Pharmaceuticals, Inc., Cambridge, MA Phase I/II trial complete	Palliative care	Increased overall survival Increased progression-free survival Improved quality of life
Tivozanib (AV-951) for treatment of advanced renal cell carcinoma	Patients in whom advanced primary RCC has been diagnosed	Tivozanib (AV-951) is a small-molecule inhibitor of VEGFR1, VEGFR2, VEGFR3 (see above information); inhibition of these receptors blocks angiogenesis to cut off blood supply to tumors, aiding in their destruction. Biologic is given after primary surgical resection of tumor and after disease recurrence; taken orally. AVEO Pharmaceuticals, Inc., Cambridge, MA Phase III trial ongoing	Sorafenib Sunitinib Avastin Temsirolimus IL-2 Cryoablation	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
TroVax for treatment of hormone-refractory prostate cancer	Patients in whom metastatic hormone-refractory prostate cancer has been diagnosed	Novel cancer therapies for hormone-refractory prostate cancer that may increase treatment efficacy and survival are needed. TroVax® is a modified vaccinia Ankara (MVA) virus vector encoding the oncofetal antigen 5T4 intended to induce cellular immune responses to tumors; oncofetal antigen 5T4 is expressed in many solid tumors. In current trial, TroVax is being administered in combination with the chemotherapy drug docetaxel. Oxford BioMedica, Oxford, UK Phase II trial ongoing (was halted in development for RCC in 2009)	Docetaxel alone	Increased overall survival Increased progression-free survival Improved quality of life
TRU-016 for treatment of chronic lymphocytic leukemia	Patients in whom CLL has been diagnosed	Many patients with CLL do not achieve an initial treatment response and most patients eventually relapse, demonstrating the need for new and effective treatments. TRU-016 is a CD37-directed small modular immunopharmaceutical (SMIP) protein intended to treat CLL; TRU-016 uses a different mechanism of action from currently available CD20-directed therapies and may be used alone or in combination with chemotherapy (bendamustine) and/or other CD20-directed therapeutics. Emergent BioSolutions, Inc., Rockville, MD Phase I/II trials ongoing	Bone marrow transplantation Chemotherapy (including bendamustine) Monoclonal antibodies (alemtuzumab [anti-CD52]), rituximab and ofatumumab [anti-CD20]) Radiation therapy Splenectomy	Increased overall survival Increased progression-free survival Improved quality of life
Tumor treating fields therapy (NovoTTF-100L device) for treatment of brain cancer	Patients in whom recurrent glioblastoma has been diagnosed	Therapy is delivered with the NovoTTF-100L device as adjunct to chemotherapy; intended to deliver local alternating electrical fields to a tumor site; electrical fields are proposed to interfere with charged molecules that are involved the cell's mitotic processes. NovoCure Ltd., Haifa, Israel FDA approved for recurrent glioblastoma in Apr 2011; phase III trial in newly diagnosed glioblastoma ongoing	Cyberknife radiation therapy Stereotactic beam radiation therapy Proton beam radiation therapy Brain brachytherapy Combination therapies	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tumor treating fields therapy (NovoTTF-100L device) for treatment of nonsmall cell lung cancer	Patients in whom stage IIIb to IV NSCLC has been diagnosed	NovoTTF-100L device delivers tumor treating fields (local alternating electrical fields) to tumor site. Electrical fields are proposed to interfere with charged molecules that are involved the cell's mitotic processes. Delivered in conjunction with chemotherapy. NovoCure Ltd., Haifa, Israel Phase I/II trial complete	Surgical resection/chemotherapy Radiation therapy/chemotherapy Chemotherapy alone	Increased overall survival Increased progression-free survival Improved quality of life
Urine test (PSP94) for prostate cancer screening	Men undergoing routine prostate cancer screening (generally men older than 50 years of age)	PSP94 (microseminoprotein-beta, inhibin-like peptide, prostate secretory protein) is expressed in normal prostate tissue; however, studies have shown that its levels are reduced in cancerous prostate cells; test kit is an enzyme-linked immunosorbent assay-based urine assay to detect reduced levels of PSP94 Miraculins, Inc., Winnipeg, Manitoba, Canada Kit was made available as a research-use-only reagent in Aug 2010; company plans to develop a commercially available diagnostic test kit	Digital rectal examination Prostate-specific antigen screening Other blood marker tests in development	Improved sensitivity and specificity for screening Improved predictive values Avoided unnecessary biopsies Better treatment planning Improved quality of life
Urocidin for treatment of nonmuscle-invasive bladder cancer	Patients in whom nonmuscle-invasive bladder cancer (cancer on the surface of the bladder) has been diagnosed	Urocidin™ is a mycobacterial cell wall/DNA preparation proposed to create a localized immune response (mechanism of action unclear). Administered by transurethral catheter directly into the bladder. Bioniche Life Sciences, Inc., Belleville, Ontario Endo Pharmaceuticals (licensee in U.S.), Chadds Ford, PA Phase II/III trial ongoing	Bacillus Calmette-Guerin treatment Cystectomy	Increased overall survival Increased progression-free survival Improved quality of life Avoidance of cystectomy

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vandetanib (Caprelsa) for treatment of metastatic medullary thyroid cancer	Patients in whom metastatic medullary thyroid cancer has been diagnosed	No treatments are currently approved for metastatic medullary thyroid cancer, which has a 28% rate of survival for 5 years. Vandetanib (Caprelsa®) is a tyrosine kinase inhibitor with activity against various growth factors: VEGFR, EGFR, and recombined in transfection (RET); approximately 25% of medullary thyroid cancer is caused by a mutation in the RET proto-oncogene. Administered orally, once daily. AstraZeneca Pharmaceuticals, LP, Wilmington, DE FDA approved Apr 2011	Chemotherapy (off label) Radiotherapy Surgery	Increased overall survival Increased progression-free survival Improved quality of life
VGX-3100 for treatment of high-grade cervical dysplasia	Patients in whom HPV 16 or 18-attributed high-grade cervical dysplasia (CIN 2 or 3) has been diagnosed	Current HPV preventive vaccines do not treat women already infected with HPV 16/18, the main cause of cervical cancer, or who have confirmed CIN; surgical excision is the usual treatment and noninvasive alternatives are needed. VGX-3100 is a therapeutic DNA vaccine encoding regions of HPV 16 and 18, E6 and E7 proteins, which are believed to be important in oncogenesis; intended to elicit cellular immune responses against the two most common HPV types associated with cervical cancer to lead to regression of high-grade precancerous lesions. VGX-3100 is administered as a 1 mL intramuscular injection followed by electroporation at day 0, week 4, and week 12. Inovio Pharmaceuticals, Inc., Blue Bell, PA Phase II ongoing	Colposcopy/excision Imiquimod	Increased CIN regression rate Increased HPV clearance rate Reduced incidence of cervical cancer

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vismodegib (GDC-0449) for treatment of basal cell carcinoma	Patients in whom advanced/metastatic basal cell carcinoma has been diagnosed	No systemic treatment is currently approved for treatment of basal cell carcinoma and patients with advanced/metastatic disease that is not amenable to surgical resection have few treatment options. Activation of the hedgehog signaling pathway, which is normally silenced following early development, has been implicated in the development and survival of a large percentage of basal cell carcinomas. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trials ongoing; NDA submitted to FDA and accepted for priority review with a PDUFA date of Mar 8, 2012	No currently approved systemic treatment option available	Increased overall survival Increased progression-free survival Improved quality of life
Vismodegib (GDC-0449) for treatment of gastric or gastroesophageal junction cancer	Patients in whom advanced gastric cancer or gastroesophageal junction cancer that is not amenable to surgical resection has been diagnosed	Hedgehog signaling is involved in normal gut epithelial homeostasis; however, aberrant hedgehog signaling may lead to carcinogenesis of the gut epithelium. No hedgehog pathway inhibitors are currently available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. In the current gastric cancer trial, vismodegib is being administered in combination with the FOLFOX cytotoxic chemotherapy regimen. National Cancer Institute/New York Cancer Consortium Phase II trial ongoing	FOLFOX chemotherapy alone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vismodegib (GDC-0449) for treatment of multiple myeloma	Patients in whom multiple myeloma has been diagnosed and who have previously been treated by autologous stem cell transplant	The hedgehog signaling pathway has been implicated in the maintenance of a population of cells ("cancer stem cells") that drive the proliferation of lymphocytes that underlies the multiple myeloma phenotype. No hedgehog pathway inhibitors are currently available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. National Cancer Institute/Sidney Kimmel Comprehensive Cancer Center Phase Ib trial ongoing	Lenalidomide/thalidomide Bortezomib	Increased overall survival Increased progression-free survival Improved quality of life
Vismodegib (GDC-0449) for treatment of chondrosarcoma	Patients in whom metastatic or unresectable locally advanced chondrosarcoma has been diagnosed	Aberrant hedgehog pathway activation has been implicated in the development of chondrosarcomas, a cancer with few treatment options. No hedgehog pathway inhibitors are currently available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. National Cancer Institute/Institute Bergonié Phase II trial ongoing	Doxorubicin	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vismodegib (GDC-0449) for treatment of pancreatic cancer	Patients in whom recurrent or metastatic pancreatic cancer has been diagnosed or in whom pancreatic ductal adenocarcinoma has been diagnosed and who are undergoing surgical resection	Aberrant hedgehog signaling has been implicated in the development of pancreatic cancer. Hedgehog signaling may promote tumor growth in a paracrine manner through signaling to the tumor stroma or may play a role in the maintenance of pancreatic "cancer stem cells". Currently no hedgehog pathway inhibitor is available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. National Cancer Institute/University of Chicago Sidney Kimmel Comprehensive Cancer Center Cambridge University Hospitals/NHS Foundation Trust National Cancer Institute/University of Michigan Cancer Center Phase II trials ongoing	Gemcitabine Gemcitabine plus erlotinib Gemcitabine plus cisplatin or oxaliplatin Gemcitabine plus a fluoropyrimidine	Increased overall survival Increased progression-free survival Improved quality of life
Vismodegib (GDC-0449) for treatment of locally advanced prostate cancer	Patients with locally advanced prostate cancer who are undergoing neo-adjuvant hormone therapy prior to radical prostatectomy	Aberrant hedgehog signaling has been implicated in the development of some prostate adenocarcinoma; however, no hedgehog pathway inhibitors are currently available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. National Cancer Institute Phase II trial ongoing	Neo-adjuvant hormone therapy alone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vismodegib (GDC-0449) for treatment of medulloblastoma	Patients in whom recurrent or treatment refractory medulloblastoma has been diagnosed	Activation of the hedgehog signaling pathway, which is normally silenced following early development, has been implicated in the development and survival of up to a third of medulloblastomas; however, no hedgehog pathway inhibitors are currently available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Curis Pharmaceuticals, Lexington, MA National Cancer Institute Phase II trials ongoing	Various chemotherapy regimens (high-dose cyclophosphamide plus or minus etoposide; etoposide; temozolomide plus or minus 13-cis retinoic acid) High-dose chemotherapy plus autologous stem cell reinfusion	Increased overall survival Increased progression-free survival Improved quality of life
Vismodegib (GDC-0449) for treatment of recurrent glioblastoma multiforme	Patients in whom recurrent glioblastoma multiforme has been diagnosed and who have undergone surgical resection of the recurrent tumor	Aberrant hedgehog pathway activation has been implicated in maintaining the features of glioblastoma multiforme that resemble “cancer stem cells”, which are largely resistant to conventional chemotherapy treatments. No hedgehog pathway inhibitors are currently available. Vismodegib (GDC-0449) is an inhibitor of the protein Smoothened, which is essential for transducing hedgehog signaling. If trials are successful, this could be the first hedgehog pathway inhibitor to be approved. National Cancer Institute Phase II trial ongoing	Temozolomide Radiation therapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vosaroxin for treatment of platinum-resistant ovarian cancer	Patients in whom platinum-resistant ovarian cancer has been diagnosed	Ovarian cancer usually has a poor prognosis because of the lack of effective early detection/screening tools and clear disease symptoms, resulting frequently in diagnosis at late stages when currently available chemotherapy regimens are largely ineffective. Vosaroxin is a first-in-class, anticancer quinolone derivative; during normal topoisomerase activity, the enzyme cleaves and then religates double-strand breaks to maintain DNA topology during replication; vosaroxin is purported to intercalate into DNA and inhibit topoisomerase II activity that results in replication-dependent, site-selective double-strand breaks in DNA leading to G2 arrest and apoptosis; compared with other topoisomerase II inhibitors, vosaroxin is not a P-glycoprotein substrate, evading the most common mechanism for multidrug resistance. Administered as an intravenous infusion. Sunesis Pharmaceuticals, Inc., South San Francisco, CA Phase II trial complete	Radiation Chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Vosaroxin for treatment of relapsed or refractory acute myeloid leukemia	Patients in whom acute myeloid (AML) cancer has been diagnosed	For patients with relapsed AML, the only potentially curative treatment is a hematopoietic stem cell transplant; however, in some patients, disease relapses after transplantation, or they are not candidates or cannot find a suitable donor. Vosaroxin is a first-in-class, anticancer quinolone derivative; during normal topoisomerase activity, the enzyme cleaves and then religates double-strand breaks to maintain DNA topology during replication; vosaroxin is purported to intercalate into DNA and inhibit topoisomerase II activity that results in replication-dependent, site-selective double-strand breaks in DNA leading to G2 arrest and apoptosis; compared with other topoisomerase II inhibitors, vosaroxin is not a P-glycoprotein substrate, evading the most common mechanism for multidrug resistance; it may be used in combination with cytarabine. Administered as an intravenous infusion, 90 mg/m^2 for days 1 and 4 for induction and 70 mg/m^2 for all other cycles. Sunesis Pharmaceuticals, Inc., South San Francisco, CA Phase III trial ongoing	Clofarabine (off label) Cytarabine Hematopoietic stem cell transplant Gemtuzumab ozogamicin	

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Zanolimumab for treatment of cutaneous T-cell lymphomas	Patients in whom treatment-refractory cutaneous T-cell lymphoma (mycosis fungoides or Sezary syndrome) has been diagnosed	Patients whose disease has progressed following second-line treatment have poor prognosis and few treatment options. The malignant T-cells of the majority of cutaneous T-cell lymphomas express CD4; Zanolimumab is a CD4 specific monoclonal and acts by downregulating T-cell activation/proliferation to deplete these malignant T cells from the patient. In trials, eligible patients must have disease that progressed following treatment with bexarotene and one additional systemic therapy. TenX BioPharma, Philadelphia, PA Phase III trial ongoing	Denileukin diftitox Photopheresis Vorinostat	Increased overall survival Increased progression-free survival Improved quality of life

Table 3. AHRQ Priority Condition: 03 Cardiovascular Disease: 95 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Adenosine diphosphate receptor antagonist (ticagrelor, Brilinta) for treatment of acute coronary syndrome	Adults in whom acute coronary syndrome has been diagnosed	The efficacy of clopidogrel varies because it is a pro-drug. It must be metabolized to become active, which can lead to variable platelet inhibition, and that in turn can increase a patient's risk of bleeding, stent thrombosis, and ischemia. Ticagrelor (Brilinta™) is an orally administered blood thinner (to reduce clumping of platelets and clotting, prevent heart attacks, prevent strokes). First reversibly binding oral adenosine diphosphate (ADP) receptor antagonist, and similar to the action of the thienopyridines prasugrel, clopidogrel, and ticlopidine, ticagrelor blocks ADP receptors of subtype P2Y12. It differs from other antiplatelet drugs because it has a different binding site from ADP; it is an allosteric antagonist, and the blockage is reversible. Also, the drug is not activated by the liver, so, researchers believe, it might work better for patients with genetic variants of the enzyme cytochrome P-450 (CYP)2C19. AstraZeneca, London, UK FDA approved for acute coronary syndrome Jul 2011; approval included labeled warning that states not to take it with a daily aspirin dose of more than 100 mg	Clopidogrel Prasugrel Ticlopidine	Reduced incidence of heart attacks and strokes Increased overall survival Reduced side effects compared with other antiplatelet drugs
Allogeneic mesenchymal stem cell therapy (Revascor) for treatment of heart failure	Patients in whom heart failure (HF) has been diagnosed	Current therapy for HF is not disease-modifying and addresses only symptoms; stem cell therapy is proposed as a potential treatment to regenerate the heart muscle, and thereby its function, in several ways. Revascor™ is an allogeneic adult mesenchymal stem cell product intended to be an off-the-shelf product that can be administered as a single injection delivered through a minimally invasive cardiac catheterization procedure; intended effects include rebuilding blood vessels and heart muscle. Cephalon, Inc., Frazer, PA Mesoblast Ltd., Melbourne, Australia Phase II trials ongoing	Pharmaceutical therapy Implantable medical devices (cardiac rhythm therapy devices, implantable cardioverter defibrillators, left ventricular assist devices [LVADs]) Surgery	Slowed, halted, or reversed HF progression Improved left-ventricular ejection fraction Increased survival Reduced hospital admissions for HF treatment Improved activities of daily living Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Allogeneic precultured adult bone-marrow-derived mesenchymal stem cells (Prochymal) for cardiac repair after myocardial infarction	Patients in whom recent myocardial infarction (MI) has been diagnosed	No regenerative therapies are currently approved for MI. Prochymal® consists of allogeneic bone-marrow-derived human mesenchymal stem cells (hMSCs) intended to preserve and improve cardiac function following an acute MI; manufacturer has developed a specific "expansion" process for these cells, which are intended to be used "off the shelf," and delivered intravenously within 10 days of a patient's first MI. Osiris Therapeutics, Inc., Baltimore, MD Phase II trial ongoing	Pharmaceutical therapy (e.g., beta blockers) Biodegradable scaffold (BL-1040, in development)	Increased ejection fraction Increased left ventricular volume Improved cardiac function Decreased cardiovascular events Improved quality of life
Anacetrapib for lipid management in coronary artery disease	Patients in whom coronary artery disease (CAD) has been diagnosed or who are at risk of developing the disease	Cholesterol ester transfer protein inhibitor intended to raise high-density lipoprotein (HDL) by 100% and reduce low-density lipoprotein (LDL), thereby improving lipid profile; precursor was torcetrapib; stopped development because of high rate of cardiovascular adverse events; anacetrapib has been reported to not raise blood pressure of subjects in clinical trials thus far. Merck & Co., Inc., Whitehouse Station, NJ Phase III trials ongoing; company anticipates filing new drug application (NDA) with FDA in 2015	Statins (anacetrapib can be used alone or in conjunction with statins) Omega-3 fatty acids Other drug therapies Lifestyle changes	Reduced risk of heart attack Improved cardiovascular outcomes
Angiotensin II-targeted vaccine (CYT006-AngQb) for treatment of hypertension	Patients in whom hypertension has been diagnosed	Vaccine (CYT006-AngQb) intended to produce sustained decrease in blood pressure. Cytos Biotechnology, AG, Schlieren, Switzerland Phase II trials completed	Oral antihypertensive medication	Normal level blood pressure

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Apo-B synthesis inhibitor (mipomersen) for treatment of familial hypercholesterol-emia	Patients in whom heterozygous or homozygous familial hypercholesterol-emia (FH) has been diagnosed	Outcomes with current medication for FH are suboptimal; mipomersen represents a new mechanism-of-action/drug class for this disease state. Mipomersen is a first-in-class apo-B synthesis inhibitor; intended to decrease production of apo-B (structural protein for atherogenic lipids, such as low-density lipoprotein C [LDL-C]), and reduce LDL-C (bad cholesterol) by preventing its formation. Drug is delivered via weekly self-administered injection. Genzyme Corp., Cambridge, MA, a subsidiary of Sanofi-Aventis Group ISIS Pharmaceuticals, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ Phase III trials completed; NDA filing with FDA expected by end of 2011for homozygous FH; FDA requested additional 12-month data before NDA filing for heterozygous FH	Bile acid-sequestering resins Extracorporeal apheresis Ezetimibe Fibrates (such as gemfibrozil) Nicotinic acid Statins	Reduced LDL levels Improved cardiovascular outcomes Improved quality of life Improved long-term health outcomes
APOCIIIRx for treatment of hypertriglyceride-mia	Patients in whom hypertriglyceride mia has been diagnosed	APOCIIIRx is an antisense drug that inhibits production (liver) of apolipoprotein C-III (apoC-III); lower production of apoC-III is linked to lower triglycerides and LDL-C levels, increased HDL levels and lower risk of cardiovascular disease. The new drug is intended to avoid side effects of current triglyceride-lowering medications. ISIS Pharmaceuticals, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ Phase I trial ongoing	Diet and exercise Fibric acid derivatives Niacin Omega-3 (N-3) fatty acids Gemfibrozil (Lopid) Fenofibric acid (Trilipix) with a statin (for mixed dyslipidemia) Lovaza for triglycerides (≥500 mg/dL)	Reduction in triglycerides Reduced cardiovascular risk Improved metabolic syndrome

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Autologous bone marrow-derived mesenchymal stem cells for myocardial repair after myocardial infarction	Patients who need cardiac repair after MI	No regenerative therapies are available for patients experiencing cardiac damage secondary to MI; 20% of MIs are severe enough to cause ventricular remodeling, which leads to HF. Autologous mesenchymal (or mononuclear, which includes mesenchymal and hematopoietic cells) stem cells are harvested from patient's own bone marrow, enriched, then injected/infused into patients (e.g., transendocardial or arterial delivery) at some point after their MI. Under development by several entities including University of Miami, Miami, FL, and Amorcyte, Allendale, NJ Phase I/II trials ongoing	Pharmaceutical management (e.g., beta blockers) Biodegradable scaffold (BL-1040, in development)	Myocardial tissue regeneration Improved cardiac function Reduced cardiovascular events Improved quality of life
Autologous heart stem cell transplantation for postmyocardial infarction revascularization	Patients who have experienced a heart attack within the past month	A biopsy performed under local anesthesia is done to harvest cardiac cells from the patient. The harvested heart stem cells are cultured and reintroduced to the patient's coronary arteries. Cedars-Sinai Heart Institute, Los Angeles, CA Phase I trial ongoing	Coronary artery bypass surgery Percutaneous coronary interventions (angioplasty, stenting) Medical management Gene therapy Stem cell implantation with transmyocardial laser revascularization	Reduced mortality and morbidity (MACE events) Improved quality of life Improved activities of daily living Reduced need for coronary reintervention
Autologous stem cell therapy (C-Cure) for heart failure	Patients in whom severe HF has been diagnosed	Stem cell product (C-Cure®) is derived from the patient's own bone marrow and (in vitro, before transplantation) cultured to become cardiac lineage cells intended to improve heart function. Cardio3 BioSciences, Mont-Saint-Guibert, Belgium Phase II completed; phase III trial planned for second half of 2011	Drug therapy Cardiac rhythm therapy devices Implanted cardioverter defibrillator Surgery	Increased left ventricular ejection fraction and other heart function outcomes Improved activities of daily living Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Biased angiotensin II type 1 receptor ligand (TRV120027) for treatment of acute heart failure	Patients in whom acute HF has been diagnosed	Current drugs for acute HF are associated with life-threatening safety risks. TRV120027 is a beta-arrestin biased angiotensin II type 1 receptor (AT1R) ligand with a new mechanism of action; it stimulates beta-arrestin recruitment and activates several kinase pathways, potentially eliciting a different pharmacologic effect from unbiased agonists; intended to have minimal effects on heart rate and reduced mean arterial pressure, while increasing the slope of end-systolic pressure-volume relationship and preserving cardiac stroke volume; first in biased ligand class to be tested in humans. Administered intravenously. Trevena, Inc., King of Prussia, PA Phase I/II trial ongoing	Diuretics Vasodilators Inotropic agents	Improved symptoms Improved hemodynamics Improved clinical status Improved long-term outcomes Increased survival Improved quality of life
Bioabsorbable polymer-coated stent (Synergy) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed and who are eligible for stenting	Stent (Synergy™) coated with bioabsorbable polymer and implanted in the occluded coronary vessel; coating resorbs into the body, leaving behind a bare-metal stent intended to maintain patency of coronary artery. Boston Scientific Corp., Boston, MA Phase I trial ongoing	Drug-eluting stents (DESs) Drug-eluting balloons Coronary artery bypass graft surgery Cutting balloons Cryoplasty	Reduced restenosis rates Angina relief Faster vessel healing after implantation than other stents Reduced risk of (late stent) thrombosis Earlier discontinuation of antiplatelet therapy
Biodegradable scaffold (IK-5001) for support postmyocardial infarction in patients at high risk for heart failure	Patients at risk of HF or ventricular remodeling after acute MI	IK-5001 (formerly BL-1040) is a partially cross-linked, alginate-based liquid polymer designed to provide physical support to the heart; it acts like a three-dimensional scaffold intended to prevent the left ventricular wall from thinning to prevent additional HF. Reabsorbed and excreted through kidney after 6 weeks. Injected at site of occlusion or distal to site after revascularization of occluded vessel. BioLineRx, Ltd., Jerusalem, Israel, licensed to Ikaria, Hampton, NJ Phase I/II trial completed; phase II expected to begin in 2011	Drug therapy to prevent HF Emerging stem cell scaffolding therapies	Improved left ejection fraction Slowed progression of HF Improved activities of daily living Improved survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bioengineered sirolimus-eluting stent (Combo) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed and who are eligible for stenting	The Combo™ stent features antibodies immobilized on the stent that capture circulating endothelial progenitor cells (EPCs), which in turn quickly form an endothelial layer over and between the stent struts. This is intended to protect against thrombus and minimize restenosis. The company terms it "endothelial progenitor cell (EPC) capture technology" and asserts that it promotes accelerated natural healing of vessel walls after implantation and could reduce need for anticoagulation therapy. OrbusNeich, Wanchai, Hong Kong Phase II trial ongoing	Other DESs	Decreased neointimal hyperplasia Improved endothelial coverage Accelerated healing Reduced restenosis Reduced thrombosis Improved cardiovascular outcomes
Bioresorbable sirolimus-eluting stent (ReZolve) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed and who are eligible for stenting	Sirolimus-eluting stent (ReZolve™) is made of a bioresorbable polymer (an iodinated, tyrosine-derived polycarbonate) that gradually degrades over time and is resorbed by the body. Reva Medical, Inc., San Diego, CA Pilot trial planned for third quarter 2011	Other DESs Combination bioabsorbable polymer/DESs Bare-metal stents Drug-eluting balloons	Reduced MI Reduced reintervention for target lesion and target vessel Reduced angina pain Increased survival
Bioresorbable stent (Absorb) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed and who are eligible for stenting	Bioresorbable DES (Absorb™) made of polylactide polymer that elutes everolimus; designed to dissolve over the course of 2 years and intended to reduce risk of late thrombosis and reduce need for dual-antiplatelet therapy compared with currently available DESs that are not bioresorbed. Abbott Laboratories, Abbott Park, IL Phase I/II trial ongoing	Bare metal stents Other bioresorbable stents in development (e.g., ReZolve) Coronary artery bypass graft surgery Conventional DESs	Reduced risk of late-stent thrombosis (LST) Improved cardiovascular outcomes (angina, repeat intervention, heart attack) Reduced need for dual antiplatelet therapy (DAPT)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cardiac contractility modulation (Optimizer system) for treatment of heart failure	Patients in whom HF has been diagnosed	Optimizer™ system delivers nonexcitatory electrical signals during the absolute refractory period (between beats) to produce more forceful contraction during heartbeat; intended as adjunct to optimal medical therapy. Impulse Dynamics, N.V., Willemstad, Netherlands Antilles Confirmatory trial ongoing	Digitalis Implanted pacemakers and/or defibrillators Optimal medical management	Improved quality of life Symptom relief Improved 6-minute walk test Fewer hospital admissions Delayed progression of heart failure Delay need for ventricular assist devices
Cardiac pacing system (Revo) for patients who may require future magnetic resonance imaging	Patients with pacemakers who need to undergo magnetic resonance imaging (MRI) scanning	Revo MRI™ SureScan® pacing system is intended for patients who may need to undergo MRI in the future. Pacemaker implants had previously been a contraindication for MRI because of potential risks of malfunction during MRI. Revo includes hardware modifications that are designed to reduce/eliminate pacemaker hazards produced by MRI environment. Pacemaker includes a feature that sets device into appropriate mode for MRI environment. Medtronic, Inc., Minneapolis, MN FDA approved Feb 8, 2011	Currently, no pacemakers exist that can be used in MRI environment Modified MRI environments	Ability for physicians to use MRI for patients who require pacemaker therapy
CardioWest total artificial heart with portable Freedom driver system as bridge to heart transplantation	Patients in whom nonreversible biventricular failure has been diagnosed who are candidates for heart transplantation	Temporary Total Artificial Heart (TAH) functions in place of ventricles/valves by pumping blood to both the pulmonary and systemic circulation. This TAH is distinguished from prior TAHs by its portable driver (Freedom® driver) that is intended to allow patients to recover and remain at home. SynCardia Systems, Inc., Tucson, AZ Total Artificial Heart was FDA approved in 2004; clinical trial investigating use of Freedom driver system ongoing under FDA IDE trial status	Ventricular assist devices outside of the hospital	Restored mobility Possible recovery at home (reduction in hospitalization costs) Extend survival for patients awaiting heart transplantation

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Catheter-based renal denervation (Symplicity System) for treatment-resistant hypertension	Patients in whom uncontrolled hypertension has been diagnosed	The Symplicity® catheter system is intended to accomplish renal denervation through a minimally invasive procedure. The device is used to affect the output of the sympathetic nerves outside the renal artery walls. The system consists of a proprietary generator and flexible catheter that is inserted through the femoral artery and threaded into the renal artery near each kidney. Once in place, the catheter tip delivers low-power radio-frequency (RF) energy to deactivate surrounding sympathetic nerves. Renal denervation does not involve a permanent implant. Renal sympathetic nerves are believed to often cause chronic hypertension. Medtronic, Inc., Minneapolis, MN Phase III trial SYMPLICITY HTN-3 ongoing	Renal artery stents Alpha agonists Alpha blockers Angiotensin-converting enzyme (ACE) inhibitors Angiotensin receptor blockers (ARBs) Beta blockers Calcium channel blockers Combination medications Diuretics Renin inhibitors	Controlled hypertension without medications Controlled blood pressure to reduce incidence of blindness, heart attacks, kidney failure, and stroke
Catheter-delivered biodegradable adhesive (Sapheon Closure System) for treatment of venous reflux	Patients in whom varicose veins have been diagnosed who are eligible for treatment	While many options exist for treatment of varicose veins, treatments are sought that offer shorter intervention time than other methods, and offer faster recovery phase than surgery, thermal, or chemical treatments. Sapheon Closure System™ consists of a catheter to deliver biodegradable adhesive intended to treat varicose veins by closing off and destroying the target vein or veins. Sapheon, Inc., Santa Rosa, CA First-in-human trial completed in U.S.; CE marked Sept 2011	Laser Radiofrequency ablation Surgery (vein stripping) Support stockings Sclerotherapy	Improved healing of wounds Improved blood flow Prevention of blood clots Reduced pain Restored functional capacity (walking)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CER-001 for treatment of acute coronary syndrome	Patients in whom acute coronary syndrome has been diagnosed	Treatment for HDL levels alone (as a single target) is not available. CER-001 is an HDL mimetic that consists of recombinant human apolipoprotein A (ApoA-I, the major structural protein of HDL) and phospholipids; HDL is responsible for reverse cholesterol transport, and the drug is intended to mobilize cholesterol, thus reducing atherosclerotic plaque burden. Administered as a weekly infusion for 6 weeks in clinical trials. Cerenis Therapeutics, Inc., Ann Arbor, MI Phase II trial ongoing	Anacetrapib (in development) Niacin Rosuvastatin RVX-208 (in development)	Improved HDL levels Improved heart function Fewer cardiac events
Cholesteryl ester transfer protein modulator (dalcetrapib) for prevention and treatment of coronary artery disease	Patients in whom dyslipidemia or CAD has been diagnosed	Despite availability of effective pharmaceutical interventions, cardiovascular disease remains the leading cause of mortality worldwide. Dalcetrapib is a *cholesteryl ester transfer protein* (CETP, plasma protein responsible for lipid transport) modulator intended to raise functional HDL by modulating CETP activity through a mechanism that differs from other CETP inhibitors in development F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trial ongoing	Anacetrapib (in development) Lifestyle changes Omega-3 fatty acids Statins	Improved lipid parameters Improved cardiovascular outcomes
Contrast agent removal system (Cincor) for prevention of contrast-induced nephropathy	Patients undergoing CT angiography, especially those at risk of contrast-induced nephropathy	Cincor™ contrast removal system consists of an 11-French diameter coronary sinus aspiration catheter and a coronary sinus support device placed via a 14-French diameter right internal jugular vein sheath to aspirate contrast media from coronary sinus; purported to be the only direct contrast removal system; other approaches to contrast removal differ in that they use fluid to try to flush the contrast medium from patients' system; intended especially for patients with pre-existing chronic renal impairment, contrast load, diabetes, and advancing age. Osprey Medical, St. Paul, MN Phase III trial registered, not yet recruiting	None known	Prevention of acute renal injury

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Controlled-release diazoxide choline for treatment of hyper-triglyceridemia	Patients in whom dyslipidemia has been diagnosed; patients on a statin drug	ATP-dependent potassium channel agonist Essentialis, Carlsbad, CA Phase III trial registered; not yet recruiting	Lovaza® Fenofibrate	Reduced risk of CAD
Dabigatran (Pradaxa) for prevention of thrombosis associated with atrial fibrillation	Patients in whom atrial fibrillation (AFib) has been diagnosed	For this population, warfarin (Coumadin, a vitamin K antagonist) is the anticoagulant routinely used long-term to prevent blood clots that cause stroke or pulmonary embolism; warfarin use is associated with high risk of bleeding and appropriate dosing is a challenge; its use requires daily/weekly monitoring of clotting parameters and dose adjustment as needed. Dabigatran (Pradaxa®) represents a new mechanism of action/new drug class for this disease state; recently approved by FDA for prevention of stroke in patients with AFib as an oral direct thrombin inhibitor intended to reduce risk of stroke by reducing blood clot formation; according to prescribing information, treatment does not require blood monitoring or related dose adjustments and has no recommended dietary restrictions. Boehringer Ingelheim, Ingelheim, Germany FDA approved Oct 2010	Aspirin Vitamin K antagonists (e.g., warfarin) Factor Xa inhibitors in development (e.g., rivaroxaban, apixaban)	Reduced blood clotting Reduced need for monitoring clotting parameters Reduced stroke incidence Improved long-term outcomes
Double left ventricular-assist device implantation for treatment of heart failure	Patients in whom advanced HF has been diagnosed	Two left ventricular-assist devices are implanted on different sides of the heart instead of a standard biventricular assist device pump, which sits outside the body and has a high complication and mortality rate. HeartWare, Inc., Framingham, MA Two ventricular assist devices were implanted in one patient under "emergency use" rule by FDA	Conventional biventricular assist device	Improved quality of life Improved cardiac function Reduced complication/mortality rate

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Drug-eluting balloon (Moxy) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed who are eligible for angioplasty	Drug-coated balloon (Moxy™) delivers drug dose (paclitaxel, antiproliferative) over several minutes during a percutaneous transluminal angioplasty procedure; drug remains resident in deep layers of artery wall and is intended to inhibit restenosis and restore inner arterial surface. Lutonix, Inc., Maple Grove, MN Phase I/II trials ongoing	Standard balloon angioplasty DESs Bioengineered stents Bioabsorbable stents	Reduced restenosis rates Reduced repeat intervention in treated coronary vessel Reduced major coronary events
Drug-eluting balloon (Moxy) for treatment of peripheral artery disease	Patients in whom peripheral in-stent restenosis has been diagnosed	Drug-coated balloon (Moxy™) delivers paclitaxel for several minutes during a percutaneous transluminal angioplasty procedure; drug remains resident in deep layers of artery wall to try to inhibit restenosis; allows for restoration of the inner arterial surface. Lutonix, Inc., Maple Grove, MN Phase II trials ongoing	Standard balloon angioplasty DESs	Reduced restenosis Reduced pain Improved quality of life Avoid need for stent implantation
Drug-eluting absorbable metal scaffold (Dreams) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed	Permanent DESs are associated with potential complications, such as LST. Dreams is a stent made of biodegradable magnesium alloy combined with a paclitaxel; it is intended to open occluded vessels and reduce neointimal proliferation, while possibly avoiding LST, because of the stent's ability to degrade over time. Biotronik SE & Co., KG, Berlin, Germany First-in-human trial ongoing	Bare metal stents Other bioresorbable stents in development (e.g., ReZolve) Coronary artery bypass graft surgery Conventional DESs	Reduced incidence of LST Reduced cardiovascular outcomes (angina, repeat intervention, heart attack) Reduced need for DAPT

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Drug-eluting balloon (Pantera Lux) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed who are candidates for angioplasty	Repeated percutaneous coronary intervention (PCI) with DESs of small vessels is associated with restenosis and adverse outcomes, such as inflammation and injury, which can lead to LST. Pantera® Lux angioplasty balloon is intended to elute the antiproliferative drug paclitaxel during a percutaneous transluminal angioplasty procedure; drug is intended to remain resident in deep layers of the artery wall, thereby inhibiting restenosis; allows for restoration of the inner arterial surface. Biotronik SE & Co., KG, Berlin, Germany Trial ongoing (no phase listed)	Moxy drug-eluting balloon DESs Non-drug-eluting balloons	Stent complications (breakage, thrombosis, inflammation, restenosis) Reduced restenosis of treated vessel Reduction in major adverse cardiac events
Drug-eluting balloon (Pantera Lux) for treatment of peripheral artery disease	Patients in whom peripheral artery disease (PAD) has been diagnosed who are candidates for angioplasty	Stents (drug eluting or bare metal) have not proven viable options for treating long-diffuse disease, small vessels, the infrapopliteals, or in lesions below the knee, because of issues with stent fractures, thrombosis, and restenosis. Pantera® Lux angioplasty balloon is intended to elute the antiproliferative drug paclitaxel during a percutaneous transluminal angioplasty procedure; drug is intended to remain resident in deep layers of the artery, wall thereby inhibiting restenosis; allows for restoration of the inner arterial surface. Biotronik SE & Co., KG, Berlin, Germany Trial ongoing (no phase listed)	Moxy drug-eluting balloon DESs Non-drug-eluting balloons	Stent complications (breakage, thrombosis, inflammation, restenosis) Maintained vessel patency Improved peripheral vascular outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Dual natriuretic peptide receptor agonist (Cenderitide) for treatment of postacute decompensated heart failure	Patients in whom acute decompensated heart failure (ADHF) has been diagnosed	According to the American Heart Association, more than 1.2 million patients are admitted for ADHF annually; about 40% of these patients are re-admitted within 90 days, so novel interventions are needed to prevent a recurrence of acute symptoms. Cenderitide is a chimeric natriuretic peptide receptor agonist that is intended to offer dual mechanisms of action, which may provide a unique therapeutic window to relieve symptoms of HF. Intended to be administered in a continuous subcutaneous pump for 90 days to provide symptomatic relief in the outpatient setting, which could contribute to a reduction in postacute hospitalizations and persistent improvement in cardio-renal functions. Nile Therapeutics, Inc., San Mateo, CA Phase I trial ongoing; FDA granted fast track status; company is seeking "post-ADHF" indication with this drug	Diuretics Natrecor (single natriuretic peptide receptor agonist, approved in U.S. for ADHF)	Reduced hospital readmissions Reduced HF symptom burden Improved cardiovascular outcomes
Electrical stimulation of carotid baroreceptors (Rheos System) for treatment of drug-resistant hypertension	Patients in whom severe, drug-resistant hypertension has been diagnosed	Electrical stimulation of carotid baroreceptors through a pulse generator inserted subcutaneously (CVRx Rheos® System), which delivers electrical signals to baroreceptors in both carotid arteries in the neck through carotid sinus leads. CVRx, Inc., Minneapolis, MN Phase II/III trials ongoing	Optimal medical management	Reduced hypertension Reduced stoke incidence Reduced cardiovascular events Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Elinogrel for prevention of heart attack and stroke and treatment of acute coronary syndrome	Patients in whom acute coronary syndrome has been diagnosed	Elinogrel is a reversible, direct-acting oral and intravenous P2Y12 ADP receptor antagonist. It is a novel small-molecule, antiplatelet compound that inhibits the ADP receptor (P2Y12) on platelets to block platelet aggregation and prevent thrombosis. It is the only compound in this class with both oral and intravenous (IV) formulations, and it could potentially be used for acute and chronic indications. The IV formulation is intended to provide immediate onset and high levels of platelet inhibition. Elinogrel requires no metabolism for activation (similar to Brilinta™); as a result, elinogrel avoids the issue of delayed action and wide interpatient variability seen with thienopyridines (e.g., clopidogrel [Plavix®] and prasugrel [Effient®]). The developer claims that elinogrel's ability to compete directly with ADP for the P2Y12 binding site may favorably affect the balance of its influence on thrombosis (low ADP state) versus hemostasis/bleeding (high ADP state), leading to a better risk-benefit ratio. Portola Pharmaceuticals, Inc., South San Francisco, CA Novartis AG, Basel, Switzerland Phase II trial for IV and oral formulations completed; phase III trials planned to begin 2012	Clopidogrel Prasugrel Ticagrelor (Brilinta, first reversible oral only P2Y12 ADP receptor antagonist) Ticlopidine	Fewer side effects from anticlotting medication regimen Reduced stroke incidence Reduced heart attack incidence Increased survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Factor Xa inhibitor (apixaban; Eliquis) for prevention or treatment of arterial or venous thromboembolism	Patients at risk of or with a history of deep vein thrombosis (DVT) or pulmonary embolism (PE)	Apixaban (Eliquis™, BMS-562247-01) is an oral, highly selective Factor Xa inhibitor intended to reduce the risk of or recurrence of venous or arterial thrombosis or PE in patients at risk of, or with a history of these events, including patients with AFib at risk of stroke. Joint development: Bristol-Meyers Squibb Co., Princeton, NJ Pfizer, Inc., New York, NY Phase III trials ongoing for non-AFib indications; for prevention of stroke in AFib, the phase III trial stopped early because of evidence of clinically important benefit and acceptable safety profile; filed for NDA for stroke prevention in AFib in early 2011. Approved May 2011 by the European Medicines Agency for venous thromboembolism prevention after knee or hip replacement surgery	Warfarin (Coumadin) Enoxaparin (Lovenox) injection Aspirin Dabigatran Comparators in development: idraparinux, biotinylated idraparinux, LY517717, YM150, DU-176b, apixaban, betrixaban, and rivaroxaban	Reduced DVT events Reduced stroke incidence Reduced PE events

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Factor Xa inhibitor (betrixaban) for prevention of deep vein thrombosis or pulmonary embolism	Patients at high risk of thrombosis	Betrixaban is a direct coagulation factor Xa inhibitor and is the only agent with potential to be used in patients with severe renal impairment (excluding dialysis patients); betrixaban keeps prothrombin from converting to thrombin to decrease clot formation; it differs from dabigatran (thrombin inhibitor), the only alternative to warfarin on the market; it is primarily eliminated unchanged in the bile so it is metabolized through cytochrome 450 enzyme system. Portola Pharmaceuticals, San Francisco, CA Phase III trial planned for 2012	Aspirin Coumadin Dabigatran Lovenox (injectable blood thinner) Factor Xa inhibitor comparators in development: idraparinux, biotinylated idraparinux, LY517717, YM150, DU-176b, apixaban, betrixaban, and rivaroxaban	Prevention of thrombosis Prevention of pulmonary embolism Decreased stroke events
Factor Xa inhibitor (edoxaban) for prevention of thromboses	Patients at risk for venous thromboembolism or AFib-related stroke	Current standard of care (warfarin) for this indication is associated with limitations, including a narrow therapeutic window and the need for frequent measurements of clotting parameters; no factor Xa inhibitors are currently approved for use in the U.S. Edoxaban is in a new class of anticoagulants in development designed to inhibit factor Xa, which is known to be an important component of the coagulation cascade. It is intended to be administered orally, once daily. Daiichi Sankyo, Tokyo, Japan Phase III trials ongoing; received approval in Japan in Apr 2011 for prevention of venous thromboembolism (VTE) after major orthopedic surgery; in the U.S., the manufacturer seeking indications only for treatment of VTE and prevention of stroke in patients with AFib	Aspirin Coumadin Dabigatran Lovenox Apixaban Betrixaban Rivaroxaban	Reduced thrombosis rate Reduced stroke incidence Reduced pulmonary embolism incidence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Factor Xa inhibitor (rivaroxaban, Xarelto) for prophylaxis of deep vein thrombosis	Patients eligible for anticoagulation (patients in whom risk of thrombosis has been diagnosed)	Rivaroxaban (Xarelto®) is a coagulation factor Xa inhibitor; keeps prothrombin from converting to thrombin, decreasing clot formation; different from dabigatran (thrombin inhibitor), which is only alternative to warfarin on the market. Fewer interactions expected; should not require frequent blood checks like Coumadin. It is an oral medication taken daily (dabigatran is taken twice a day). Johnson & Johnson, New Brunswick, NJ FDA approved Jul 1, 2011 for the prophylaxis of deep vein thrombosis (DVT) which may lead to pulmonary embolism (PE) in patients undergoing knee or hip replacement surgery.	Aspirin Coumadin Dabigatran Lovenox (injectable blood thinner)	Reduced stroke events
Gene therapy (Mydicar) for heart failure	Patients in whom HF has been diagnosed (additional trials needed to identify appropriate candidate population)	Genetically targeted enzyme replacement therapy (Mydicar®) as adjunct to treat HF. Intended to correct or replace faulty genes, restore levels of key proteins, and restore the heart's pumping capacity. Celladon Corp., La Jolla, CA Targeted Genetics Corp., Seattle, WA Phase II trial completed	Current drug therapies	Improved left ventricular ejection fraction Improved cardiovascular outcomes (reduction in cardiovascular events) Improved quality of life
Glial growth factor 2 for treatment of heart failure	Patients in whom HF has been diagnosed	Existing medications for HF treatment primarily aim to modify the workload of the heart, rather than promote ventricular repair. Glial growth factor 2 (GGF2) is a neuregulin (part of a family of proteins) believed to act directly on cardiomyocytes to repair tissue damage from heart disease, thereby improving contractility. Administered as single IV infusion. Acorda Therapeutics, Hawthorne, NJ Phase I trial ongoing	ACE inhibitors ARBS Beta blockers Digitalis Diuretics Stem cell therapies	Increased ventricular repair Improved cardiac output Improved cardioprotection Improved long-term cardiac outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Human monoclonal antibody (BI-204) for treatment of coronary artery disease	Patients in whom CAD has been diagnosed	BI-204 is a human monoclonal antibody that specifically targets oxidized form (apoB100) of a LDL that has been linked to increased inflammatory processes leading to plaque formation in blood vessel walls, leading to CAD. BioInvent International AB, Lund, Sweden Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trial ongoing	Mainly statins Other drug therapy Lifestyle changes	Prevent plaque formation Reduced existing plaques Prevent breakdown of unstable plaques Reduced cardiac events in high-risk patients
Icatibant (Firazyr) for treatment of acute hereditary angioedema	Patients in whom acute hereditary angioedema (HAE) of mild, moderate, or severe type has been diagnosed	HAE is a genetic disorder caused by dysfunction or deficiency of the plasma protein C1 inhibitor (C1INH). C1INH is an inhibitor of the C1 protease that is responsible for activating the complement pathway in the immune system. If C1INH is deficient, the immune system reacts with an inflammatory response that leads to swelling. Unlike bradykinin receptor-1, BR2 receptors do not appear to be involved in chronic inflammatory diseases but may mediate acute inflammatory processes. Icatibant (Firazyr®) is a peptidomimetic drug consisting of 10 amino acids and is a selective and specific antagonist of bradykinin B2 receptors. Administered by subcutaneous injection. Shire Pharmaceuticals, plc, Dublin, Ireland FDA approved on Aug 25, 2011 for treatment of acute attacks of HAE	Antihistamines C1-INH (concentrate from donor blood) Fresh-frozen plasma Pain relievers and fluids given intravenously	Faster symptom relief of primary symptom Reduced severity of symptoms Reduced mortality
Implantable cardiac monitor for detecting myocardial infarction	Patients at high risk of MI	Implantable electronic device designed to warn patients of an impending MI; measures electrical changes in the heart. Angel Medical Systems, Shrewsbury, NJ Phase III trial ongoing	Conventional, external MI detection technologies Patient report	Earlier detection of impending heart attack Prevention of heart damage Improved overall survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Injectable biopolymer (Algisyl-LVR) for prevention or treatment of heart failure	Patients in whom an enlarged left ventricle (from mitral valve regurgitation, ischemia, dilated cardiomyopathy and/or other disorders) has been diagnosed	No treatments are available to reverse the progression of HF. Algisyl-LVR™ is a polysaccharide biopolymer made from marine algae; it is intended to be injected (during open heart surgery) directly into myocardium in the left ventricle and to thicken upon injection, forming gel-like bodies that remain in heart muscle as permanent implants; intended to thicken heart muscle wall, reduce chamber size, decrease local muscle wall stress, allow for reshaping of dilated ventricle; material is inert (i.e., does not interact with the human immune system). Cardio Polymers, now part of LoneStar Heart, Inc., Laguna Hills, CA Phase II trial ongoing	Drug therapy to prevent HF Emerging stem cell scaffolding therapies BL-1040	Increased left ejection fraction Reduced progression of HF Reduced regression of HF Improved cardiovascular outcomes Improved quality of life
Intravenous methamphetamine HCl for neuroprotection during stroke	Patients experiencing an acute ischemic stroke	Only one drug, tissue-plasminogen activator (tPA) is FDA approved for this indication, but is effective only when administered within the first 3 hours of symptom onset, and only a very small percentage of patients experiencing an acute stroke receive tPA. Methamphetamine is currently marketed in pill form for attention deficit disorder with hyperactivity. Abuse of methamphetamine is known to cause arterial injury, stroke, brain hemorrhage and death at high doses. The manufacturer has created new low-dose version and new route of administration (intravenous injection). The company claims that preclinical models have shown neuroprotection for up to 12 hours. It is believed to exert its effects by inhibiting apoptosis (programmed cell death) and upregulating antiinflammatory cytokines, as well as downregulating proinflammatory cytokines, through dopaminergic pathways. Sinapis Pharma, Inc., Jacksonville, FL Phase I trial completed; phase II trial planned to begin by late 2011	tPA	Improved poststroke neuron survival Improved patient outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ivabradine for treatment of heart failure	Patients in whom symptomatic (New York Hospital Association class II to IV) chronic HF and systolic dysfunction have been diagnosed who are on stable background therapy and in a normal sinus rhythm	Ivabradine is an oral selective inhibitor of hyper-polarization-activated cyclic-nucleotide-gated funny current involved in pacemaking and responsiveness of the sinoatrial node; intended to slow heart rate and allow more time for blood to flow to the heart. Servier, Neuilly sur Seine, France Phase III trial (sponsored by IRCCS San Raffaele) ongoing; approved in European Union in 2005 as Procoralan	Beta blockers Calcium channel blockers	Reduced HF hospitalizations Reduced coronary events Reduced incidence of MI Improved quality of life
JVS-100 for treatment of critical limb ischemia	Patients in whom critical limb ischemia (CLI) has been diagnosed	No regenerative or disease-modifying therapies are available to treat this condition and this drug has that potential. JVS-100 is an agent that encodes stromal-cell derived factor 1 (SDF-1). SDF-1 recruits EPCs to site of injury, thereby potentially inducing neovascularization and angiogenesis (sustained vessel formation necessary for adult tissue to become fully revascularized, particularly after ischemia); natural SDF-1 expression lasts for less than a week so natural stem cell homing signals fade quickly. Juventas Therapeutics, Cleveland, OH Phase II trial registered, not yet recruiting	Endovascular intervention Medication to reduce contributing factors (e.g., cholesterol) or pain Surgical intervention	Reduced pain Improved blood flow Reduced need for amputation Improved functional ability Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Left ventricular assist device (HVAD) as bridge to transplantation for end-stage heart failure	Patients in whom end-stage HF has been diagnosed who are eligible for heart transplantation	HeartWare is developing an LVAD (HVAD™) for treatment of advanced HF. The LVAD propels blood centrifugally from the center of a spinning disc, which is suspended by magnetics and blood; smaller than currently marketed devices, it can be implanted directly in left ventricle and surrounding space (does not require abdominal surgery to create pocket). The device is implanted with less invasive surgery which could enable more patients to be candidates for the devices and at earlier stages of disease progression. HeartWare International, Inc., Framingham, MA U.S. multicenter late-phase clinical trial under FDA IDE status ongoing; CE marked in Europe in 2009	Optimal medical management Other LVADs Total artificial heart	Improved survival Improved quality of life prior to transplant Reduced incidence of internal bleeding compared with continuous-flow devices
Left ventricular end diastolic pressure-based hydration for renal protection during coronary angiography	Patients at high risk for renal damage (diabetes mellitus, history of congestive HF, hypertension, or age older than 75 years) who are undergoing coronary angiography	Hydration with different sodium chloride protocols for the prevention of contrast-medium-induced nephropathy. Strategy intended to adjust fluid rate according to left ventricular end diastolic pressure. Kaiser Permanente Health System, Los Angeles, CA Phase III trial ongoing	Conventional hydration strategies used during coronary angiography	Reduced contrast-induced renal toxicity
Low-dose tPA for treatment of intraventricular hemorrhage	Patients in whom intraventricular hemorrhage has been diagnosed	TPA is a thrombolytic agent (clot-busting drug) long used for treatment of stroke; it may be useful to treat intraventricular hemorrhage clots that form once bleeding has been stopped; current strategy is to remove the clots with intraventricular catheter, which can clog and take days. TPA could offer a less invasive, faster treatment option. Johns Hopkins University, Baltimore, MD Phase III trial ongoing	Intraventricular catheter alone	Improved clot evacuation Decreased time to clot evacuation Improved cardiovascular outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Minocycline with tPA for treatment of stroke	Patients in whom acute ischemic stroke has been diagnosed	Minocycline, a tetracycline antibiotic, is given with tPA to reduce stroke-associated inflammatory factors and bleeding. Georgia Health Sciences University, Augusta, GA Phase I/II trial ongoing	Nonsteroidal anti-inflammatory drugs (NSAIDs)	Reduced bleeding in stroke Improved overall outcomes
Membrane active chelator (DP-b99) for neuroprotection during acute stroke	Patients experiencing an acute ischemic stroke	Only one drug, tPA is FDA approved for this indication, but tPA is effective only when administered within the first 3 hours of symptom onset, and only a very small percentage of patients experiencing an acute stroke receive tPA. When a cell is deprived of oxygen, the ability of membranes to control ion flux is disrupted, resulting in the loss of metal ion homeostasis, which can significantly impair cell or organ function and eventually lead to cell death. DP-b99 is a lipophilic chelator of calcium, zinc, and copper ions; it is intended to sequester metal ions only within and near cell membranes. The manufacturer claims it can bind to pathological levels of metal ions, making it useful for the suppression of cell damage in stroke patients. The technology is based on lipid modification of metal ion chelators, which sequester metal ions in all aqueous environments, causing potential toxic effects. The modified version binds metal ions selectively, which makes it potentially safer and is intended to increase treatment window to 9 hours. DP-b99 is delivered via intravenous infusion. D-Pharm, Ltd., Rehovot, Israel Phase III trial ongoing; FDA granted fast track status	tPA	Improved poststroke neuron survival Faster recovery Reduced need for rehabilitation services

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mitochondrial pore modulator (TRO-40303) to prevent reperfusion injury after heart attack	Patients receiving cardiac reperfusion after heart attack or coronary bypass surgery	Experimental studies show that reperfusion injury accounts for as much as 50% of the final size of a myocardial infarct in patients having a heart attack; protecting the heart during reperfusion of ischemic areas is therefore, important; as oxygen is reintroduced into an ischemic area after heart attack or heart bypass surgery, oxygen free radicals are generated, resulting in cellular damage in the form of swelling and/or contracture; this leads to what is termed a “no-reflow phenomenon”; this effect limits recovery of some heart cells and is believed to contribute to irreversible injury of other heart cells. TRO-40303 targets mitochondria to protect cells from apoptosis; intended to prevent reperfusion injury that occurs in virtually all patients when ischemic tissue in the heart is reperfused after a heart attack or coronary artery bypass surgery. Administered intravenously. Trophos SA, Marseille, France Phase II trial registered, not yet recruiting	Reperfusion with and without TRO-40303	Reduced myocardial cell death Improved cardiovascular function Increased survival
Mitochondrial-targeted compound (Bendavia) for treatment of ischemia reperfusion injury	Patients experiencing ischemia reperfusion injury during reperfusion post-MI and coronary bypass surgery	As oxygen is reintroduced into an ischemic area after heart attack or heart bypass surgery, oxygen free radicals are created, resulting in cellular damage in the form of swelling and/or contracture. This leads to what is termed a "no-reflow phenomenon." This effect limits recovery of some heart cells and is believed to contribute to irreversible injury of other heart cells. Bendavia™ is a compound that targets mitochondria to protect cells from undergoing cellular death. It is intended to prevent reperfusion injury that occurs in virtually all patients as ischemic tissue in the heart is being reperfused after a heart attack or coronary artery bypass surgery. Stealth Peptides, Inc., Newton Centre, MA Phase II trial planned, not yet registered	Fibrinolytic therapy (i.e., drugs (tPA) used to break up clots that are blocking a vessel) Angioplasty and stenting	Improved electron transport efficiency Maintained mitochondrial respiration and adenosine triphosphate levels Prevented mitochondrial swelling and depolarization Reduced apoptosis (cell death) Improved cardiovascular outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mitral contour system (Carillon) for functional mitral valve repair	Patients in whom functional mitral regurgitation has been diagnosed	Nonsurgical, minimally invasive device intended to repair the mitral valve (implantable device and percutaneous delivery system). Cardiac Dimensions, Inc., Kirkland, WA Trials ongoing, not registered; approved for marketing in Europe in 2009	Optimal medical management Minimally invasive surgery Open surgery	Reduced risk of cardiac events Reduced mitral regurgitation Improved quality of life Reduced operative morbidity Reduced mortality
Mobile phone electrocardiography (iPhoneECG)	Patients in need of an electrocardiogram (ECG) who have access to a mobile device	Access to ECG machines is limited in some rural or emergency rescue locations; patients are required to visit health care facilities for ECG readings; "portable" ECG machines still require 12 leads. The iPhoneECG is a slim device in a case that fits over an iPhone (also available as the iCard, which sticks to the back of any mobile device, including iPads), has low-power electrodes on the case that are pressed against the fingers or chest of a patient to display full ECG and heart rate; intended to record and upload the reading onto a server, which converts it to a PDF for analysis by a medical professional; manufacturer intends device to be used to aid diagnosis of heart blockage or unstable heartbeat, or to monitor heart rate during exercise or stress reduction techniques; manufacturer claims that the device will work in any location with wireless coverage. AliveCor, Seattle, WA Premarket notification for 510(k) clearance from FDA in progress	Standard ECG machines Portable ECG machines	Increased access to ECG technology Reduced morbidity from heart conditions monitored by ECG Reduced health disparities

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
MTP inhibitor (lomitapide) for treatment of homozygous familial hyper-cholesterolemia	Patients in whom homozygous familial hyper-cholesterolemia (HoFH) has been diagnosed	Outcomes with current medication for HoFH are suboptimal. Lomitapide represents a novel class of medication - a microsomal triglyceride transfer protein inhibitor (MTP-I) that is intended to lower both cholesterol and triglycerides. MTP is a lipid transfer protein that is required for moving lipid molecules from their site of synthesis, so inhibiting MTP prevents both hepatic very-low-density lipoproteins and intestinal chylomicron secretion (from food/diet), which in turns lowers plasma lipids. Lomitapide is intended to replace statins. Taken orally. Aegerion Pharmaceuticals, Inc., Cambridge, MA Pivotal phase III trial ongoing; FDA granted orphan drug status; company plans to submit NDA to FDA by end of 2011	Bile acid-sequestering resins Extracorporeal apheresis Ezetimibe Fibrates (such as gemfibrozil) Nicotinic acid Statins	Reduced LDL levels Improved cardiovascular outcomes Improved quality of life Improved long-term health outcomes
Myocardial stem cell delivery via transmyocardial laser revascularization (Phoenix system) for treatment of coronary artery disease	Patients in whom diffuse CAD has been diagnosed who are not candidates for surgical bypass or percutaneous coronary intervention	Phoenix™ system transmyocardial revascularization creates channels in the myocardium through which autologous stem cells can be injected to try to improve cardiac vascularization. CryoLife, Inc., Kennesaw, GA (acquired Cardiogenesis May 2011) Phase II trial ongoing in Spain; CE marked in Europe 2006; company plans to submit request to FDA in 2011 for permission to begin IDE trial	Optimal medical management Gene therapy	Reduced angina Improved cardiac function Reduced cardiovascular events Improved quality of life
Nitroxyl donor (CXL-1020) for treatment of acute decompensated heart failure	Patients in whom acute decompensated HF has been diagnosed	CXL-1020 is a proprietary nitroxyl donor intended to enhance heart contractility (inotropy) and relaxation (lusitropy) and peripheral vasodilation without increasing heart rate or myocardial oxygen consumption. Administered intravenously. Cardioxyl Pharmaceuticals, Inc., Chapel Hill, NC Phase II trial ongoing	Diuresis (for fluid removal) Vasodilation (for preload and afterload reduction) Other intravenous inotropic agents (dobutamine, milrinone)	Improved symptoms, hemodynamics, and clinical status of patients with acute decompensated HF

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oxygenated pegylated hemoglobin (MP4OX) for treatment of hemorrhagic shock	Patients in whom trauma-related oxygen deprivation (hemorrhagic shock) has been diagnosed	Standard of care for hemorrhagic shock is limited because treatments do not reach capillaries or ischemic tissues; many patients treated with optimal care for traumatic injuries still experience organ dysfunction and failure; treatments are needed to improve the perfusion and oxygenation capabilities of standard of care. MP4OX is oxygenated, pegylated hemoglobin that is intended to prevent the premature release of oxygen in the vascular system and to open capillary beds for perfusion and targeted oxygen delivery; it is designed to be at a certain optimal oxygen affinity, diffusion potential, and molecular size so it has the potential to perfuse capillaries and delivery oxygen to tissues at risk for ischemia; intended for use as an adjunctive treatment to standard of care (transfused blood or packed red blood cells). Sangart, Inc., San Diego, CA; MP40X's development is part of a Dec 2010 cooperative research and development agreement (CRADA) with the U.S. Navy Phase IIb trial ongoing	Standard of care with and without MP4OX	Improved perfusion of capillaries and oxygenation of ischemic tissues Resolution of hemorrhagic shock Reduced rate of organ failure Improved survival
PAR-1 antagonist (Atopaxar) for prevention of atherothrombosis	Patients in whom a risk of atherothrombosis has been diagnosed	Current standard of care, DAPT, for reducing ischemic events in patients with atherothrombotic disease is associated with limitations, including the risk of bleeding and the possibility of recurrent thrombotic events; these agents do not modulate thrombin, a potent receptor for platelet activation; atopaxar represents a new mechanism of action for this disease state. Atopaxar (E5555): protease-activated receptor 1 (PAR-1) antagonist; thrombin mediates its effects though PAR-1 on the platelet surface, so inhibition of PAR-1 may represent a viable approach for reducing platelet activation, without causing prolongation of bleeding time (because other thrombin-mediated effects associated with hemostasis are not affected). Administered orally, once daily. Eisai, Inc., Tokyo, Japan Phase II trials completed	Aspirin Clopidogrel	Reduced platelet aggregation Fewer ischemic events Improved bleeding rates Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PerClot blood-clotting agent for perioperative and postoperative hemostasis	Surgical patients at risk of perioperative and postoperative hemorrhage	Hemostatic agent (PerClot®) in form of absorbable powder used adjunctively when control of bleeding from capillary, venous, or arteriolar vessels by pressure, ligature, and other conventional means is either ineffective or impractical. Cryolife, Inc., Atlanta, GA Company filed IDE application with FDA in Apr 2011 to begin U.S. trials; has marketing approval in Europe	Conventional hemostatic techniques (fibrin sealants, mechanical hemostasis) used during surgery	Adequate, timely hemostasis
Percutaneous left atrial appendage occlusion (Watchman) for prevention of atrial fibrillation-associated stroke	Patients in whom AFib has been diagnosed who are not good surgical candidates	Intended to block left atrial appendage opening and prevent clots from entering general circulation. Atritech, Inc., Plymouth, MN Phase III trial ongoing	Long-term anticoagulation therapy	Reduction in stroke risk
Pipeline embolization device for treatment of brain aneurysms	Patients in whom brain aneurysms have been diagnosed	Pipeline embolization device is a self-expanding, microcatheter-delivered, cylindrical mesh "flow diversion" device intended to divert blood flow away from the aneurysm sac and assist in reconstruction of the parent artery while leaving the side vessels open. ev3 Neurovascular, Menlo Park, CA Received FDA approval Apr 2011; continued follow-up for 5 years of individuals in the pivotal clinical cohort and continued access cohort required	Endovascular coiling Stent-assisted coiling Surgical clipping or bypass	Prevented rupture of brain aneurysms Reduced mortality form aneurysm

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Placenta-derived cell therapy (PLX-PAD) for critical limb ischemia	Patients with CLI including pain at rest and tissue necrosis, Fontaine class III to IV	Treatment is needed for patients with CLI whose CLI is not responding to medical or surgical interventions; these patients are at risk of amputation. Placenta-derived cell therapy (PLX-PAD) for PAD consists of mesenchymal-like stromal cells derived from a full-term placenta; PLX-PAD cells originate from the human placenta harvested after a caesarean section and cultured in a bioreactor (PluriX™). Delivered by intramuscular injection to a patient's limb with the intent to improve blood flow. Pluristem Therapeutics, Inc., Haifa, Israel Phase I trial ongoing	Antiplatelet therapy Cilostazol and pentoxifylline (improve walking distance) Cholesterol-lowering agents (statins) Percutaneous angioplasty and stenting Surgery In development: JVS-100 (repair through recruitment of endogenous stem cells to the damaged organ)	Less pain Increased amputation-free survival rate (amputations and death) Improved quality of life
PMX-60056 for management of coagulation in the use of heparin and low molecular weight heparins	Patients receiving heparin or low molecular weight heparins (LMWHs) in routine surgical procedures or in cases of bleeding complications	Currently, no drugs are FDA approved to completely reverse the anticoagulant activity of LMWH given during surgery if bleeding becomes uncontrolled. Thus, developing a drug that allows for complete reversal of the anticoagulant activity of both heparin and LMWH has become an area of interest. Synthetic small-molecule (PMX-60065) is intended to completely reverse anticoagulant activity of heparin or LMWHs and is believed to be the first such agent with the potential to do so. PolyMedix, Inc., Radnor, PA, Phase II trial ongoing	Protamine	Fast, complete reversal of anticoagulation Reduction in bleeding complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Point-of-care autologous bone marrow for treatment of critical limb ischemia	Patients in whom CLI has been diagnosed who are not eligible for revascularization surgery	Treatment is needed for patients with CLI whose disease is not responding to medical or surgical interventions; these patients are at risk of amputation. The Magellan ® MAR01™ system enables the production of a concentrate of aspirated bone marrow at the patient's bedside that yields an injectable tissue rich in platelets, hematopoietic stem cells, and mesenchymal stem cells (key cells in tissue repair); intervention will evaluate administration of concentrated bone marrow injections (using the 510[k] cleared Magellan MAR01 technology) at the bedside; injected concentrate intended to improve perfusion in ischemic tissue in affected limbs of patients with CLI who are not candidates for revascularization surgery. Arteriocyte, Inc., Cleveland, OH Phase I trial under IDE status ongoing	Antiplatelet therapy Cilostazol and pentoxifylline (improve walking distance) Cholesterol-lowering agents (statins) Percutaneous angioplasty and stenting Surgery In development: Placenta-derived cell therapy (PLX-PAD) JVS-100 (encodes Stromal-cell Derived Factor 1, repair through recruitment of endogenous stem cells to the damaged organ)	Increased amputation-free survival rate (amputations and death) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Polymer strands (cPAX system) for treatment of giant and wide-neck cerebral aneurysms	Patients in whom a large, giant and wide-neck cerebral aneurysm has been diagnosed.	Large, giant and wide-neck cerebral aneurysm remain the most difficult to treat, and conventional platinum coils have been suboptimal. CPAX is polymeric strand delivered into the aneurysm using a technique similar to currently available platinum coil technologies (endovascular embolization); the difference is that cPAX is a soft polymeric material designed to achieve more complete filling of the giant or wide-neck aneurysm than is possible with currently available platinum coils; translucency of its polymeric material allows for non-invasive \CT and MRI scans with little or no artifact for more accurate patient assessment and followup. NeuroVasx, Inc., Maple Grove, MN FDA approved under Humanitarian Device Exemption in Apr 2011	Endovascular embolization-detachable coils (spirals of platinum wire) Microvascular clipping (clothespin-like clip on the aneurysm's neck) Occlusion of artery that leads to the aneurysm	Decreased incidence of ruptured aneurysm (about 27,000 individuals per year in the U.S.) Reduced incidence of hemorrhagic stroke, vasospasm (the leading cause of disability or death following a burst aneurysm) Short-term and/or permanent brain damage Decreased mortality
Potassium binder (RLY5016) for prevention of hyperkalemia	Patients in whom HF or HF with underlying renal impairment has been diagnosed	Renin-angiotensin-aldosterone-system-inhibitor drugs cannot be used in HF patients and renal impairment because of concerns about hyperkalemia; an effective drug therapy would allow better management of HF patients; current agents are poorly tolerated and cause bowel necrosis. RLY5016 is a novel potassium binder (orally absorbed resin; high capacity cation binder) that is intended to lower serum potassium, thereby preventing hyperkalemia in patients with HF or HF and renal impairment; appears to be better tolerated and potentially has twice the potassium-binding capacity compared with current agents. Relypsa, Santa Clara, CA Phase IIb trial ongoing	Other potassium binders (e.g., sodium polystyrene sulfonate)	Improved side effect profile Decreased incidence of hyperkalemia Optimal medical management of HF Improved long-term cardiac outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Recombinant neuregulin-1 (Neucardin) for treatment of heart failure	Patients in whom HF has been diagnosed	No disease-modifying treatments for HF exist; only the symptoms are treated. Neucardin™ (rhNRG-1) represents a potential disease-modifying approach to treatment; it is a recombinant peptide fragment of human neuregulin-1 (NRG-1); NRG1 is a tyrosine kinase receptor agonist (member of the endothelial growth factor [EGF] family) and is known to activate multiple intracellular signaling pathways in cardiomyocytes, including MAPK pathway (associated with protein synthesis and muscle hypertrophy) and PI3K-Akt-mTOR (mammalian target of rapamycin) pathway (associated with prosurvival effects and activation of cellular metabolism); the NRG signaling cascade is challenged by stress factors and has limited ability to compensate for myocardial cell loss, so rhNRG-1 is intended to aid in development, differentiation, and function of myocardial cells. Zensun (Shanghai) Sci & Tech Co., Ltd., Shanghai, China Phase IIa trial registered, not yet recruiting	Pharmacotherapy (ACE inhibitors, beta blockers) Polymer scaffolds Emerging stem cell therapies	Increased cell survival Improved cell metabolism Increased cell proliferation Improved symptoms Improved morbidity and decreased mortality
REG1 system for anticoagulation during elective percutaneous coronary interventions	Patients who are undergoing elective percutaneous coronary intervention	Two-component drug technology that includes selective coagulation Factor IXa inhibiting aptamer (pegnivacogin) and its specific reversal agent (anivamersen). Regado Biosciences, Inc., Basking Ridge, NJ Phase IIb trial completed.	Unfractionated heparin Other anticoagulants	Reduced bleeding episodes during percutaneous coronary intervention Reduced complications from ischemia

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Robotic system (CorPath 200) for remotely controlled percutaneous coronary intervention	Patients undergoing PCI	PCI, as it is currently performed, is associated with procedural challenges, radiation exposure, and spinal strain for interventional cardiologists. CorPath™ 200 is a console or cockpit with radiation shielding placed several feet from patient that allows the physician to use robotic-assisted tools to place coronary guidewires and stent/balloon catheters; the physician does not have to wear a lead shield apron during PCI; system is intended to fixate and hold devices to enable the cardiologist (while seated) to control contrast injection and manipulate the guidewire; intended to enhance visualization, minimize fatigue, and protect against exposure to radiation and back strain. According to manufacturer, improved control of contrast injection and visualization of angiography may also reduce the volume of contrast media and radiation dose administered to the patient. Corindus Vascular Robotics, Inc., Natick, MA Phase II trial ongoing; company pursuing FDA 510(k) clearance	Manually performed PCI	Improved procedural visualization Reduced radiation exposure Reduced physician spinal strain Reduced physician fatigue Increased number of PCI procedures performed Improved patient safety
RVX-208 for treatment of dyslipidemia	Patients in whom sub-optimal HDL levels (dyslipidemia) have been diagnosed	Treatment of HDL as a single target is not available. RVX-208 is a novel, small-molecule inducer of Apo-1 synthesis; intended to generate functional HDL particles (that facilitate reverse cholesterol transport). Resverlogix, Calgary, Alberta, Canada Phase II trial ongoing	Anacetrapib (in development) Niacin Rosuvastatin	Improved HDL levels Decreased plaque burden Improved cardiovascular outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
School-wide electrocardiogram screening (Young Hearts for Life) for cardiac abnormalities in students	Students in high school or college, who may or may not participate in organized sports	More than 1,000 young adults die from sudden cardiac death annually in the U.S. The Young Hearts for Life Cardiac Screening Program is intended to provide free electrocardiograms (ECGs) to all high school students (who choose to participate) to identify students at risk for sudden cardiac death; screenings are conducted during the school day, usually during physical education classes, and echocardiograms are available on site at no cost for selected students who have an inconclusive screening ECG (intended to give additional information regarding whether further evaluation is necessary); ECGs are interpreted by volunteer cardiologists; parents receive test results approximately 3 weeks after the screening and are instructed to follow up with primary care physician if necessary. Midwest Heart Foundation, Lombard, IL Studies have been completed with more than 55,000 students screened	American Heart Association (AHA)-recommended screening that includes physical examination and family and personal medical history	Increased detection of potential cardiac abnormalities Earlier diagnosis of abnormalities Reduced incidence of SCD Increased costs from screening general student population who would otherwise not be screened by ECG
Selective serotonin-4 (RO1160367, SER101) antagonist for treatment of heart failure	Patients in whom HF has been diagnosed	RO1160367 is a 5-HT4 (serotonin) antagonist; 5-HT4 receptors have been discovered on muscle cells in failing cardiac ventricles and failing cardiac ventricle expresses 5-HT4 receptors as a response to the serious condition. Serodus ASA, Oslo, Norway, licensed from Hoffmann-La Roche, Basel, Switzerland Phase I trial completed	ACE inhibitors ARBS Beta blockers Digitalis Diuretics	Increased cardiac output Improved cardioprotection Improved long-term cardiac outcomes
Self-expanding stent (Sesame) for use in saphenous vein graft lesions	Patients undergoing angioplasty of degenerated saphenous vein graft lesions	Preemptive embolic protection stent (Sesame Stent™) is designed specifically for saphenous vein graft lesions Covered with microporous mesh (purported to be more biocompatible than polymer covered) that limits plaque protrusion through stent struts and limits stent strut migration into underlying plaque (important because lesions are associated with a higher risk of plaque and thrombus embolization). Palmaz Scientific, Dallas, TX First-in-human trial completed	No self-expanding stents available specifically used to treat saphenous vein graft disease Antiplatelet agents Polymer-covered stents	Reduced restenosis Reduced major adverse cardiovascular events Improved health outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Self-expanding stent (Stentys) for treatment of straight and bifurcated coronary lesions	Patients in whom CAD has been diagnosed and have a bifurcated vessel lesion and who are eligible for stenting	Stent malapposition increases the risk of stent thrombosis; no approved stents are specifically designed to address malapposition or bifurcated lesions. The Stentys stent represents a new class of coronary stent; it is a self-expanding, self-apposing stent that is made in both bare metal and drug-eluting (paclitaxel) forms; it has potential for utility in bifurcated lesions because of the ability of the stent struts to "detach" during balloon angioplasty, providing a mechanism by which a second stent can be placed through the stent into another vessel without damaging the main vessel stent; the self-expanding stent is designed to accommodate to arterial enlargement (which occurs due to changes in thrombus load and vasoconstriction in the days/weeks after acute MI percutaneous coronary intervention), thereby reducing the risk of malapposition and subsequent stent thrombosis; stent is made of nitinol Z-shaped mesh, which is linked by small interconnections. Stentys SA, Paris, France Phase III trial completed in patients with acute MI; CE marked in 2010	Dual stenting using two conventional stents for bifurcated lesions Single stenting using a DES (one only in the bifurcated lesion) Other bifurcation stent technologies currently in development	Prevention of restenosis of side branch artery (in addition to main artery) Reduced thrombosis (short-term and long-term) Improved cardiovascular outcomes Prevented malapposition
Side branch stent system (Tryton) for treatment of bifurcation lesions	Patients in whom CAD has been diagnosed and have a bifurcated vessel lesion and who are eligible for stenting	Tryton Side Branch Stent System™ is intended to treat a type of complex Y-shaped coronary lesion that exists in two vessel—one branching off the other. Such lesions are typically treated by using two separate stents, one in each branch, which has caused significant complications. The Tryton cobalt chromium stent is deployed in the side branch artery using a standard single-wire balloon-expandable stent delivery system so that a conventional DES can be placed in the main vessel by being threaded through the Tryton stent. Tryton Medical, Inc., Durham, NC Phase I/II trial ongoing; CE marked	Approaches using more than one conventional stent DESs (one only) Other bifurcation stent technologies currently in development	Reduced restenosis of side branch artery (in addition to main artery) Reduced thrombosis Improved cardiovascular outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Sildenafil (Viagra) off-label to improve pediatric exercise tolerance after Fontan surgery for heart defect	Pediatric patients with exercise intolerance after undergoing Fontan operation to correct heart defect	No medical therapies have demonstrated a benefit in improving exercise tolerance in patients who have undergone a Fontan operation. The Fontan procedure is a palliative surgery for patients who have a single pumping ventricle; a staged reconstruction of the heart and the major blood vessels whereby the veins that usually bring blood back to the heart are connected directly to the pulmonary arteries; this creates a "new" circulatory system, in which blood from the body bypasses the heart and flows directly to the lungs; importantly, blood flow through the lungs is passive (not pumped) and the efficiency of flow through the cardiovascular system is related to the resistance to blood flow in the vessels of the lungs, or pulmonary vascular resistance (PVR). Sildenafil (Viagra®) is a phosphodiesterase 5 inhibitor that has potent selective vasodilatory effects on pulmonary vasculature; may decrease PVR, resulting in increased pulmonary blood flow. Children's Hospital of Philadelphia, Philadelphia, PA Pfizer, Inc., New York, N Phase IV trial ongoing	Exercise training	Improved PVR Improved pulmonary blood flow Improved cardiac filling Increased stroke volume Improved cardiac output response to exercise Increased exercise tolerance Increased time to transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Standardized protocol and integrated system (RACE Project) for treatment and transfer of patients with ST-elevated myocardial infarction	Patients in whom an ST-elevated myocardial infarction (STEMI) has been diagnosed	Current guidelines recommend that patients with STEMI receive fibrinolysis within 30 minutes, and primary PCI within 90 minutes, of symptom onset, yet fewer than half of patients receive this care within the recommended time frame. Additionally, only 4% of patients who are transferred to a second (PCI-capable) hospital are treated within the 90-minute time frame. Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments (RACE) Project: Statewide initiative to identify and overcome barriers to recommended rapid reperfusion times by establishing optimal regional systems of care (with parallels to existing trauma systems). Goal is to improve both the rate and speed of STEMI care though specific interventions with a systemic approach. PCI and non-PCI hospitals are assessed to determine barriers to rapid reperfusion, and customized plans for improvement are developed. Interventions include: educational symposia (on topics such as ECG interpretation, STEMI recognition, treatment options), placing ECG and transmittal equipment on EMS transport vehicles, and establishing a single telephone number to access transfer to a PCI hospital. Transfer-specific interventions include: leaving patient on the original stretcher and creating system-compatible intravenous (IV) tubing and pumps, and/or eliminating the need for IV pumps (e.g., through administration of IV bolus of unfractionated heparin). Sponsored by North Carolina Chapter of the American College of Cardiology (ACC) Pilot study with 436 patients at 55 hospitals completed; data available	Current STEMI practices (vary between hospitals)	Reduced door-in-to-door-out (DIDO) time Reduced time to treatment Improved cardiovascular morbidity Improved mortality outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Stromal cell-derived factor-1 for treatment of heart failure	Patients in whom HF has been diagnosed	About 5.4 million Americans have HF, and because of the lack of regenerative treatments, the vast majority of patients will die within 8 years of first diagnosis. JVS-100 (also called ACRX-100) is an agent that encodes SDF-1; SDF-1 recruits EPCs to site of injury or ischemia, thereby potentially inducing neovascularization and angiogenesis (sustained vessel formation necessary for adult tissue to become fully revascularized, particularly after ischemia). Natural SDF-1 expression lasts for less than a week, so natural stem cell homing signals fade quickly. In clinical trial, agent is being injected directly into the myocardium as a single dose at multiple sites through a percutaneous, left ventricular approach using a needle injection catheter. Juventas Therapeutics, Inc., Cleveland, OH Phase I trial ongoing	ACE inhibitors Angiotensin receptor blockers (ARBs) Beta blockers Digitalis Diuretics Mydicar (gene therapy in development)	Increased neovascularization and angiogenesis Reduced symptom burden Disease regression or slowed disease progression
Subcutaneous implantable cardioverter defibrillator (S-ICD System) for treatment of cardiomyopathy	Patients in whom cardiomyopathy has been diagnosed who are at risk for sudden cardiac arrest	This subcutaneous implantable cardioverter defibrillator's (S-ICD®) wires do not connect to the heart and reduce risk of wires bending and causing unnecessary shocks; no imaging equipment required for placement. Cameron Health, Inc., San Clemente, CA IDE trial ongoing; CE marked in 2009	Other implantable defibrillators	Quicker recovery after implantation Reduced risk of unnecessary shocks Reduced risk of failures to shock Improved quality of life
TB-402 for prevention of deep vein thrombosis associated with orthopedic surgery	Patients undergoing orthopedic surgery	More effective antithrombotic therapy is needed for patients undergoing orthopedic surgery. TB-402 is human monoclonal antibody binding to Factor VIII (blood clotting factor); being developed as an anti-coagulant for the treatment and prevention of venous thromboembolism post-orthopedic surgery; injected as a single dose intravenous bolus 18 to 24 hours after total knee replacement surgery; potential to reduce the risk of bleeding events and need for anticoagulation monitoring; overcome poor patient compliance to antithrombotic therapy (single dose). ThromboGenics, Inc., Heverlee, Belgium BioInvent Inc., Lund, Sweden Phase II trial ongoing	Enoxaparin (Lovenox) low molecular weight heparin Short-term warfarin (Coumadin) therapy	Decreased adverse effects Decreased bleeding

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Transcatheter aortic valve (CoreValve) implantation for treatment of severe aortic stenosis	Patients in whom severe aortic stenosis has been diagnosed	Aortic stenosis (AS) occurs in about 4% to 5% of people aged 75 years or older and more than 300,000 people are estimated to have the condition worldwide; causes of severe AS include buildup of calcium deposits on the aortic valve, prior radiation therapy, certain medications, and/or a history of rheumatic fever; an estimated 30% of all patients with symptomatic severe AS are not suitable candidates for valve replacement performed as an open heart surgery procedure. The transcatheter aortic valve (CoreValve®) procedure uses fluoroscopic guidance to replace the native aortic heart valve without open heart surgery; an 18 French diameter catheter is used for delivery of a self-expanding nitinol frame stent with a porcine pericardial tissue valve. Medtronic, Inc., Minneapolis, MN Two pivotal U.S. trials begun in 2011 under FDA IDE status; late-phase and postmarket international trials completed; CE marked in 2007; available outside U.S. in 34 countries	Open heart aortic valve surgery In development: Melody transcatheter aortic valve for severe AS	Improved cardiac function Increased survival Improved quality of life
Transcatheter aortic valve implantation (Sapien) for treatment of severe aortic stenosis	Patients with severe calcific aortic stenosis who are considered to be high-risk or non-operable for conventional open-heart valve replacement surgery	Sapien transcatheter aortic valve is a tissue valve deployed into the heart using a minimally invasive transcatheter-based procedure (transfemoral or transapical) to try to repair aortic valve. Edwards Lifesciences, Irvine, CA Phase III pivotal trial ongoing; (PARTNER I and II trials); FDA approved Nov 2011 for use in patients who cannot be treated by open-heart surgery. American Heart Association featured special session on transaortic valve replacement at its meeting in late Nov 2011. Centers for Medicare and Medicaid Services opened national coverage analysis Sept 2011 to try to coincide with anticipated FDA decision in late 2011 or early 2012.	Optimal medical management Open surgery for valve replacement	Freedom from death Accurate valve replacement Avoided open surgery Improved quality of life Decreased rehospitalization for HF

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Transcatheter mitral valve repair (MitraClip) for treatment of mitral regurgitation	Patients in whom degenerative mitral valve disease with prolapse has been diagnosed who are not good candidates for open surgical repair	Minimally invasive transcatheter approach requires transseptal puncture to access the left heart chambers; in lieu of sutures, metal clip (MitraClip®), a flexible metal clip covered in polyester fabric is used. Intended for patients whose valve disease originates mainly from the center of the valve. Evalve, Inc., Menlo Park, CA; being acquired by Abbott Laboratories, Abbott Park, IL Phase III trial ongoing; CE marked in 2008	Open surgical mitral valve repair Drug therapy for patients for whom surgery is not an option	Improved quality of life for patients who are not good surgical candidates Reduction in mitral regurgitation and associated cardiovascular outcomes Decreased cost because of slowing disease progression Decreased cost compared with open surgery
Transcatheter pulmonary valve (Melody) for treatment of regurgitant or stenotic right ventricular outflow tract conduit	Adults and children with a regurgitant or stenotic right ventricular outflow tract conduit (≥16 mm in diameter when originally implanted)	A catheter is inserted into the patient's femoral vein, and the catheter holding the Melody® valve stent is placed in the vein and guided into the patient's heart in desired position. Balloon is inflated, and valve expands to enable blood to flow between the patient's right ventricle and lungs. Fluoroscopy is used to confirm function. Medtronic, Inc., Minneapolis, MN Received FDA Humanitarian Device Exemption approval in 2010; CE marked in Oct 2006	Surgery for valve replacement	Improved blood flow and ejection fraction(due to valve) Improved symptoms Delay of open-heart surgery

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Transcatheter pulmonary valve (Sapien) replacement for treatment of pulmonary valve disease	Pediatric patients in whom a malformed pulmonary valve has been diagnosed	Interventional cardiac catheterization procedure with the Sapien stent valve intended to replace a worn-out pulmonary valve Edwards Lifesciences, Irvine, CA Clinical trial ongoing under FDA IDE status; company intends to seek HDE from FDA	Open heart surgery	Accurate deployment of valve Avoided open surgery Reduced hospital stay Reduced pain Reduced bleeding/transfusion Quicker recovery and return to normal activity Improved quality of life
Trans-sodium crocetinate for treatment of peripheral artery disease	Patients in whom PAD has been diagnosed	Trans-sodium crocetinate is a small molecule intended to treat hypoxia and enhance diffusion of oxygen selectively to oxygen-deprived tissues in arms and legs; intended to enhance diffusion of oxygen through plasma to alleviate pain and ischemia caused by narrowed or blocked peripheral vessels. Diffusion Pharmaceuticals, LLC, Charlottesville, VA Phase I/II trials completed	Angioplasty Surgery Medications to prevent blood clots: Aspirin Plavix Symptom-relief medications: Cilostazol (Pletal)	Improved circulation in arms and legs Reduced pain Improved ability to walk
Urocortin 2 for treatment of heart failure	Patients in whom HF has been diagnosed	Urocortin 2 (infusion) is intended to mimic the effect of the newly discovered protein urocortin 2, which selectively stimulates the corticotropin-releasing factor (CRF2) receptor, thereby improving cardiac output with minimal increase in heart rate; new mechanism of action for cardioprotection by regulating calcium cycling enzymes/channels in heart muscle cells. Neurocrine Biosciences, Inc., San Diego, CA Phase II trials completed	ACE inhibitors ARBS Beta blockers Digitalis Diuretics	Increased cardiac output Improved cardioprotection Improved long-term cardiac outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vagus nerve stimulation (CardioFit) for treatment of congestive heart failure	Patients in whom severe congestive HF has been diagnosed	CardioFit® vagus nerve stimulation (VNS) is an implantable device intended to improve heart-pumping capacity in patients with severe congestive HF. BioControl Medical, Yehud, Israel Phase III trial (INOVATE-HF) ongoing	Optimal medical management Minimally invasive heart surgery Ventricular assist devices Heart transplantation	Improved left ventricular ejection fraction Improved 6-minute walk test Improved quality of life Reduced need for medication
Varespladib methyl (A-002) for treatment of acute coronary syndrome	Patients in whom acute coronary syndrome has been diagnosed	Varespladib methyl (A-002) secretory-type PLA2 inhibitor. Phospholipid molecules in the blood and vessel wall are broken down by sPLA2, producing two potentially bioactive fats that can be involved in atherosclerosis; intended to be used as adjunct to statin therapy. Anthera Pharmaceuticals, Inc., Hayward, CA Phase III trial ongoing	Lifestyle changes Lipoprotein-associated PLA2 drugs (also being studied)	Reduced atherosclerosis Reduced death Reduced MI Reduced stroke Improved unstable angina
Vernakalant (Kynapid) injection for treatment of acute atrial fibrillation	Patients in whom acute AFib has been diagnosed	Vernakalant (Kynapid™) is an injection intended to selectively block ion channels in the atria. Cardiome Pharma Corp., Vancouver, British Columbia, Canada, and Merck & Co., Inc., Whitehouse Station, NJ Phase III U.S. trial halted by FDA in Oct 2010 due to cardiogenic shock; FDA is reviewing data before allowing trial to restart; additional phase III trial ongoing; injection formulation approved in European Union Sept 2010	Ibutilide (Corvert) Electrical cardioversion	Reduced life-threatening ventricular arrhythmias Reduced hospital admissions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vernakalant (Kynapid) orally for treatment of atrial fibrillation	Patients in whom AFib has been diagnosed, whose rhythm has been successfully restored via cardioversion	Vernakalant (Kynapid) is a longer-acting, slow-release oral formulation of the injectable vernakalant potassium channel inhibitor; intended to selectively block ion channels in the atria; selectively inhibits IKur (Kv1.5), a current that is more predominant in atrial tissue (than in ventricular tissue). It is intended for use after successful cardioversion. Cardiome Pharma Corp., Vancouver, British Columbia, Canada and Merck & Co., Inc., Whitehouse Station, NJ Phase II trial to begin in late 2012.	Amiodarone (Cordarone®, Pacerone®) Dronedarone (Maltaq®) Propafenone (Rythmol®) Sotalol (Betapace®) Dofetilide (Tikosyn®) Flecainide (Tambocor™)	Increased time to recurrence of AFib Decreased ventricular arrhythmias Decreased hospital admissions

Table 4. AHRQ Priority Condition: 04 Dementia (including Alzheimer's): 19 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anavex 2-73 for treatment of Alzheimer's disease	Patients in whom Alzheimer's disease (AD) has been diagnosed	Anavex 2-73 acts as a sigma-1 receptor agonist and has muscarinic cholinergic effects and affects modulation of endoplasmic reticulum stress to prevent oxidative stress and apoptosis (programmed cell death); intended to alleviate neurotoxicity and cognitive deficits. Anavex Life Sciences Corp., Hoboken, NJ Phase I trial completed; phase IIa trial being planned	Current drug therapy for Alzheimer's disease	Delayed memory loss Delayed cognitive decline Longer maintenance of independent living
Anti-a-beta monoclonal antibody for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	Currently, no disease-modifying agents for AD are available, though several are in development. Anti-Abeta (also known as MABT5102A) is a humanized monoclonal antibody intended to be used for passive immunotherapy against beta amyloid (a-beta, main constituent of a-beta plaques); it is intended to promote clearance of a-beta protein from damaged sites of the brain; according to the manufacturer, the agent binds both monomeric and oligomeric forms of a-beta, inhibits a-beta aggregation, and promotes a-beta disaggregation. In clinical trials, being administered in both subcutaneous and intravenous formulations. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trials ongoing	Bapineuzumab Ponezumab Solanezumab	Reduced a-beta load in brain Slowed progression of AD Increased survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Antiamyloid monoclonal antibody (ponezumab) for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	Current drug therapy for AD has nonspecific antibodies that interact with many other brain processes; there is a need for therapy to reduce toxicity or presence of a-beta without creating other side effects. Ponezumab is a human monoclonal antibody intended to promote clearance of a-beta protein from damaged sites of the brain while minimizing adverse effects that may result from less-specific binding (i.e., monoclonal antibody to bind specifically to a-beta, but not to amyloid precursor protein [APP] also); it recognizes and binds to the free carboxy terminal amino acids 33 to 40 of the a-beta 1-40 peptide; also called PF-04360365. Pfizer, Inc., New York, NY Phase II trials completed	Galantamine Rivastigmine Donepezil Memantine	Decreased A-beta 40 load in brain Slowed disease progression Improved cognitive function Improved memory Increased ability to live independently longer Improved quality of life
AZD1446 for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	AZD1446 is a selective modulator of alpha4beta2. Targacept, Inc., Winston-Salem, NC Phase II trial completed	Medications to slow progression of AD	Delayed progression of AD symptoms Delayed need for intensive assistance with activities of daily living Improved quality of life Improved functional capacity
Bapineuzumab for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	Human monoclonal antibody intended to promote clearance of a-beta protein from damaged sites of the brain. Intended to minimize adverse effects that may result from less specific binding (i.e., monoclonal antibody to bind specifically to a-beta, but not to APP also); current drug therapy has nonspecific antibodies that interact with many other brain processes. Janssen Alzheimer Immunotherapy, Dublin, Ireland Pfizer, Inc., New York, NY Phase III trials ongoing	Other drug therapy for AD	Halted or delayed disease progression Preserved cognitive function Preserved memory Improved quality of life Ability to live independently longer

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Beta-amyloid immunotherapy (CAD-106) for Alzheimer's disease	Patients in whom mild to severe AD has been diagnosed	No disease-modifying treatments for AD are approved or available. CAD-106 is an active immunization targeting a-beta, which is thought to contribute to AD progression; CAD-106 is intended to induce a-beta-specific antibodies without stimulating A-beta-reactive T cells; the stimulation effect has been a safety concern with earlier attempts at immunotherapy for this population; in preclinical studies, the vaccine was shown to reduce amyloid burden in the brain. Administered via subcutaneous injection. Novartis AG, Basel, Switzerland Phase II clinical trials ongoing	Donepezil Galantamine Memantine Rivastigmine	Reduced AB load in brain Regression or slowing of disease progression Reduced morbidity and mortality Improved quality of life
Davunetide for treatment of mild cognitive impairment and/or Alzheimer's disease	Patients in whom mild cognitive impairment and/or AD has been diagnosed	Effective treatments to slow or halt progression of AD are needed. Davunetide is first-in-class agent intended to target tangles, rather than a-beta plaques; is an intranasal formulation of a microtubule-interacting peptide that is intended to promote neurite growth and restore transmission between nerve cells; derived from naturally occurring activity-dependent neuroprotective protein (ADNP); also known as AL-108. Allon Therapeutics, Inc., Vancouver, British Columbia, Canada Phase II trial completed	Galantamine Rivastigmine Donepezil Memantine	Improved working memory test scores (e.g., digit span) Delayed disease progression Improved quality of life
Estrogen receptor beta-selective phytoestrogenic formulation (phyto-beta-SERM) for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	No disease-modifying treatments for AD exist. This drug represents a novel mechanism of action for AD; phyto-beta-SERM is an estrogen receptor beta (ERbeta)-selective phytoestrogenic formulation comprised of three phytoestrogens. Phytoestrogens mimic the effects of estrogen at low doses, but may not be associated with an increase in breast cancer risk. Evidence suggests that phytoestrogens may be neuroprotective against toxic compounds, including a-beta. This mechanism is unclear, but may involve suppression of mitochondrial apoptosis (extrinsic cell death) and reduction of inflammation/oxidative stress. University of Southern California (USC), Los Angeles, CA Trial ongoing at USC	Donepezil Galantamine Memantine Rivastigmine	Delayed disease progression, or regression Improved outcomes (e.g., morbidity and mortality) Improved quality of life for patients and caregivers

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Exebryl-1for treatment of Alzheimer's disease	Patients in whom mild to moderate AD has been diagnosed	Exebryl-1 inhibits a-beta protein aggregate formation in the brain and disaggregates amyloid plaques already present; it targets both a-beta and tau protein (specificity toward tau protein aggregates) and is intended to slow AD progression. ProteoTech, Inc., Kirkland, WA Tasly Pharmaceuticals, Inc., Rockville, MD Phase I trial ongoing	Other drug therapy for Alzheimer's disease	Delayed or halted progression of Alzheimer's disease Preservation of cognitive ability and memory
Florbetapir F18 injection (Amyvid) contrast for positron emission tomography for beta-amyloid plaque imaging	Patients suspected of having an a-beta associated disease (e.g., AD, Lewy body dementia, Guam Parkinson dementia complex) who are undergoing positron emission tomography (PET)	Currently, there is no method for detecting a-beta in living patients suspected of having an a-beta-associated disease. Florbetapir F18 (Amyvid™) is a radiopharmaceutical that binds specifically to a-beta and is visualized by PET. Contrast agent would be indicated for visualization of a-beta aggregates; a negative result could help to rule out presence of pathologically relevant levels of a-beta plaques. Avid Radiopharmaceuticals, a subsidiary of Eli Lilly & Co., Indianapolis, IN Mar 2011, Lilly received complete response letter from FDA stating that company must institute a training program for those who will interpret results of an Amyvid-PET scan before FDA will grant approval	No current method of detecting a-beta in live patients Flutemetamol in development for same indication	Increased sensitivity of a-beta plaque detection Increased specificity of a-beta plaque detection
Flutemetamol-enhanced positron emission tomography for diagnosis of Alzheimer's disease	Patients in whom AD is suspected	A PET imaging agent to detect normal or raised amyloid levels and confirm a diagnosis of AD. General Electric Co., Fairfield, CT (GE Healthcare, Chalfont St. Giles, UK) Phase III trial ongoing	Other imaging agents used with PET Clinical exam and history Blood tests and other biomarkers	Sensitivity and specificity of PET for diagnosing AD Improved positive and negative predictive values Earlier diagnosis of AD Earlier intervention for management of early AD

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gamma secretase inhibitor (BMS-708163) for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	Currently, no disease-modifying treatments for AD exist. BMS708163 inhibits cutting of APP by gamma secretase, which in turn prevents the creation of a-beta 42, thought to contribute to the pathophysiology of AD. According to the manufacturer, does not disrupt the Notch signaling pathway. Administered as oral capsules. Bristol-Myers Squibb, New York, NY Phase II trials ongoing	Donepezil Galantamine Memantine Rivastigmine	Reduced a-beta load Slowing of disease progression, or regression Improved long-term outcomes Improved quality of life
Handheld event-related potential/ quantitative electroencephalo-graphy system (Cognision) for diagnosis of Alzheimer's disease	Patients in whom a diagnosis of AD is suspected	No means are available to definitively diagnose AD (prior to autopsy), and a significant gap exists between AD onset and the point at which treatment begins. There is an unmet need for diagnostic/screening tools that can detect the condition before significant loss of memory, cognition, and activities of daily living occur. Cognision™ System is a device intended to provide objective assessment of cognitive function via noninvasive technology using electrodes attached to a hat-like frame, which is placed on the head. The system is designed to measure auditory event-related potentials (ERP); according to the manufacturer, ERPs are generated in response to auditory stimuli and can accurately measure the cognitive performance of a patient's brain before overt AD symptoms are present; patient data are located into central data bank, which analyzes data and classifies the patient's brainwaves based on similarities to known neurologic risk profiles. Neuronetrix, Inc., Louisville, KY Trial ongoing (no phase listed)	Cerebrospinal fluid tests Neuropsychological test battery Positron emission tomography (PET) scans	Improved ability to diagnose, rule out, and/or screen for AD Earlier intervention Improved outcomes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Home-based behavioral therapy for dementia	Patients in whom dementia has been diagnosed who are living in a home environment with a caregiver	Nonpharmacologic, biopsychosocial-environmental intervention; goal of home-based therapy is to decrease physical and cognitive demands of daily activities to bring them more in line with patient capabilities. Occupational therapists interview caregivers to determine patient routines, habits, interests and caregiver concerns. Therapists then review the information and tailor training for caregivers to enable them to modify activities and approaches to patient support. Thomas Jefferson University, Philadelphia, PA Randomized controlled trial completed	Patient/caregiver educational programs (e.g., phone-based, one-time educational sessions) Drug therapy: Antipsychotics Cholinesterase inhibitors such as donepezil, galantamine, rivastigmine Memantine No intervention	More realistic expectations and understanding of patient Improved functional dependence Improved daily activities dependence Improved activity engagement Improved perceived well-being Improved confidence in using activities Improved quality of life
Immunoglobulin intravenously for treatment of Alzheimer's disease	Patients in whom mild to moderate AD has been diagnosed	No effective treatments for slowing the progression of AD are available. Intravenous immunoglobulin (IVIG) infusion is approved for treatment of many immune disorders; in patients with AD, IVIG is intended to clear a-beta from the brain, thereby blocking A-beta's detrimental effects on the brain. Dosing is still being determined, but will be administered as an infusion, every 2 or 4 weeks, depending on physician recommendation. Baxter International, Inc., Deerfield, IL Phase III trial ongoing	Galantamine Rivastigmine Donepezil Memantine	Reduced A-beta load in brain Halted or slowed disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Insulin sensitizer (MSDC-0160) for treatment of Alzheimer's disease	Patients in whom mild AD has been diagnosed	No disease-modifying treatments for AD currently exist; currently available drugs only treat symptoms, not the underlying causes of AD. MSDC-0160 is a novel insulin sensitizer that modulates mitochondrial metabolism. Research has suggested that that loss of mitochondrial function and decline in brain glucose metabolism may contribute to the pathology of AD. The manufacturer received a $773,000 grant from the Alzheimer's Drug Discovery Foundation (ADDF) to conduct a pilot phase IIa trial for this indication. Intended to be administered orally, 150 mg/daily. Metabolic Solutions Development Co., LLC, Kalamazoo, MI Phase II trial ongoing	Cholinesterase inhibitors Memantine	Delay or halt in progression of AD Improved long-term outcomes Improved quality of life
Solanezumab (LY2062430 beta-amyloid monoclonal antibody) for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	Current treatments for AD treat symptoms only, and are not effective for many patients. Current treatments also have no effect on disease progression. Solanezumab is a human monoclonal antibody that binds specifically to soluble a-beta and is intended to draw the peptide away from the brain through the blood to promote clearance of a-beta protein from damaged sites in the brain. Eli Lilly & Co., Indianapolis, IN Two phase III trials ongoing (EXPEDITION; EXPEDITION II)	Bapineuzumab Cholinesterase inhibitors Memantine	Decreased a-beta load in brain Slowed or halted disease progression Improved memory and cognition Improved survival Improved quality of life
Statins for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	Statins are hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (class of drug used to reduce cholesterol biosynthesis; upregulate low-density lipoprotein receptors in the liver, thereby promoting clearance of LDL from bloodstream); studies have demonstrated a link between statin use and a decreased prevalence of AD, so the drugs are under investigation for use in patients suspected of having AD; exact mechanism of action is unknown. National Institute on Aging, National Institutes of Health, Bethesda, MD Phase III trial completed	Galantamine Rivastigmine Donepezil Memantine	Slowed disease progression Decreased symptoms Improved long-term health outcomes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Viral delivery of nerve growth factor (CERE-110) for treatment of Alzheimer's disease	Patients in whom mild to moderate AD has been diagnosed	CERE-110 uses a deactivated virus (i.e., one that cannot replicate on its own) to transfer a gene to nerve cells in the brain to make nerve growth factor; nerve growth factor is a protein shown to be neuroprotective in the brain by maintaining nerve cell survival in brain tissue; injected into brain during surgical procedure. Ceregene, Inc., San Diego, CA Phase II trial ongoing	Currently, no treatment exists for changing the underlying neurobiology of the disease Drug therapies for relief from cognitive symptoms	Reduced apoptosis (programmed cell death) Reduced brain degeneration Preserved cognition Preserved memory Preserved independence Improved quality of life Reduced need for caregivers

Table 5. AHRQ Priority Condition: 05 Depression and Other Mental Health Disorders: 34 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Acupuncture for treatment of posttraumatic stress disorder	Patients in whom posttraumatic stress disorder (PTSD) has been diagnosed	Many patients with PTSD do not adequately respond to available treatments, which include pharmacotherapy (e.g., antidepressants) and psychotherapy; additional efficacious treatments are needed. Acupuncture is a type of Traditional Chinese Medicine (TCM) in which needles are inserted into specific points along meridians of the body. From a Western medicine perspective, acupuncture's efficacy may be related to its regulatory effects on the nervous system, which increases the activity of biochemicals (such as endorphins and immune system cells) at specific sites in the body, or related to its effect on brain chemistry and the release of neurotransmitters and neurohormones, which affect immune reactions and processes that regulate a person's blood pressure, blood flow, and body temperature. It is being investigated for use in patients with PTSD to reduce anxiety, sleep disruption, and other signs and symptoms. Department of Veterans Affairs (VA) Trials ongoing (no phase listed)	Pharmacotherapy Psychotherapy	Reduced symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ADX71149 (glutamate positive allosteric modulator) for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	About one-third of patients with schizophrenia do not respond adequately to currently available treatments and almost all currently available pharmacotherapies for schizophrenia cause extrapyramidal side effects (EPSs) to some degree. ADX71149 has a novel mechanism of action as a positive allosteric modulator (PAM) of glutamate receptor 2 (mGluR2) that is intended to fine-tune glutamate transmission, presumably by increasing the activity of the mGluR2; glutamate (specifically, mGluR2 activation) acts on the N-methyl-D-aspartate (NMDA) and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors and is known to play a role in schizophrenia; clinical data suggests EPSs are not associated with this drug, which is being investigated as both a monotherapy and adjunctive treatment. Addex Pharmaceuticals, Geneva, Switzerland Ortho-McNeil-Janssen Pharmaceuticals, Inc., Titusville, NJ Phase II trial ongoing	Atypical antipsychotics (e.g., quetiapine)	Decreased positive symptoms of schizophrenia Decreased EPSs Improved quality of life
Antipsychotic (LY-2140023) for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	LY-2140023 is an oral agent that acts through a novel pathway (glutamate receptors rather than dopamine receptors) and is intended to relieve schizophrenia symptoms. Eli Lilly & Co., Indianapolis, IN Phase III trials ongoing	Atypical antipsychotic drugs (e.g., Seroquel, Zyprexa)	Reduced symptoms Reduced side effects compared with other drugs Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bright light therapy for nonseasonal major depressive disorder	Patients in whom nonseasonal MDD has been diagnosed	Many pharmacologic and psychotherapeutic options are available for major depression, yet fewer than half of patients achieve remission, and antidepressant drugs have undesired side effects for many patients. Bright light therapy (BLT) has long been diffused for seasonal affective disorder but not for nonseasonal MDD. The exact mechanism of action unknown, but BLT is thought to target depression-associated neurotransmitter systems (serotonin, noradrenaline, dopamine) and the same brain structures as antidepressant pharmacotherapy. It would likely be used as an adjunct to other treatments. U.S. National Institute of Mental Health Trial completed	Antidepressant medication (SSRIs, SNRIs, etc.) Psychotherapy Combination therapy	Improved depression rating scale scores Improved sleep patterns Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Buspirone and melatonin combination (BCI-952) for treatment of major depressive disorder	Patients in whom MDD has been diagnosed	These patients have high rates of inadequate response to currently available medications. BCI-952 is a combination of low dose buspirone (generic antianxiety medication) and melatonin that is being investigated for the treatment of MDD. The company claims that the compound has shown neurogenic effects on human neural stem cells in vitro and produced neurogenesis in vivo, and it states that this activity can improve the MDD condition. BrainCells, Inc., San Diego, CA Phase II trial completed.	Atypical antipsychotic drugs (off-label) Selective serotonin reuptake inhibitors	Neurogenesis Improved depression symptoms Improved quality of life
Citizen soldier peer support outreach program (Buddy-to-Buddy) for returning veterans	Returning veterans in whom mental health or substance abuse conditions have been, or may be, diagnosed	Twenty-five percent to 40% of citizen soldiers (National Guard, Reserves) develop PTSD, clinical depression, sleep disturbances, or suicidal thoughts, but when veterans return home, barriers exist to receiving appropriate care, and about half of those needing medical or psychological intervention are not receiving care. The Buddy-to-Buddy (B2B) is a veteran outreach peer support program; according to the program's developers, returning soldiers are assigned a "Buddy One," who is a veteran who has received training in peer support and systematically makes contact (via telephone) with each of his or her assigned veterans to try to identify those who may benefit from further evaluation or referral; "Buddy Two" volunteers receive more intensive training in motivational interviewing approach, local resources, and they also receive weekly telephone supervision; these Buddies visit armories during drill weekends and are available by telephone to all soldiers. Currently available only to veterans in Michigan, but intending to scale up nationally. Developed by Michigan Army National Guard (MI ARNG); Michigan State University, East Lansing, MI; University of Michigan, Ann Arbor, MI; Buddy One funded by MI ARNG and the National Guard Bureau (NGB); Buddy Two funded by Major League Baseball charities, New York, NY; and McCormick Foundation, Chicago, IL Fully implemented in Michigan; outcomes evaluation is ongoing	Vet-to-Vet (peer support group meeting) program No peer support Professional only support	Increased access for veterans to medical and psychological support resources Improved mental health outcomes Improved substance abuse outcomes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Deep brain stimulation (Reclaim system) therapy for severe obsessive-compulsive disorder	Patients in whom severe OCD has been diagnosed	Electrode leads (Reclaim™ system) connected from chest to anterior limb of the internal capsule stimulate the patient's brain. Medtronic, Inc., Minneapolis, MN Approved under humanitarian device exemption as adjunct to medications and alternative to anterior capsulotomy in patients whose disease has failed to respond to three selective serotonin reuptake inhibitors	Anterior capsulotomy Psychotherapy alone Drug therapy alone Combination therapy	Reduced scores on OCD measures Improved quality of life
Deep brain stimulation (Reclaim system) therapy for treatment-resistant depression	Patients in whom treatment-resistant depression has been diagnosed	Neurostimulator (Reclaim system) implanted subcutaneously in chest; intended to deliver controlled electrical stimulation to targeted parts of the brain via thin wire electrodes. Medtronic, Inc., Minneapolis, MN Phase III trial ongoing	Transcranial magnetic stimulation Electroconvulsive therapy VNS Antidepressant medications	Reduced scores on depression scales Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Deep brain stimulation for treatment of Tourette syndrome	Patients in whom Tourette syndrome (TS) has been diagnosed	Approximately 200,000 people in the U.S. have been diagnosed with TS; however, many people with debilitating cases do not respond to currently available pharmacotherapy. Deep brain stimulation (DBS) involves implanting a battery-operated medical device (neurostimulator) in the brain to deliver electrical stimulation to targeted areas that control movement (e.g., subregions of the globus pallidus internus, centromedian-parafascicular [CM-Pfc], and ventralis oralis complex of the thalamus). The type of DBS device being used was not indicated. University of Florida, Gainesville, FL Trial ongoing (no phase listed) at University of Florida; University holds only FDA investigational device exemption approved for DBS for TS in U.S.	Antidepressants Botulinum toxin type A (Botox) injections Central adrenergic inhibitors Fluphenazine Pimozide Stimulant medications	Reduced symptom burden Improved quality of life
Deep brain stimulation of Brodmann's area 25 (Libra System) for treatment of major depressive disorder	Patients in whom treatment-resistant MDD has been diagnosed	Once multiple medications, psychotherapy, and electroconvulsive therapy (ECT) have failed, no proven treatment options exist for MDD; many patients do not respond to initial therapy. The Libra™ Deep Brain Stimulation System sends mild pulses of current from an implanted device to stimulate the brain. DBS leads are surgically placed within a target area in the brain and connected to a neurostimulator that is usually implanted under the skin near the collarbone. For depression, the manufacturer is investigating placement of the leads in Brodmann's area 25 (high concentration of serotonin). St. Jude Medical, Inc., St. Paul, MN FDA IDE trial ongoing	DBS using Medtronic Reclaim System in anterior capsule Deep transcranial magnetic stimulation Repetitive transcranial magnetic stimulation VNS	Reduced symptom burden Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Dimethoxy-benzylidene anabaseine for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	Dimethoxybenzylidene anabaseine (DMXB-A) is an alpha-7 neural nicotinic receptor (NNR) agonist, which is a novel target for schizophrenia because no drugs are currently indicated for treatment of cognitive symptoms of the disorder; patients with schizophrenia have poor psychosocial/cognitive functioning (e.g., cognitive symptoms), which has been associated with decreased expression of the alpha-7 NNR. Department of Veterans Affairs Phase II trial ongoing	Atypical antipsychotics Other NNR agonists in development	Improved cognitive function Improved clinical schizophrenia rating scales Improved quality of life
Gamma-aminobutyric acid agonist (BL-1020) for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	BL-1020 may address cognitive and negative symptoms, an unmet need in this population for which no therapies exist. Negative symptoms may be more common and detrimental on quality of life than positive symptoms and can be difficult to recognize; negative symptoms are an absence of normal responses, including blank stares, monotone and monosyllabic speech, few gestures, and disengagement or disinterest; these often persist in the lives of people with schizophrenia during periods of low (or absent) positive symptoms. BL-1020 has a novel mechanism of action (i.e., first in class) as a gamma aminobutyric acid (GABA) ester of perphenazine (Trilafon, typical antipsychotic, no efficacy in negative or cognitive symptoms); it blocks dopamine (DA) and serotonin (5HT) while increasing GABA activity (lowered levels of GABA participate in the pathogenesis of schizophrenia). BioLineRx, Ltd., Jerusalem, Israel Cypress Bioscience, Inc., San Diego, CA Phase II/III trial ongoing	Atypical antipsychotics DMXB-A TC-5619	Improved cognition Decreased negative symptoms Improved social functioning Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Glycine reuptake inhibitor (RG1678) for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed and who present with predominantly negative symptoms (e.g., flat affect, unable to experience pleasure, blank gaze)	Most drugs for schizophrenia treat the positive symptoms (e.g., hallucinations) and treatments are needed for the negative symptoms; RG1678 is a first-in-class glycine reuptake inhibitor; normalizes glutamate neurotransmission by increasing synaptic levels of glycine, an essential cofactor for N-methyl-D-aspartic acid receptors (NMDARs), which likely have a role in the pathophysiology of schizophrenia; without it, receptor does not work properly. Genentech, Inc., South San Francisco, CA, subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trials ongoing	Novel mechanism of action, so no comparators in class Atypical antipsychotics (e.g., quetiapine) Lithium	Meaningful reduction in negative symptoms of schizophrenia, as measured by clinical rating scales (e.g., Positive and Negative Syndrome Scale [PANSS]) Improved personal and social functioning
GLYX-13 for treatment-resistant depression	Patients in whom treatment-resistant depression has been diagnosed	GLYX-13 (glycine-site functional partial agonist selective modulator of NMAR) is an oral medication intended for treatment-resistant depression. Naurex, Inc., Evanston, IL Phase II trial ongoing	Other NMDAR modulators (e.g. ketamine) Selective serotonin reuptake inhibitors Cognitive behavioral therapy Psychotherapy Combination treatment	Improved score on standardized depression measures Reduced side effects Improved quality of life
Ketamine for treatment-resistant severe depression	Patients in whom treatment-resistant major depressive disorder or bipolar depression has been diagnosed	Oral NMDA (ketamine, a recreational drug) for rapid (within 40 minutes) relief of severe treatment-resistant depression. National Institutes of Health, Bethesda, MD Phase II trial ongoing	Other antidepressant medicines Electroconvulsive therapy Transmagnetic stimulation Psychotherapy Cognitive behavior therapy Combination therapies	Rapid response Improved treatment adherence Reduced symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Lisdexamfetamine (Vyvanse) for treatment-resistant major depressive disorder and bipolar depression	Patients in whom treatment-resistant MDD has been diagnosed	Lisdexamfetamine (Vyvanse®) is a prodrug of dextroamphetamine; currently indicated to treat attention-deficit/hyperactivity disorder; induces release of neurotransmitters dopamine and norepinephrine, which are known to contribute to maintaining alertness, focus, thought, effort, and motivation. Shire Pharmaceuticals, plc, Dublin, Ireland Phase III trials ongoing	Other amphetamines	Improved symptoms on major depression scales Improved quality of life
Lisdexamfetamine (Vyvanse) for treatment of negative symptoms in schizophrenia	Patients in whom schizophrenia has been diagnosed	Currently, no therapies exist for the effective treatment of negative symptoms in schizophrenia; negative symptoms may be more common and detrimental on quality of life even than positive symptoms; described as an absence of normal responses including, but not limited to, blank stares, monotone and monosyllabic speech, few gestures, disengagement or disinterest. Lisdexamfetamine is a prodrug of dextroamphetamine; currently indicated to treat attention deficit hyperactivity disorder; induces release of dopamine and norepinephrine, which contribute to maintaining alertness, focus, thought, effort, and motivation. Shire Pharmaceuticals, plc, Dublin, Ireland Phase II trial completed	Atypical antipsychotics BL-1020 (in development) RG-1678 (in development) RO4917838 (in development)	Reduced negative symptoms Improved social functioning Improved quality of life
Low-dose ondansetron (TO-2061) for treatment of obsessive compulsive disorder	Patients in whom obsessive compulsive disorder (OCD) has been diagnosed who have not adequately responded to selective serotonin reuptake inhibitors	Low-dose ondansetron (TO-2061) (a 5-HT3 [serotonin] receptor antagonist; downregulates dopamine), which is approved for chemotherapy-induced nausea and vomiting, is intended as an adjunctive therapy to selective serotonin reuptake inhibitors for patients with OCD who have not responded to other medications. Administered orally. Transcept Pharmaceuticals, Inc., Port Richmond, CA Phase II trial ongoing	Selective serotonin reuptake inhibitors Atypical antipsychotic drugs (off-label) Other combination therapy Cognitive behavioral therapy Psychotherapy	Reduced scores on OCD measures Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Loxapine (AZ-004) inhalation aerosol for acute agitation in schizophrenia or bipolar disorder	Patients with acute agitation related to underlying schizophrenia or bipolar disorder	Inhaled aerosol delivery of loxapine (Adusuve Staccato) using "novel" delivery method is intended to alleviate acute agitation episodes. Alexza Pharmaceuticals, Inc., Mountain View, CA FDA rejected NDA in 2010, requesting additional data on pulmonary safety; company resubmitted approval application in Aug 2011, FDA approval date set for Feb. 4, 2012	Atypical antipsychotics Typical antipsychotics Benzodiazepines	Rapid reduction in agitation symptoms Increased quality of life
Magneto-encephalography for diagnosis of posttraumatic stress disorder	Patients in whom PTSD is suspected	Magnetoencephalograph (measure of extremely weak magnetic fields generated by the brain) is proposed as a new "biomarker" for PTSD; abnormal brain signals found in part of brain are associated with memory (connected to ability to suppress bad memories). It is purported to identify patients with PTSD 97% of time. Brain Sciences Center in Minneapolis VA Medical Center, Minneapolis, MN Trial completed	Patient reports Clinical interviews	Increased sensitivity and specificity Improved positive and negative predictive value Earlier intervention and treatment
Extended intensive psychotherapy assisted by MDMA (methylenedioxymethamphetamine) for treatment of posttraumatic stress disorder	Patients in whom treatment-refractory PTSD has been diagnosed	Methylenedioxymethamphetamine (MDMA; ecstasy) has pharmacologic effects that include serotonin release, 5HT2 receptor stimulation, and increased levels of oxytocin, prolactin, and cortisol. exact mechanism of action unclear, but lowers inhibitions in a way that some think might make psychotherapy more productive. Patients receive 125 mg of pure methylenedioxymethamphetamine before two 8-hour sessions of intensive psychotherapy followed by overnight stay. MDMA is not given as long-term drug therapy (e.g., selective serotonin reuptake inhibitors). Its purpose is only to enhance psychotherapy to enable patients to engage in discussion. Funded by Multidisciplinary Association for Psychedelic Studies Phase II trial ongoing, with permission from FDA and the Drug Enforcement Administration (DEA)	Intensive psychotherapy alone Selective serotonin reuptake inhibitors alone Combination therapy	Improved efficacy of intensive psychotherapy sessions Improved rating scales (e.g., Clinician-Administered PTSD Scale [CAPS]) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Nicotinic receptor (TC-5619) agonist for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	No therapies exist to treat the cognitive symptoms of schizophrenia. TC-5619 is an alpha-7 NNR partial agonist and novel target for schizophrenia; patients with schizophrenia have poor psychosocial/cognitive functioning (e.g., cognitive symptoms), which has been associated with decreased expression of the alpha-7 NNR. Targacept, Winston-Salem, NC Phase II trial completed	Atypical antipsychotics Other NNR agonists in development	Improved cognitive symptoms Improved social functioning Improved quality of life
Psilocybin for treatment of anxiety in patients with advanced cancer	Patients with advanced cancer who are not responsive to conventional anxiety and mood therapies	Moderate dose (0.2 mgs/kg of body weight) is intended to reduce anxiety and pain for up to six months without adverse psychological or physiological events. Various organizations, including New York University and Los Angeles Biomedical Research Institute Trials ongoing	Conventional depression/anxiety drug therapy; psychotherapy	Reduced anxiety Reduced need for pain medication Improved quality of life
Reversible inhibitor of monoamine oxidase A (TriRima) for treatment-resistant depression	Patients in whom treatment-resistant depression has been diagnosed	Reversible and selective inhibitors of monoamine oxidase A (TriRima™); novel class of drugs; if approved, will be first monotherapy indicated for treatment-resistant depression. CeNeRx BioPharma, Inc., Cary, NC Phase II trials ongoing	Aurorix (only approved reversible inhibitor of monoamine oxidase A; not marketed in U.S.; approved in other countries) Monoamine oxidase inhibitors Selective serotonin reuptake inhibitors	Improved score on validated depression scales Reduced serious cardiovascular side effects associated with other monoamine oxidase A inhibitors

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Riluzole (Rilutek) off-label for treatment of major depressive disorder	Patients in whom treatment-resistant MDD has been diagnosed	Fewer than one-half of patients with MDD achieve remission with currently approved antidepressant therapy. The mechanism of action of riluzole (Rilutek®) would be novel for this disease state. Riluzole is a glutamatergic modulator currently FDA approved for treatment of amyotrophic lateral sclerosis (ALS); glutamate is the primary excitatory neurotransmitter in the brain, and the glutamatergic system plays a major role in MDD. Riluzole has been shown to inhibit glutamate release, enhance glutamate reuptake, and protect glial cells against glutamate excitotoxicity. National Institute of Mental Health, Bethesda, MD Sanofi-Aventis, Bridgewater, NJ, makes the drug but is not sponsoring the trial Phase II trials ongoing	Antidepressant pharmacotherapy (selective serotonin reuptake inhibitors) DBS Electroconvulsive therapy Psychotherapy Transcranial magnetic stimulation VNS	Glutamatergic modulation Improved MDD symptoms Improved quality of life
RO4917838 for treatment of negative symptoms of schizophrenia	Patients in whom schizophrenia has been diagnosed	Glycine transporter type 1 inhibitor (RO4917838); elevation of extracellular synaptic glycine concentration by blockade of glycine transporter type 1 has been hypothesized to potentiate N-methyl-D-aspartic acid receptor function. Intended to mediate negative symptoms (blank stares, monotone and monosyllabic speech, lack of animation, seeming lack of interest in the world and other people, inability to feel pleasure). Current treatment focuses on positive symptoms. F. Hoffmann-La Roche Ltd., Basel, Switzerland Phase III trials ongoing	Current drug therapy for schizophrenia (positive symptoms, e.g., hallucinations)	Symptom improvement Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Serotonin-norepinephrine-dopamine reuptake inhibitor (EB-1010) for treatment of depression	Patients in whom MDD has been diagnosed who do not respond adequately to selective serotonin reuptake inhibitors	A novel, unbalanced, triple serotonin-norepinephrine-dopamine reuptake inhibitor (EB-1010) antidepressant that acts simultaneously as a reuptake inhibitor for the three monoamines; demonstrates greatest affinity for transporters that inhibit serotonin reuptake, half as much against norepinephrine reuptake, and an eighth as much against dopamine reuptake. Euthymics Biosciences, Inc., Cambridge, MA Phase II/III trial ongoing	DBS Electroconvulsive therapy Psychotherapy Transcranial magnetic VNS Medicines: Selective serotonin reuptake inhibitors Serotonin and norepinephrine reuptake inhibitors	Increased serotonin, norepinephrine, and dopamine neurotransmission Improvement in symptoms, as measured by standard depression rating scales Improved quality of life
Serotonin receptor antagonist (ITI-007) for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	ITI-007 acts as a 5-HT2A (serotonin) receptor antagonist intended to alter phosphorylation status of phosphoproteins downstream from dopamine receptor to treat symptoms of schizophrenia with fewer side effects (cardiovascular, weight gain, cognitive defects) than current schizophrenia treatments; taken orally. Intra-Cellular Therapies, Inc., New York, NY Phase Ib/II trial completed; phase II trial planned	Other schizophrenia drugs Cognitive behavioral therapy Psychotherapy Combination drug/behavioral therapy	Decreased symptoms Reduced concomitant depression Fewer side effects

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Synthetic neurosteroid (Ganaxolone) for treatment of posttraumatic stress disorder	Patients in whom PTSD has been diagnosed	Despite pharmacotherapy and psychotherapy, many patients have treatment-resistant PTSD. Ganaxolone (3 alpha-hydroxy-3 beta-methyl-5 alpha-pregnan-20-one) is a 3beta-methylated synthetic analog of allopregnanolone (a naturally occurring neuromodulator that is a neurosteroid metabolite of progesterone); researchers believe that neurosteroid (allopregnanolone) levels play a role in the severity and outcomes for patients with PTSD. Ganaxolone is intended to regulate inhibitory GABA as a positive allosteric modulator (PAM). Marinus Pharmaceuticals, Inc., Branford, CT, in public-private collaboration with INTRuST Consortium (group of clinical study centers in the U.S. funded by Department of Defense) Phase II trial ongoing	Acupuncture (in development) Counseling (e.g., cognitive behavior therapy; group therapy) Selective serotonin reuptake inhibitors (SSRIs)	Improved symptoms Improved quality of life
TC-5214 (mecamylamine) for treatment of major depressive disorder	Patients in whom treatment-resistant MDD has been diagnosed	Mecamylamine blocks alpha 3, beta 4 nicotinic receptors in brain; depression symptoms are associated with an overstimulation of neuronal nicotinic receptors and other receptors in the brain that are activated by the neurotransmitter acetylcholine. AstraZeneca, London, UK Targacept, Inc., Winston-Salem, NC Phase III trials (five trials) ongoing; phase I trial ongoing in elderly patients who are medically stable	Other antidepressants Combination therapy Psychotherapy Transcranial magnetic stimulation Electroconvulsive stimulation DBS for treatment-resistant depression Vagus-nerve stimulation for treatment-resistant depression	Improved depression scores on validated depression instruments Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Text-messaging therapy for bulimia nervosa	Patients in whom bulimia nervosa has been diagnosed	Feelings of shame affect willingness to undergo treatment, and access to treatment and duration of treatment are significant issues with eating disorders because of chronic nature of the disorders. New approaches to behavioral therapies that engage participants ongoing are needed. In this program, participants send nightly text message to clinicians to report the number of binge eating and purging episodes and rate their urges to binge and purge; participants receive automatic feedback message tailored to their self-reported symptoms. This approach is being studied in conjunction with a cognitive behavioral therapy program to keep patients engaged in therapy. University of North Carolina at Chapel Hill Trial completed (no phase stated)	Antidepressant medication Cognitive behavioral therapy and other psychological counseling Nutritional counseling Combination therapy	Reduced number of binge eating and purging episodes Improved symptoms of depression, eating disorder, and night eating Enhanced self-monitoring and treatment, leading to improved attendance, adherence, and engagement in treatment Increased remission

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Trigeminal nerve stimulation (eTNS) for treatment of major depressive disorder	Patients in MDD has been diagnosed	Available pharmacotherapies for MDD are characterized by limitations, including lack of efficacy for many patients and unwanted side effects; options for treatment-resistant MDD (e.g., deep brain stimulation, VNS, transcranial magnetic stimulation, or repetitive transcranial magnetic stimulation [rTMS]) are surgically invasive and must be performed in a hospital setting. Trigeminal nerve stimulation (eTNS) is noninvasive; mild electrical signals pass through electrodes placed on the patient's forehead. Stimulation is intended to transcutaneously stimulate the various branches of the trigeminal nerve (the largest cranial nerve), which projects to the amygdala (mood regulation). The stimulation is controlled by an external pulse generator worn by patient during 8 hours of sleep. Researchers are also developing sTNS version (subcutaneous electrodes and implantable pulse generator). University of California, Los Angeles, CA, and NeuroSigma, Inc., Los Angeles, CA Phase II trial ongoing	DBS Electroconvulsive therapy Pharmacotherapy rTMS VNS	Improved depression symptoms Improved quality of life
Trigeminal nerve stimulation (eTNS) for treatment of posttraumatic stress disorder	Patients in whom PTSD has been diagnosed	Many patients with PTSD do not adequately respond to pharmacotherapy and psychotherapy; additional efficacious treatments are needed. eTNS is a noninvasive therapy in which mild electrical signals pass through electrodes placed on the forehead. It is intended to transcutaneously stimulate the various branches of the trigeminal nerve (the largest cranial nerve), which projects to the amygdala (mood regulation). The stimulation is controlled by an external pulse generator and worn by patient during 8 hours of sleep. Researchers are also developing sTNS version (subcutaneous electrodes and implantable pulse generator). University of California, Los Angeles, CA, and NeuroSigma, Inc., Los Angeles, CA Phase I trial ongoing	Pharmacotherapy Psychotherapy	Improved symptom burden Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Wisdom therapy for posttraumatic embitterment disorder	Patients in whom posttraumatic embitterment disorder (PTED) has been diagnosed	PTED is an emerging condition and does not have an established therapeutic regimen. Wisdom therapy is a relatively young field of psychology; somewhat related to motivational interviewing; based on the concept that cognition and reflection (central aspects of wisdom) may help one to overcome bitterness. Embitterment is the outcome of a particular way of handling life experiences, as is wisdom, so wisdom therapy may provide an avenue for growth while dealing with negative life experiences. First described by Michael Linden, Charité University Hospital, Berlin, Germany Pilot trial completed	Pharmacotherapy (e.g., selective serotonin reuptake inhibitors)	Improved symptoms Improved quality of life

Table 6. AHRQ Priority Condition: 06 Developmental Delays, ADHD, and Autism: 18 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
AFQ056 for treatment of fragile X syndrome	Patients in whom fragile X syndrome (FXS) has been diagnosed	There is no cure for FXS; medications and behavioral interventions alleviate individual symptoms but do not address the cause of FXS. Individuals with FXS have DNA mutations in the *FMR1* gene that basically turn off the gene; normal *FMR1* gene produces a protein that controls the synthesis of proteins at synapses that are stimulated via metabotropic glutamate receptors (mGluRs); without this control provided by the FMR1 protein, synaptic protein synthesis is excessive and connections do not develop normally. AFQ056, a selective, noncompetitive antagonist of the metabotropic glutamate receptor 5 (mGluR5), may potentially normalize the excessive protein synthesis and control symptoms associated with FXS. Dose range will be 25, 50, and 150 mg twice a day. Drug is also under study for Parkinson's disease and Huntington's disease. Novartis AG, Basel, Switzerland Phase II/III trials ongoing	Physical and behavioral interventions including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Medications: Antipsychotics Central nervous system (CNS) stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors	Change baseline in behavioral symptoms using the Aberrant Behavior Checklist
Detector (Q Sensor) to predict severe emotional distress in autism	Children in whom autism spectrum disorders have been diagnosed	The Q Sensor is a device worn on a wristband or anklet and is intended to records physiologic signs of stress and excitement by measuring slight electrical changes in the skin; intended to help predict impending emotional meltdowns for early intervention; includes software for viewing, comparing, and annotating data in a PC or Mac computer. Affectiva, Inc., Waltham, MA Commercially available (not subject to FDA regulation)	Biofeedback monitors Human observation (teachers, therapists, parents, other caregivers)	Reduced number of meltdowns Reduced self-harm behaviors (e.g., head banging) Improved ability to proactively intervene with calming measures Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Donepezil (Aricept) off-label for treatment of fragile X syndrome	Patients in whom FXS has been diagnosed	There is no cure for FXS; medications and behavioral interventions alleviate individual symptoms but do not address the cause of FXS. FXS is a neurodevelopmental disorder caused by mutations of the *FMR1* gene and is the most common known heritable cause of cognitive and behavioral disability; abnormalities of cholinergic pathway function and neurochemistry observed with functional magnetic resonance imaging (fMRI) in FXS patients makes researchers believe that functional cholinergic deficits contribute to cognitive-behavioral dysfunction in FXS. Aricept® (donepezil HCl) is a cholinesterase inhibitor that is intended to improve memory, attention, social interaction, reasoning and language abilities, and ability to perform activities of daily living by increasing the amount of acetylcholine in the brain by reversibly inhibiting its hydrolysis by acetylcholinesterase; may potentially augment the cholinergic system in adolescents affected by FXS. Approved to treat mild, moderate and severe Alzheimer's disease and is under study for various other types of cognitive impairment, including Down syndrome. Under study by Autism Speaks, New York, NY, National Institute of Mental Health, Rockville, MD, and Stanford University, Palo Alto, CA Phase II trial ongoing	Physical and behavioral intervention including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Medications: Antipsychotics CNS stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors	Improvements in specific measures of behavior and cognition Improved scores on behavior assessments Improved scores on working memory tests
Enzyme (CM-AT) to enhance protein digestion in children with autism	Children in whom autism has been diagnosed	An enzyme (CM-AT) is intended to enhance protein digestion, affecting amino-acid building. It is believed that many children in whom autism has been diagnosed do not digest protein properly. Enzyme is formulated as a powder, and given orally, with food. Curemark, LLC, Rye, NY Phase III trial ongoing; has fast-track status from FDA	Medications Behavioral and educational programs Other dietary supplements	Improved core symptoms

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Functional magnetic resonance imaging for differentiating autism from bipolar disorder in children	Children suspected of having autistic spectrum disorder	Bipolar disorder and autism can have similar signs and symptoms in young children and differentiating between the two when making a diagnosis can be very difficult. Functional MRI is being investigated as a means of differentiating the two conditions by observing patterns of activity in the brain during MRI. Twenty individuals previously diagnosed with autism spectrum disorder were studied; next goal is to test in children suspected of having autism. Institute of Psychiatry, King's College, London, UK Phase I trial completed	Assessments based on interviews and behavioral observation	Early diagnosis Early intervention and treatment Improved quality of life
Ganaxolone for treatment of fragile X syndrome	Patients in whom FXS has been diagnosed	There is no cure or specific treatment for FXS; pharmacologic treatments that address FXS social deficits are needed because impairments in social function are a core feature of FXS. Ganaxolone is the 3beta-methylated synthetic analog of the neurosteroid allopregnanolone, a metabolite of progesterone; reduced gamma aminobutyric acid A (GABA-A) receptor expression in FXS includes heightened sensitivity to sensory stimuli, anxiety, and seizures in some patients; developers theorize that ganaxolone, which demonstrates high affinity for GABA-A/delta receptors, could increase signaling at existing receptors to normalize GABA-mediated inhibition to reduce anxiety, hyperactivity, and learning disabilities associated with FXS. Marinus Pharmaceuticals, Inc., Branford, CT Early phase trial planned to start 4Q 2011	Physical and behavioral intervention including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Medications: Antipsychotics CNS stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors To address sleep disturbances To treat seizures and mood instability	Improved behavioral and cognitive measures Increased sociability and communication Improved scores on scales of sociability

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Hyperbaric oxygen therapy for treatment of autism spectrum disorders	Patients in whom an autism spectrum disorders have been diagnosed	Patients are exposed to high concentration oxygen at elevated pressure for short periods of time over the course of a few months (about 40 treatments of 1 hour each). Johnson Center for Child Health and Development, Austin, TX; Various academic medical research centers Phase I trial completed; other pilot trials ongoing	Risperidone Off-label treatments, including: acetylcholinesterase inhibitors, alpha-2 adrenergic agonists, carnitine, immunomodulation and anti-inflammatory treatments, melatonin, music therapy, naltrexone, oxytocin, tetrahydrobiopterin, and vitamin C Behavioral programs for autistic children	Improvement in symptoms as measured by Clinical Global Impression Scale, Aberrant Behavior Checklist, and Autism Treatment Evaluation Checklist
Interactive robotic dolls for improving social skills in childhood autism	Children in whom autism has been diagnosed	Robotic doll-based therapy intended to improve communication skills and interaction abilities of children who have limited or no verbal skills. Carnegie Mellon University Entertainment Technology Center, Autism Center, Pittsburgh, PA Early phase development	Educational and behavioral programs for autistic children Other robotic dolls in development	Improved social skills and human interaction Improved quality of life Improved activities of daily living

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
N-acetylcysteine for treatment of autism	Children receiving a diagnosis of autism	According to the U.S. Centers for Disease Control and Prevention, autism spectrum disorders are diagnosed in about 9 of 1,000 people in the U.S. Current therapies include behavioral programs, devices, and pharmacotherapies. N-acetylcysteine is (NAC) a glutamate modulator and antioxidant known to increase glutathione in children diagnosed with autism. For children in whom autism has been diagnosed, NAC is administered orally, 900 mg twice daily, or 900 mg three times daily, in one study; in another study evaluating NAC for treatment of autism spectrum disorders, NAC is being administered orally, 60 mg three times daily, with a maximum dose of 4,200 mg/day. Stanford University School of Medicine, Stanford, CA, and Indiana University School of Medicine, Indianapolis, IN, in collaboration with National Alliance for Autism Research, Princeton, NJ Stanford University School of Medicine: phase II trial completed Indiana University School of Medicine: phase II trial completed	Behavioral programs for autistic children Risperidone Off-label treatments, e.g. Acetylcholinesterase inhibitors Alpha-2 adrenergic agonists Carnitine Immunomodulation and antiinflammatory treatments Melatonin Naltrexone Oxytocin Tetrahydrobiopterin	Improved Clinical Global Rating Scale results Improved Repetitive Behavioral Scale score Improved social responsiveness Improved speech and language Improved metabolic measures Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label memantine (Namenda) for treatment of Down syndrome	Patients in whom Down syndrome has been diagnosed	Trisomy 21, or Down syndrome, is a genetic disorder that causes both physical and mental limitations or delays and health problems. Down syndrome occurs in about 1 in 700 births. Currently, some treatments are known to improve complications of Down syndrome, but few options are intended to improve brain function. Memantine (Namenda®) is in a class of medications called N-methyl-D-aspartate (NMDA) receptor antagonists and is already approved by FDA for Alzheimer's disease. It is intended to work by decreasing abnormal activity in the brain by binding to NMDA receptors on brain cells to block activity of the neurotransmitter glutamate. At normal levels, glutamate is believed to aid in memory and learning, but if levels are too high, glutamate appears to cause neuronal death. University of Colorado School of Medicine, Aurora, CO, in collaboration with Forest Laboratories, Inc., New York, NY Phase IV trial ongoing	Counseling and behavioral training Medications to treat disease complications	Increased brain function and cognitive activity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label intranasal oxytocin for treatment of social dysfunction in autism spectrum disorders	Patients in whom autistic spectrum disorder (ASD) or Asperger's syndrome has been diagnosed	Most individuals with ASD are treated through highly structured behavioral programs to try to improve social cognition and functioning; pharmacologic therapies address symptoms of hyperactivity and depression; pharmacologic treatments for social deficits in individuals with ASD are lacking; a pharmacologic treatment targeted at the core social deficits of ASD in early childhood could affect developmental pathways to make other psychosocial interventions possible. Oxytocin acts on smooth muscle cells (causes uterine contractions and milk ejection); it also can influence activity in brain amygdala, an area involved in social and emotional processing; oxytocin may increase visual contact to eye region of human faces, increase memory for faces, and improve the ability of people to infer the mental states of others, which are challenges associated with autism; potential improvements in social function and quality of life and reductions in certain types of repetitive behaviors may be realized with oxytocin therapy. Clinical trial dose: 0.4 IU/kg morning and lunch. Montefiore Medical Center, Bronx, NY; Mount Sinai School of Medicine, New York, NY; Victoria Apotheke, Zurich, Switzerland is the source of the oxytocin; trial is funded by U.S. Department Of Defense, Washington, DC, University of Illinois, Urbana, IL, and Holland Bloorview Kids Rehabilitation Hospital, Toronto, Ontario, Canada Phase II trials ongoing in Canada and U.S.	Applied behavior analysis Floortime Gluten free, casein free diet Occupational therapy PECS (communicate using picture cards) PRT (teach language, decrease disruptive/self-stimulatory behaviors) Relationship development intervention SCERTS (practices and strategies from other approaches) Sensory integration therapy Speech therapy TEACCH (special education program) Verbal behavior intervention	Improved Diagnostic Analysis of Nonverbal Accuracy (DANVA2) results Improved Change Social Responsivity Scale (SRS) score Improved Change Clinical Global Impressions Scale - Improvement(CGI-I) score
Mecasermin (Increlex) for treatment of Rett's syndrome	Children aged 2 to 12 years in whom Rett's syndrome has been diagnosed	Mecasermin (Increlex®) is a synthetic form of insulin-like growth factor-1 to stimulate synaptic maturation and is intended to improve cognitive function in children with Rett's syndrome. Ipsen (acquired developer Tercica Pharmaceuticals), Paris, France Phase II trial ongoing	Educational programs	Improved neurodevelopmental symptoms (severe cognitive, motor, and language problems and autistic behaviors)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ND0801 dermal patch for cognitive improvement in adults with attention deficit hyperactivity disorder	Adults in whom attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) has been diagnosed	ND0801 dermal patch is intended to work by preventing desensitization of nicotinic receptors, thereby improving cognition and focus. NeuroDerm, Ltd., Ness Ziona, Israel Phase IIa trial ongoing	Standard medications for ADHD	Cognitive improvement Fewer side effects than current ADHD stimulant medications Improved quality of life
Off-label minocycline for treatment of fragile X syndrome	Patients in whom FXS has been diagnosed	There is no cure for FXS; medications and behavioral interventions alleviate individual symptoms but do not address the cause of FXS. In FXS, synaptic protein synthesis is excessive and connections do not develop normally. Minocycline is an antibiotic used in children for infection and is being investigated for treatment of FXS; minocycline lowers matrix metalloproteinase 9 (MMP9) levels, which are high in FXS, and it also strengthens brain connections according to animal models of FXS; potential benefits include improved language, behavior and/or cognition in children with FXS. Administration is orally once a day for 3 months. University of California, Davis, CA Trial ongoing (phase unstated)	Medications to address sleep and behavior and mood symptoms: Antipsychotics CNS stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors	Improved behavior, perceptual and cognitive development Improved daily living skills Improved gross motor skill development Increased sociability and communication Improved speech and language

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
RO4917523 for treatment of fragile X syndrome	Patients in whom FXS has been diagnosed	There is no cure for FXS; medications and behavioral interventions alleviate some individual symptoms, but do not address the underlying cause of FXS. Individuals with FXS have DNA mutations in the *FMR1* gene that basically turn off the gene; normal *FMR1* gene produces a protein that controls the synthesis of proteins at synapses that are stimulated via metabotropic glutamate receptors (mGluRs); without this control provided by the FMR1 protein, synaptic protein synthesis is excessive and connections do not develop normally. RO4917523, an antagonist of one type of mGluR receptor, mGluR5, may potentially normalize the excessive protein synthesis and control symptoms associated with FSX. F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trial completed	Physical and behavioral intervention including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Medications: Antipsychotics CNS stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors To address sleep disturbances To treat seizures and mood instability	Improved behavioral and cognitive measures Improved daily living skills Improved gross motor skill development Increased sociability and communication Improved sensory system Improved speech and language skills
STX107 for treatment of fragile X syndrome	Patients in whom FXS has been diagnosed	There is no cure for FXS; medications and behavioral interventions alleviate individual symptoms but do not address the cause of FXS. Individuals with FXS have DNA mutations in the *FMR1* gene that basically turn off the gene; normal *FMR1* gene produces a protein that controls the synthesis of proteins at synapses that are stimulated via metabotropic glutamate receptors (mGluRs); without this control provided by the FMR1 protein, synaptic protein synthesis is excessive and connections do not develop normally. STX107 selectively inhibits one type of mGluR receptor, mGluR5, and may potentially normalize the excessive protein synthesis that may give rise to symptoms associated with FXS. Seaside Therapeutics, Inc., Cambridge, MA Phase II trial ongoing	Physical and behavioral intervention including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Medications: Antipsychotics CNS stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors To address sleep disturbances To treat seizures and mood instability	Improved behavioral and cognitive measures Improved daily living skills Improved gross motor skill development Increased sociability and communication Improved sensory system Improved speech and language skills

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
STX209 (arbaclofen) for treatment of fragile X syndrome	Patients in whom FXS has been diagnosed	There is no cure for FXS; pharmacologic treatments that address FXS social deficits are needed because impairments in social function are a core feature of FXS. Research suggests that individuals with FXS have abnormalities in synaptic transmission. STX209 (arbaclofen) is a selective gamma aminobutyric acid type B (GABA-B) receptor agonist; through the GABA-B receptor, STX209 may serve to restore the normal balance at the synapse and correct abnormalities associated with FXS. Seaside Therapeutics, Inc., Cambridge, MA Phase III trials ongoing	Physical and behavioral intervention including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Medications: Antipsychotics CNS stimulants Clonidine (Catapres) Folic acid Selected serotonin reuptake inhibitors To address sleep disturbances To treat seizures and mood instability	Improved behavioral and cognitive measures Increased sociability and communication

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
STX209 (arbaclofen) for treatment of social withdrawal in autism spectrum disorder	Patients in whom autism spectrum disorders (ASD) has been diagnosed	Most individuals with ASD are treated through highly structured behavioral programs to try to improve social cognition and functioning; pharmacologic treatments to address ASD-related social deficits are lacking (existing pharmacologic treatments address symptoms such as hyperactivity, irritability, anxiety, or depression, not social deficits); a pharmacologic treatment targeted at the core social deficits in areas of communication or repetitive behaviors and restricted interests is needed. Research suggests an imbalance in GABA/glutamate transmission underlies behavioral deficits of ASD; arbaclofen is intended to improve synaptic functioning by regulating glutamate and increasing GABA (the main inhibitory neurotransmitter in the CNS), an inhibitory transmitter, which counteracts the over-excitability of cells. STX209, a GABA-B agonist, has been proposed as a treatment to normalize this deficiency. Clinical trials dosage: disintegrating tablet (ODT) 5 or 10 mg twice a day, 10 or 15 mg three times a day. Seaside Therapeutics, Inc., Cambridge, MA Phase II trial ongoing	Applied behavior analysis Floortime Gluten free, casein free diet (GFCF) Occupational therapy PECS (communicate using picture cards) PRT (teach language, decrease disruptive/self-stimulatory behaviors) Relationship development intervention SCERTS (practices and strategies from other approaches) Sensory integration therapy Speech therapy TEACCH (special education program) Verbal behavior intervention Investigational: Oxytocin nasal Brief parent-mediated intervention Friendship training program	Improvement in Aberrant Behavior Checklist-Social Withdrawal Subscale

Table 7. AHRQ Priority Condition: 07 Diabetes Mellitus: 47 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Alpha-1 antitrypsin (AAT) for treatment of type 1 diabetes mellitus	Patients in whom type 1 diabetes mellitus (T1DM) has been diagnosed	Current therapies for T1DM have had variable results and other therapies are needed to more effectively treat and slow progression of T1DM. Alpha-1 antitrypsin (AAT) has shown antiinflammatory properties and although the level of AAT in diabetes patients is normal, its activity appears to be significantly lower. These anti-inflammatory properties are believed to have potential to interfere with or even prevent autoimmune destruction of beta cells in the pancreas. AAT is administered intravenously at 40, 60, or 80 mg per dose, in four-week intervals. Kamada, Ltd., Ness Ziona, Israel National Institute of Allergy and Infectious Disease, Bethesda, MD University of Colorado, Denver, CO, in collaboration with Omni Bio Pharmaceuticals, Inc., Greenwood Village, CO Phase I/II trial and Phase II trials ongoing; FDA granted orphan drug designation	Dietary and lifestyle modifications Various modifications to insulin	Reduced daily insulin usage Improved hemoglobin A_{1C} levels Reduced complications of diabetes Improved quality of life
Allogeneic fecal enema for treatment of metabolic syndrome in obese patients	Obese patients in whom metabolic syndrome (at least three of five National Cholesterol Education Project metabolic syndrome criteria) has been diagnosed	Fecal matter is harvested from healthy lean donors, processed, and transferred into obese patients with metabolic syndrome in an effort to treat insulin resistance and obesity by populating the lower intestinal tract with the flora of a healthy, lean person. Academic Medical Center/University of Amsterdam, the Netherlands Pilot trial completed	Dietary and exercise changes Bariatric surgery Anti-obesity drugs	Improved fecal flora composition Weight loss Resolution of metabolic syndrome

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anakinra interleukin-1 receptor antagonist for treatment of type 2 diabetes	Patients in whom type 2 diabetes (T2DM) has been diagnosed	Research has implicated inflammation in the development of insulin resistance associated with T2DM; however, no antiinflammatory treatments are currently approved for treatment of T2DM. Anakinra is a recombinant protein inhibitor of interleukin-1 (IL-1) receptors that has been approved since 2001 for treatment of rheumatoid arthritis; IL-1 is a proinflammatory cytokine that has been observed in pancreatic sections obtained from patients with T2DM and may play a role in the inflammatory process leading to T2DM progression. Amgen, Inc., Thousand Oaks, CA (manufacturer); Radboud University Nijmegen, the Netherlands (investigator) University Hospital, Zurich, Switzerland and Steno Diabetes Center, Gentofte, Denmark (investigators) Unphased and phase II trials ongoing	Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sulfonylurea drugs (glimepiride)	Desired HbA_{1c} level control Desired fasting glucose level control Resolved insulin sensitivity
Angiotensin analog (DSC127) for treatment of diabetic foot ulcers	Patients in whom diabetic foot ulcers have been diagnosed	Current treatments for diabetic foot ulcers result in complete healing less than 30% of the time; therefore, effective treatments are intended to accelerate and complete the wound healing process. DSC127 is an analog of the human peptide signaling molecule angiotensin; angiotensin has properties that are believed to improve wound healing, including increasing keratinocyte/mesenchymal stem cell proliferation, extracellular matrix production, and vascularization; DSC127 has been modified from endogenous angiotensin to remove the normal effects of the peptide on blood pressure; applied daily as a topical gel until the wound is healed. Derma Sciences, Princeton, NJ Phase II trial completed	Cellular wound matrices Acellular wound matrices Negative pressure wound therapy Hyperbaric oxygen therapy	Increased percentage of ulcers healed Decrease in ulcer size

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Artificial pancreas for treatment of diabetes	Patients in whom T1DM or T2DM has been diagnosed who require insulin and are highly motivated to use the system and monitor its function	Artificial pancreas is a closed-loop system consisting of an insulin pump, a real-time glucose monitor, and a sensor to detect glucose levels. Various manufacturers have made components required for the artificial pancreas. However, no single manufacturer has created a total closed loop system. Sixteen systems are in early-phase trials. Various manufacturers Early phase development	Injected insulin External insulin pump	Reliable glycemic control at desired levels Reduced risk of acute and nighttime hypoglycemia Reduction in postprandial (after meal) hyperglycemia Halted or delayed progression of secondary complications Improved quality of life
Atrasentan for treatment of chronic kidney disease in type 2 diabetes	Patients in whom T2DM has been diagnosed and who have chronic kidney disease (CKD)	Current treatments only modestly slow disease and patients ultimately need dialysis. Atrasentan is a highly selective endothelin-A receptor antagonist, which blocks the effect of endothelin-I, a protein that constricts blood vessels and raises blood pressure, thereby decreasing kidney function. In conjunction with renin-angiotensin system inhibitors, Atrasentan may reduce albuminuria (presence of protein in urine) which occurs as kidney function decreases. Abbott Laboratories, Abbott Park, IL Phase II trial completed	Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sulfonylurea drugs (glimepiride) Various drugs under development	Reduced urine albumin-to-creatinine ratio Improved kidney function Improved quality of life
Bariatric surgery for resolution of diabetes in obese and nonobese patients	Obese and nonobese patients in whom T2DM has been diagnosed	Bariatric surgery (gastric bypass, lap banding, sleeve gastrectomy) for resolution of T2DM. Some researchers suggest that bariatric surgery could be used to treat, or possibly "cure," patients with T2DM regardless of body mass index level and independent of weight loss. Mid-phase trials ongoing	Drugs such as metformin Dietary changes and exercise	Resolution of T2DM

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Breath analysis for assessing blood glucose levels	Patients in whom T1DM or T2DM has been diagnosed	Breath analyzer uses proprietary cavity-enhanced absorption spectroscopy technology to measure acetone levels in breath. Intended as a rapid, noninvasive blood glucose test for patients with T1DM or T2DM. Oxford Medical Diagnostics, Oxford, UK Early phase trials planned	Conventional glucose testing from blood samples	Improved compliance with blood glucose testing
Breath analysis (laser-based) for diagnosing diabetes	Patients at risk of T1DM or T2DM	Uses laser-based gas analysis; intended to provide a rapid, noninvasive method for diagnosis. Avacta Group, plc, York, UK Oxford Medical Diagnostics, Oxford, UK Unphased trial ongoing	Blood glucose testing	More patients screened and diagnosed Diagnosis earlier in disease course Faster, point-of-service diagnosis
Buccal insulin (Oral-lyn) for treatment of type 1 and type 2 diabetes	Individuals in whom T1DM or uncontrolled T2DM has been diagnosed and who require insulin	Buccal insulin (Oral-lyn™ delivered via RapidMist™ device) is a fast-acting insulin that is sprayed in aerosol form on the inside of the cheek (buccal mucosa) to allow rapid absorption into bloodstream; short duration of activity; intended for dosing before and after meals; intended for use adjunctively with long-acting, injectable or infused insulin and as a substitute for injectable short-acting insulin; not intended to reach the lungs; may pose less risk of respiratory or pulmonary complications associated with inhaled insulin. Generex Biotechnology Corp., Toronto, Ontario, Canada Phase III trials ongoing in U.S.; FDA approved for patients with life-threatening T1DM or T2DM with no other treatment options Sept 2009	Adjunct to other insulin products	Achieved target HbA_{1c} levels Reduced glycemic excursions related to meals Prevented onset of T2DM in prediabetic individuals Delayed insulin dependence in T2DM Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Canakinumab interleukin-1 inhibitor for treatment of type 2 diabetes	Patients in whom impaired glucose tolerance or T2DM has been diagnosed	Research has implicated inflammation in the development of insulin resistance associated with T2DM; however, there are no currently approved antiinflammatory treatments for T2DM. Canakinumab is a human monoclonal antibody against IL-1-beta; IL-1 is a proinflammatory cytokine that has been observed in pancreatic sections obtained from patients with T2DM and may play a role in the inflammatory process leading to T2DM progression. Novartis AG, Basel, Switzerland Phase II/III trial completed	Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sulfonylurea drugs (glimepiride) Anakinra (IL-1 inhibitor in development)	Desired HbA_{1c} level control Desired fasting glucose level control Resolved insulin sensitivity
C-peptide replacement therapy (Ersatta™) for treatment of diabetic peripheral neuropathy	Patients in whom diabetic peripheral neuropathy has been diagnosed	Current treatments for diabetic peripheral neuropathy involve control of secondary symptoms (i.e., pain management). In the body, c-peptide is generated during insulin processing and is secreted along with insulin; until recently, c-peptide was not thought to possess biological activity and was used as a biomarker; however, recent studies suggest that a lack of c-peptide (which is not provided by exogenous insulin administration) may contribute to various secondary complications of diabetes. Ersatta is an extended release formulation of c-peptide, which is being studied in the treatment of various secondary complications of diabetes. Cebix, Inc., La Jolla, CA Phase Ib trial ongoing; FDA has granted Ersatta fast track status for diabetic peripheral neuropathy	Analgesics Lidocaine patches Duloxetine (antidepressant), Pregabalin (anticonvulsant) Selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, anti-epileptics	Reduced patient-reported pain on visual analog scale Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CTP-499 for treatment of diabetic nephropathy	Patients in whom diabetic nephropathy has been diagnosed	Renal failure is common in patients with long-term diabetes; CTP-499 is an antiinflammatory, antioxidant, and antifibrotic agent being developed for diabetic nephropathy and other forms of CKD. CTP-499 is a deuterium-containing new chemical entity derived from an active metabolite of a drug approved for a different indication; deuterium is a stable, nonradioactive relative of hydrogen, with strong bonds with carbon; this affinity may impact the drug's absorption, distribution, metabolism and/or excretion properties, and improve drug efficacy, safety, and tolerability. It has potential to preserve kidney function and slow disease progression when added to existing therapy. Concert Pharmaceuticals, Inc., Lexington, MA Phase I trial completed	Controlling high blood pressure is the most effective way of slowing kidney damage from diabetic nephropathy •Angiotensin-converting enzyme (ACE) inhibitors •Angiotensin receptor blockers (ARBs) Dialysis (once end-stage kidney disease develops) Kidney transplantation	Protect kidney function and slow disease progression when added to existing therapy Delay/prevent kidney transplantation
Dapagliflozin (with metformin) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed who have not achieved adequate blood glucose control with metformin	Dapagliflozin is a sodium-glucose cotransporter-2 (SGLT2) inhibitor. Facilitates excretion of glucose and associated calories in the urine, decreasing blood glucose levels. Intended for adjunctive use with metformin; taken orally once a day. Bristol-Myers Squibb, New York, NY AstraZeneca, London, UK FDA advisory panel voted 9-6 against approval Jul 2011 because of safety concerns, including risk of breast and bladder cancer, for which they wanted more data; FDA set decision date of Jan 28, 2012	Glipizide plus metformin	Achieved target HbA_{1c} levels Weight loss Decreased hypoglycemic events Halted or delayed secondary complications of diabetes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
DB 959 (PPAR agonist) delta/gamma for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	DB 959 is a PPAR (peroxisome proliferator-activated receptor) delta/gamma agonist intended to control glucose while raising high-density lipoprotein (HDL) and the ratio of HDL to low-density lipoprotein and lowering triglycerides; purported to not cause weight gain seen with other PPAR agonists. Taken once daily. DARA Biosciences, Inc., Raleigh, NC Phase Ib trial ongoing; Phase IIa planned for 2012	Non-PPAR agonist drugs Other agonist drugs that can cause weight gain and do not improve lipid profile	Achieved target HbA_{1c} levels Improved lipid profile
Diabetes Insulin Guidance System (DIGS) for management of type 1 or 2 diabetes mellitus requiring insulin	Patients with T1DM or T2DM who require daily insulin	According to the American Diabetes Association, about 5.5 million people in the U.S. manage their diabetes with daily insulin injections and two-thirds of those people do not achieve adequate glycemic control. Current standard glucose meters provide no guidance or recommendations on insulin dosage. The Diabetes Insulin Guidance System (DIGS™) is a device that uses software to analyze blood-sugar levels and recommend to patients how much insulin they should self-administer based on body chemistry. Using applied mathematics, the software program is intended to adjust insulin dosage dependent on both current and previously obtained blood glucose levels. The insulin therapy device not only provides blood glucose readings, but provides patients with a dose-by-dose insulin recommendation. Hygieia, Inc., Ann Arbor, MI Unphased trials completed	Standard glucose meters	Improved glycemic control Decreased hypoglycemic episodes Decreased secondary complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
D-tagatose (Naturlose) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	D-tagatose (Naturlose™) is a dairy-based naturally occurring sugar that is already used in food; it is intended to lower HbA_{1c} levels. Taken three times a day an adjunct to diet and exercise changes. Spherix, Inc., Bethesda, MD Phase III trial completed; company has discontinued further testing pending funding source	Other drugs for T2DM, such as metformin Dietary modifications Exercise	Reaching target HbA_{1c} levels Improved lipid profiles Weight loss Reduced hyperglycemia Reduced hypoglycemia
Exenatide extended-release (Bydureon) for treatment of diabetes	Patients in whom T2DM has been diagnosed who take oral agents for control	Extended-release exenatide (Bydureon™), a version of Byetta (approved in 2005) is taken by injection once a week. Amylin Pharmaceuticals, Inc., San Diego, CA Alkermes, Inc., Waltham, MA Drug failed to meet primary superiority endpoint in results reported Mar 2011. FDA requested additional study of the drug's cardiovascular impact as response to the new drug application (NDA) filed. FDA also requested results of DURATION-5 study to evaluate efficacy and labeling of safety and effectiveness of commercial formulation of Bydureon. The companies resubmitted the NDA in Aug 2011; in Nov 2011, Eli Lily & Co. returned all development rights to Amylin; FDA decision is expected Jan 28, 2012.	Oral agents taken daily	Blood sugar control Cardiovascular changes (QTc prolongation arrhythmias)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Exenatide (Byetta) continuous subcutaneous (Duros, or ICTA 650 pump) delivery for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed who have not achieved desired blood glucose goals with metformin	Exenatide (Byetta®) is a glucagon-like peptide-1 mimetic delivered continuously with an implantable pump, using Duros® technology; device can be inserted under the skin in a few minutes; intended to improve glucose control and result in less nausea than observed with injected exenatide. Amylin Pharmaceuticals, Inc., San Diego, CA (drug) Intarcia Therapeutics, Inc., Hayward, CA (device) Duros technology is FDA approved for drug delivery; exenatide formulation for use with pump is under study; in Nov 2011, Eli Lily & Co. returned all development rights of exenatide to Amylin; phase II trial completed; phase III trial anticipated to begin before end of 2011.	Metformin Injected exenatide	Achieving desired HbA_{1c} levels Weight loss Reduced side effects (nausea)
Fluocinolone acetonide implant (Iluvien) for treatment of diabetic macular edema	Patients in whom diabetic macular edema has been diagnosed	No FDA-approved drug therapy is available for treatment of diabetic macular edema. Iluvien™ is a tube-shaped implant that releases a steady flow of the corticosteroid fluocinolone acetonide (FAc) into the ocular space for up to 3 years; FAc is a corticosteroid that has both antiinflammatory and anti-VEGF (vascular endothelial growth factor) activity and has a history of effectiveness in treating ocular disorders. Alimera Sciences, Alpharetta, GA Phase III trials completed; NDA submitted in Jun 2010; FDA issued a complete response letter in Dec 2010 asking for additional safety data; initial 2010 NDA resubmitted in May 2011 after FDA request for more safety data; in Nov 2011, FDA issued a complete response letter to the NDA	Laser photocoagulation Intravitreal triamcinolone acetonide with or without laser photocoagulation. VEGF antagonists (pegaptanib, ranibizumab, bevacizumab)	Increased visual acuity Increased contrast sensitivity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
GFT 505 for treatment of prediabetes and diabetes	Patients in whom diabetes, abdominal obesity, or atherogenic dyslipidemia (low levels of HDL cholesterol, high triglycerides) has been diagnosed	Mixed PPAR-alpha/delta agonist (GFT 505) is based on Genfit's Selective Nuclear Receptor Modulator (SNuRM) platform; GFT 505 simultaneously targets several micro- and macro-vascular risk factors such as hyperglycemia and insulin resistance, dyslipidemia, inflammation, and hepatic steatosis. Genfit Corp., Lille, France Phase II trial completed	Drugs for treatment of prediabetes (metabolic syndrome) Drugs for treatment of diabetes	Improved blood glucose levels Improved lipid profiles Halted progression to diabetes Resolution of diabetes
Glutamic acid decarboxylase-based vaccine (Diamyd) for treatment of latent autoimmune diabetes of adults	Patients in whom latent autoimmune diabetes of adults has been diagnosed	Subcutaneous injection with Diamyd® vaccine intended to preserve insulin-producing islet cells in pancreas of patients with latent autoimmune diabetes of adults. Diamyd is thought to induce tolerance to GAD65, thereby preventing or reducing autoimmune attack on islet-beta cells and preserving the pancreas's capacity to produce insulin in patients with autoimmune diabetes. Given as two injections, administered one month apart. Diamyd Medical AB, Stockholm, Sweden Phase II trial completed	Insulin injection or infusion Islet cell transplantation	Preserved islet cell function Reduced need for insulin injections Reduced incidence of diabetes acute and secondary complications
Glutamic acid decarboxylase-based vaccine (Diamyd) for treatment of type 1 diabetes	Patients in whom T1DM has been recently diagnosed	Subcutaneous injection with Diamyd vaccine is intended to preserve insulin-producing islet cells in pancreas of patients with latent autoimmune diabetes of adults. Diamyd is thought to induce tolerance to GAD65, thereby preventing or reducing autoimmune attack on islet-beta cells and preserving the pancreas' capacity to produce insulin in patients with autoimmune diabetes. Given as two injections, administered one month apart. Diamyd Medical AB, Stockholm, Sweden Phase III trial ongoing; one phase III trial (EU) terminated because primary endpoint at 15 months was not met	Insulin injection or insulin infusion Islet cell transplantation	Improved islet cell function Reduced need for insulin therapy Decreased diabetes complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
GLY-230 (EXO-230) for treatment of diabetic nephropathy	Patients with T2DM in whom diabetic nephropathy has been diagnosed	A variety of existing treatments are available to manage symptoms of diabetic neuropathy; however, none address the underlying cause, and few slow disease progression. GLY-230 is intended to inhibit formation of Amadori-modified proteins, decrease microalbuminuria, reduce abnormalities in molecular mediators, and prevent development of renal insufficiency. Glycadia Pharmaceuticals; Philadelphia, PA Phase I/II trial completed	ACE inhibitors Angiotensin receptor blockers (ARBs) Hypoglycemic agents Anti-hypertensive agents Diet modification Dialysis Kidney transplantation C-peptide	Slowed disease progression (as measured by serum creatinine and biomarkers) Increased renal function Reduced complications of diabetic nephropathy Improved quality of life Increased survival
Hematopoietic stem cell transplantation for treatment of type 1 diabetes	Patients in whom T1DM has been diagnosed who have not achieved adequate control of blood glucose levels	Patients are given immunosuppressive drugs and then a stem cell infusion of their own previously harvested blood (hematopoietic) stem cells, which is intended to restore insulin-producing function of beta cells in the pancreas. Various research organizations and companies are developing proprietary versions of stem cell transplants Phase II trials ongoing	Injected insulin External insulin infusion pump Islet cell transplantation Pancreas transplantation	Decreased or eliminated insulin use Improved glycemic control Normal growth rate for children Restored beta cell function as measured by C-peptide levels
Implantable stimulator (Balance system) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed who do not have adequate glucose control	The Balance system paces the duodenum to control contractions and change speed of food passage through digestive track; electrical stimulation closes the pyloric sphincter to stop food from entering the duodenum causing early satiety. It also can speed transit through the duodenum, decreasing absorption, which leads to a decrease in blood glucose. Beta-Stim Ltd., Caesarea, Israel Phase I trial ongoing	Dietary modification Exercise Diabetes medications Injected insulin Subcutaneous insulin pump	Achievement of normal blood glucose levels Delayed or halted progression of disease Reduced secondary complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Inhaled insulin (Afrezza) for treatment of diabetes	Patients in whom T1DM or T2DM has been diagnosed who require insulin injections	Inhaled insulin (Afrezza®) to control blood glucose levels. MannKind Corp., Valencia, CA Mid-phase trials ongoing; in Mar 2010, company received complete response letter from FDA questioning whether the inhaler used in clinical trials was comparable to a new-generation inhaler that the company wants to market with the drug. In Jan 2011, company received a second response letter outlining additional trials needed for approval; Aug 2011, two phase III trials were planned after manufacturer meeting with FDA	Injected insulin Insulin pump therapy Other inhaled insulin products	Decreased blood glucose levels Better glycemic control Delayed or halted progression of complications Improved patient acceptance Improved quality of life
InsuPatch for improving insulin absorption in type 1 diabetes	Patients in whom T1DM has been diagnosed who use an insulin pump	InsuPatch device is intended to improve insulin delivery into the blood by heating the area of the body around the point of insulin infusion; system includes a catheter that connects to the insulin pump, electrical contacts, and embedded wires. InsuLine Medical, Ltd., Petach-Tikvah, Israel Phase III trial completed	Insulin delivered via a pump, but without heat	Improved insulin absorption Decreased frequency and severity of adverse events Avoidance of glycemic excursions
Leptin analog (Metreleptin) for treatment of type 1 diabetes	Patients in whom T1DM has been diagnosed	Metreleptin is an analog of human leptin; studied as treatment for obesity, T2DM, and severe lipodystrophy; leptin is a hormone secreted by fat cells that plays fundamental role in regulation of glucose metabolism; preclinical studies indicate metreleptin decreases blood glucose levels, blood fats, and cholesterol; taken in addition to insulin. University of Texas Southwestern Medical Center , Dallas, TX (in collaboration with Juvenile Diabetes Foundation, New York, NY and Amylin Pharmaceuticals, Inc., San Diego, CA) Phase I trial ongoing	Insulin alone	Better blood sugar control Improved lipid and cholesterol profile

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mitaglitazone (MSDC-0160) for treatment of type 2 diabetes mellitus	Patients in whom T2DM has been diagnosed	First generation thiazolidinediones (TZDs) have been used for T2DM by actively binding to PPAR gamma receptors, most notably decreasing insulin resistance and modifying adipocyte differentiation; however, these pharmacologic therapies have been associated with unwanted cardiovascular adverse effects. If approved, MSDC-0160 could potentially replace existing TZDs. MSDC-0160 is a TZD displaying the positive effect of insulin sensitizers on blood glucose, serum lipids, and blood pressure, but it does so through a PPAR gamma-sparing mechanism. MSDC-0160 does not directly activate these nuclear receptors and therefore may avoid the adverse side effects associated with first-generation TZDs, including edema, weight gain, and danger of congestive heart failure. MSDC-0160 has also shown the ability to turn committed precursor cells into functional brown fat, a specialized type of fat in the body that burns rather than stores fat. Metabolic Solutions Development Co., LLC, Kalamazoo, MI Phase IIa trial complete; phase IIb trial ongoing	First generation TZDs: Pioglitazone Rosiglitazone Troglitazone Other various drugs	Decreased hemoglobin A_{1c} levels Decreased fasting glucose levels Increased insulin sensitivity Decreased acute and secondary complications
Motilin agonist (GSK962040) for treatment of diabetes-related gastroparesis	Patients in whom gastroparesis resulting from T1DM or T2DM has been diagnosed	Current treatments for gastroparesis have significant side effects that can preclude long-term use or induce movement disorders; therefore, novel treatments for gastroparesis are needed. GSK962040 is a small molecule selective motilin agonist; activation of the motilin receptor is proposed to increase stomach wall contraction and thereby increase the rate of food passage. GlaxoSmithKline, Middlesex, UK Phase II trial completed	Erythromycin Metoclopramide Antinausea agents (e.g., prochlorperazine, ondansetron, diphenhydramine)	Faster gastric emptying (as measured by the 13C-octanoic acid breath test) Improved gastric half emptying time

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Noninvasive saliva testing (Pop Test) for glucose testing in diabetes	Patients in whom T1DM and T2DM has been diagnosed	Glucose test in the form of lollipop (Glucose Pop Test™); intended to detect glucose over the full range from hypoglycemia (equivalent to blood as low as 10 mg/dL) to hyperglycemia levels. Pop Test, LLC, Cliffside Park, NJ Received first patent Nov 2010; clinical trial status unspecified	Invasive blood glucose testing	Improved compliance with blood glucose testing, especially in children Improved diabetes management Improved health outcomes
Otelixizumab (TRX4) for early treatment of type 1 diabetes	Patients in whom T1DM has been diagnosed within the past 90 days	Otelixizumab is an anti-CD3 monoclonal antibody that preserves beta cell function if used early in the disease course; CD3-monoclonal antibodies bind to and inactivate cytotoxic T-lymphocytes, the cells that destroy beta cells. Additionally, CD3-monoclonal antibodies activate T cells, which helps control cytotoxic T-lymphocyte action. Tolerx, Inc., Cambridge, MA GlaxoSmithKline, Middlesex, UK Phase III trial completed; GSK announced Mar 11, 2011 that drug did not meet primary endpoint; GSK stated it will explore additional dosing regimens to inform decisions about future clinical development of the compound	Drugs that do not address beta cell function, but only control the disease	Improved C-peptide levels, which indicate beta cell function Improved glycemic control Daily insulin required Reduced side effects

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Peptide immune modulator (DiaPep277) for treatment of type 1 diabetes	Patients in whom T1DM has recently been diagnosed	No current treatments for T1DM are curative or address the underlying cause and dysfunction. DiaPep277® has a novel mechanism of action and is an immune-modulating therapy intended to dampen the immune system's activity against beta-islet cells, thereby promoting their survival and preserving function of the pancreas; therapy consists of a peptide derived from heat shock protein 60, which is one of the main antigens on beta-islet cells recognized by cytotoxic T cells; DiaPep277 is designed to interact with both the T cell receptor and TLR2, which has the effect of downregulating the inflammatory response induced by T helper cells. Would be delivered as a vaccine in physician's office rather than as a self-administered drug (or self-administered insulin). Andromeda Biotech, Ltd., Yavne, Israel Phase III trials ongoing	Insulin injection or insulin infusion Islet cell transplantation Pancreas transplantation Diamyd (in development)	Improved beta-cell function (measured as change from baseline in stimulated C-peptide secretion during a mixed-meal tolerance test) Increased glycemic control.
Porcine-derived cell transplant (DiabeCell) for treatment of type 1 diabetes	Patients in whom T1DM has been diagnosed	DiabeCell® is a xenotransplantation therapy (i.e., animal-based transplant) using porcine pancreatic islet cells injected into the patient's abdomen; because insulin-producing islet cells are destroyed in T1DM by an autoimmune response, replacing islet cells may improve glycemic control and overall disease management. The porcine islet cells in DiabeCell are coated with a biocapsule made of alginate gel that company claims will prevent rejection and will eliminate the need for immunosuppressants. Living Cell Technologies, Ltd., Sydney, Australia Phase IIb trial completed late 2010; phase I/IIa trial on 10 patients completed in Russia; phase II trial ongoing in New Zealand	Human islet cell transplants Insulin injection Insulin pump Pancreas transplantation	Reduced graft rejection Freedom from immunosuppressive drugs posttransplant Reduced insulin independence Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pulsed acoustic pressure device (dermaPACE) for treatment of diabetes-related foot ulcers	Patients in whom diabetic foot ulcers have been diagnosed	Approximately 3 million patients a year develop diabetic foot ulcers; current treatments achieve complete healing less than 30% of cases; therefore, effective treatments are intended to accelerate and complete the wound healing process. The dermaPACE® device is intended to work by use of acoustic pressure waves that are purported to initiate a biologic response at the cellular level to try to stimulate production of angiogenic growth factors, including endothelial nitric oxide synthase (ENOS), VEGF, and proliferating cell nuclear antigen (PCNA). This is asserted to lead to growth of newly formed vessels and increased cellular proliferation and tissue regeneration needed to heal a wound. Sanuwave, Inc., Alpharetta, GA Phase III trial completed	Acellular wound matrices Cellular wound matrices Hyperbaric oxygen therapy Negative pressure wound therapy	Increased percentage of ulcers healed Shortened time to complete healing Reduced ulcer size Reduced incidence of gangrene Reduced incidence of amputation
Pyridoxamine (Pyridorin, BST-4001, K-163) for treatment of diabetic nephropathy	Patients with T2DM who have been given a diagnosis of diabetic nephropathy	Although a variety of treatments exist to manage symptoms of diabetic neuropathy, none of these address the underlying cause, and few can slow disease progression. Pyridorin™ is an oral pharmaceutical that targets pathogenic oxidative chemistries, including advanced glycation end-products, toxic carbonyls, and reactive oxygen species, which develop in patients with diabetes and are considered a principal causative factor in the development of diabetic microvascular disease. NephroGenex, Inc., Research Triangle Park, NC Phase II trial completed; company is seeking a partner for phase III development; Nov 2011, NephroGenex and FDA have agreed on design for Phase III trial; awarded Fast Track designation by FDA	ACE inhibitors Angiotensin receptor blockers (ARBs) Hypoglycemic agents Anti-hypertensive agents Diet modification Dialysis Kidney transplantation C-peptide	Reduced disease progression (as measured by serum creatinine and biomarkers) Improved renal function Reduced complications of diabetic nephropathy Improved quality of life Increased survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Salsalate off-label for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	Research has demonstrated a link between T2DM progression and inflammation. Salsalate is a widely available antiinflammatory derivative of salicylic acid; while salicylic acid has been known for many years to aid in control of blood glucose levels, concerns regarding gastrointestinal (GI) side effects have prevented its use; salsalate may avoid these GI side effects while maintaining antiinflammatory activity. Generic drug being studied at Joslin Diabetes Center, Boston, MA Phase III trial completed	Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sulfonylurea drugs (glimepiride)	Desired HbA_{1c} level control Desired fasting glucose level control Resolved insulin sensitivity
Sodium-glucose cotransporter (LX4211) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	LX4211 is an oral dual SGLT2, SGLT1 inhibitor that increases urinary excretion of glucose; intended to lower blood glucose levels and caloric load. Lexicon Pharmaceuticals, Inc., The Woodlands, TX Phase II trial completed	Alpha-glucosidase inhibitors (acarbose and miglitol), which interfere with absorption of some glucose-containing nutrients	Rapid improvement in glycemic control Improved blood pressure Improved triglyceride levels Weight loss
Sodium-glucose transporter-2 inhibitor (ASP1941) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	ASP1941 is a SGLT2 inhibitor that blocks the reabsorption of glucose in the kidney and increases its excretion in the urine. Astellas Pharma, Inc., Tokyo, Japan Phase III trials ongoing in Japan	Other diabetes medications that do not result in weight loss	Reduced blood glucose levels Weight loss
Sodium-glucose transporter-2 inhibitor (BI 10773) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed who have not achieved adequate blood glucose control	An SGLT2 inhibitor (BI 10773); because of their unique mechanism of action, SGLT2 inhibitors have a different safety profile from other agents traditionally used to treat T2DM; intended to eliminate excess blood glucose via the urine. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing	Pioglitazone Pioglitazone plus metformin	Improved HbA_{1c} levels Delayed progression of complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Subconjunctival insert (EyeSense) for blood glucose monitoring	Patients in whom diabetes has been diagnosed and who require regular glucose monitoring	Options to improve patients' self blood-glucose monitoring are needed to improve compliance and management of diabetes. The EyeSense system has two components; ophthalmologists implant a small sensor below the conjunctiva of the patient's eye in a short office-based procedure; the implantable sensor calculates blood glucose in the subconjunctival interstitial fluid; to take readings, patients place a small hand-held device near the implantable sensor to read transmitted fluorescent light signals. EyeSense GmbH, Grosssostheim, Germany Phase II trial ongoing (in Germany); unknown when/if U.S. trials will be undertaken	Conventional blood-based glucose monitors	Improved compliance with glucose testing Better management of blood glucose levels
Oral neuronalalpha-7 neural nicotinic receptor modulator (TC-6987) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	Inflammation has been implicated in the progression of T2DM following exposure of beta-islet cells to continuously high levels of glucose; however, no antiinflammatory treatments are approved for diabetes treatment. TC-6987 is an orally administered modulator of alpha-7 neuronal nicotinic receptor (NNR), which has been shown to play a role in controlling inflammation pathways; modulation of alpha-7 NNR has been shown to lead to a reduction in the production and release of proinflammatory cytokines. Administered in trials as a 10 mg daily, hard-gel capsule or as a 20 mg loading dose gel capsule followed by 10 mg daily dosing. Targacept, Inc., Winston Salem, NC Phase II trial ongoing	Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sulfonylurea drugs (glimepiride)	Improved fasting glucose levels Achievement of target HbA_{1c} levels Decreased insulin sensitivity Delayed disease progression Avoidance of secondary complications of diabetes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Transmembrane protein antagonist (Nexagon) for treatment of type 2 diabetes mellitus-associated leg ulcers	Patients with venous leg wounds and foot ulcers associated with T2DM	Current treatments for leg wounds have been largely ineffective and may not improve patient quality of life. Nexagon™ is a gel acting as an antagonist to connexin-43, a gap junction protein that may be overproduced and may cause chronic delay of wound healing. If proven effective, this connexin-43 antagonist could potentially serve as first-line therapy for treatment of chronic wounds for patients with T2DM. Nexagon is administered topically (1 or 3 mg/mL used with compression dressings). CoDa Therapeutics, Inc., San Diego, CA Phase II trial ongoing	Antibiotics Steroids/anti-inflammatories Surgery (i.e., vascular surgery)	Reduction of wound size Complete healing of venous leg wounds and foot ulcers Improved mobility Improved quality of life
Triolex antiinflammatory (HE3286) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	Research has implicated inflammation in the development of insulin resistance associated with T2DM; however, there are no approved antiinflammatory treatments for T2DM. Triolex® is an oral novel steroid antiinflammatory whose mechanism of action may involve inhibition of the NF-kappaB pathway. Harbor BioSciences, Inc., San Diego, CA Phase II trial completed; missed primary endpoint and development is currently stalled pending further analysis of data	Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sulfonylurea drugs (glimepiride)	Desired HbA_{1c} level control Desired fasting glucose level control Resolved insulin sensitivity
Ultra-long-acting insulin (Degludec) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed who require oral medication, insulin, or both	Degludec releases over several days; flexible dosing regimen allows 8 to 40 hours between dosing, which could lead to thrice-weekly dosing, or dosing once in the evening; may also be combined with insulin aspart (NovoMix 30) to form DegludecPlus. Novo Nordisk a/s, Bagsvaerd, Denmark Phase IIIa trials completed for Degludec and DegludecPlus; phase III trial initiated May 2011; Sept 2011, Novo Nordisk filed NDAs with the FDA for Degludec and DegludecPlus	Insulin glargine, a long-acting basal insulin taken once daily (Lantus) Regular insulin	Achieve target HbA_{1c} levels Reduced progression of complications Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
XOMA-052 (gevokizumab) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed who are receiving metformin monotherapy	XOMA 052 is designed to inhibit the proinflammatory cytokine IL-1-beta that is believed to be a primary trigger of pathologic inflammation in T2DM. It is given by subcutaneous injection. Dosing is not yet established but the manufacturer expects dosage to be given once a month or less, so it could provide an option to potentially improve patient compliance with treatment due to the dosing schedule. Xoma Ltd., Berkeley, CA Phase IIb trial results announced Mar 22, 2011; did not meet primary endpoint; further development uncertain at this time	Other oral diabetes medications (metformin and sulfonylureas) Lifestyle modification	Improved blood glucose levels

Table 8. AHRQ Priority Condition: 08 Functional Limitations and Disability: 144 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
1-deoxyno-jirimycin (AT2220) to enhance efficacy of enzyme replacement therapy for Pompe disease	Patients in whom late-onset Pompe disease has been diagnosed	Pompe disease is a rare genetic disorder that results in a deficiency in alpha-glucosidase activity, leading to progressive muscle weakness and respiratory insufficiency. Current enzyme replacement therapies have multiple shortcomings, including minimal efficacy in skeletal muscle, short half-life, poor cellular uptake, and induction of allergic reactions. AT2220 acts to promote the proper folding of alpha-glucosidase, potentially increasing the effectiveness of enzyme replacement therapy and/or increasing the activity of endogenous mutant protein. Amicus Therapeutics, Inc., Cranbury, NJ Phase II trial ongoing; one phase II study recently terminated	Alpha-glucosidase enzyme replacement therapy (Myozyme, Lumizyme) with and without AT2220	Decreased muscle atrophy, increased strength and function Improved pulmonary function and/or ventilation conditions Reduced cardiomyopathy Reduced fatigue Improved quality of life
Activin receptor (ACE-031) for treatment of Duchenne muscular dystrophy	Patients in whom Duchenne muscular dystrophy (DMD) has been diagnosed	ACE-031 is an activin receptor type IIB (ActRIIB) molecule; ACE-031 is a protein that builds muscle and increases strength by inhibiting signaling through ActRIIB; a decoy of ActRIIB is created that interferes with proteins such as myostatin that limit muscle growth and regeneration. Acceleron Pharma, Inc. (developer), Cambridge, MA Shire Pharmaceuticals, plc (commercializing), Dublin, Ireland Phase II terminated (based on preliminary safety data); pending further analysis of safety data and discussion with FDA, company considering plans for a new trial; no further development news as of Nov 2011	Mutation-specific RNA-based drugs	Halted or delayed loss of muscle strength and function Decreased damage and deterioration of skeletal and cardiac muscles Improved ability to walk, breathe, and live independently Survival beyond late-20s (which is expected survival for patients with this disease)

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Adenosine A2a receptor antagonist V-81444 for treatment of Parkinson's disease	Patients in whom Parkinson's disease (PD) has been diagnosed	Patients with PD experience "on" times when medication reduces symptoms and "off" times when medication becomes ineffective and symptoms worsen before the next dose of medication can be administered. Treatments that can increase the "on" time for patients with PD could improve quality of life and management of the disease. V-81444 is an oral adenosine A2A receptor antagonist intended to increase "on" time for patients currently taking levodopa; the striatopallidal output pathway synthesizes gamma aminobutyric acid (GABA) and enkephalin as neurotransmitters, and expresses the A2A subtype of adenosine receptors. Pharmacologic inhibition of A2A adenosine receptors may inhibit the overactive striatal GABAergic inhibition on neurons associated with patients with PD. Vernalis, plc, Winnersh, UK Phase I trial ongoing	Dipraglurant Dopamine agonists Istradefylline Levodopa/carbidopa Mavoglurant Monoamino oxidase (MOA)-B inhibitors, etc. NP002	Improved motor skill functions Reduced disease progression Sustained effect of treatment over time Reduced incidence/severity of levodopa-induced dyskinesia Reduced symptoms Improved quality of life
Alemtuzumab (Lemtrada) for treatment of relapsing-remitting multiple sclerosis	Patients in whom relapsing-remitting multiple sclerosis (RRMS) has been diagnosed	Alemtuzumab represents a new mechanism of action for RRMS. Alemtuzumab is a humanized monoclonal antibody (mAb) targeted to the CD52 antigen (expressed on both T and B lymphocytes, monocytes, macrophages, and eosinophils); intended to target antigen-carrying cells, thereby rapidly removing T cells from blood, bone marrow, and organs; T-cell depletion claimed to last for more than 1 year; once-yearly treatment regimen (once a day for five days) via intravenous administration. FDA approved for treatment of refractory chronic lymphocytic leukemia. Genzyme Corp., Cambridge, MA Phase III trials ongoing	Fingolimod Glatiramer acetate Interferons (INFs) Mitoxantrone Natalizumab	Reduced frequency of relapse Slowed disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Alpha-tocopherol quinone (EPI-A0001) for treatment of Friedreich's ataxia	Patients in whom Friedreich's ataxia (FA) has been diagnosed	FA is an autosomal nDNA inherited mitochondrial disease that globally affects approximately 50,000 individuals; it is a progressively debilitating disease and patients typically present with energy failure symptoms including heart failure (HF), ataxia, diabetes, and visual and hearing deficiencies; currently FDA has not approved any drugs for treatment of FA. EPI-A0001 is a coenzyme Q10 analog that was shown to improve mitochondrial energy production and reduce oxidative stress in yeast cells by buffering free radical formation that is induced by excess mitochondrial iron. EPI-A0001 is administered orally, 1.0 or 1.5 g total daily dose, twice daily. Edison Pharmaceuticals, Inc., Mountain View, CA Phase IIa trial ongoing; FDA granted orphan drug and fast track status	Drugs currently under investigation: Idebenone (Phase III) Deferiprone EGb761 EPI-743 OX1 Pioglitazone Resveratrol TAT-Frataxin Counseling Physical therapy Speech therapy Walking aids or wheelchairs	Improved neurologic function (assessed by Friedreich's Ataxia Rating Scale) Improved quality of life
ALN-TTR01/RNAi for treatment of TTR-mediated amyloidosis	Patients who have been given a diagnosis of ATTR amyloidosis (amyloidosis caused by transthyretin deposits), which affects the heart, nerve system, and other organs	Currently, the only treatment for amyloidosis is liver transplantation, which is not an option for many patients with ATTR amyloidosis. An effective pharmacologic treatment could reduce or possibly postpone the need for transplantation. ALN-TTR is an infused RNAi therapeutic that targets the transthyretin (*TTR*) gene to treat TTR-mediated amyloidosis (ATTR). ALN-TTR01 prevents pathogenic TTR deposits in peripheral tissues, including dorsal root ganglia, sciatic nerve, stomach, and intestines, by silencing the *TTR* gene and serum levels of TTR. Alnylam Pharmaceuticals, Cambridge, MA Phase 1 trial ongoing	Liver transplantation	Reduced TTR deposits Improved function of cardiac and nervous tissues Reduced symptoms of amyloidosis (variable) Reduced need for liver transplant Improved survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Amino-benzothiazole (dexpramipexole) for treatment of amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	Only one agent (riluzole) is currently FDA approved for treatment of ALS, and it is associated with limited efficacy in improving survival time and little to no efficacy in improving motor function; novel therapies for ALS are urgently needed. Dexpramipexole likely represents a new mechanism of action for this disease state. Dexpramipexole is a synthetic amino-benzothiazole; (R)-(+) enantiomer of pramipexole (high-affinity dopamine agonist, already approved for PD and restless leg syndrome, but would be dosed at very high levels for ALS); its mechanism of action is unknown, but may be related to its ability to increase the efficiency of mitochondria, which undergo significant stress in patients with ALS. Dosed orally, daily. Biogen Idec, Inc., Weston, MA, and Knopp Bioscience, Pittsburgh, PA Phase III trial ongoing; FDA granted fast track and orphan drug status	Riluzole	Increased survival Delayed disease progression Improvement in ALS symptoms Improved quality of life
Ampakine (CX-1739) for treatment of obstructive sleep apnea	Patients in whom obstructive sleep apnea (OSA) has been diagnosed	No pharmacotherapies are FDA approved for treatment of OSA; standard therapy (continuous positive airway pressure [CPAP]) has a low compliance rate; a pharmaceutical intervention has the potential to increase compliance with therapy. CX-1739 is a "low impact" ampakine that has specificity for the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor (subtype of glutamate receptor), and lowers the amount of neurotransmitter required to generate a response, thereby increasing the amplitude of the response to glutamate; it may have utility in disorders characterized by reduced functioning of the glutamatergic pathways and research has shown a relationship between glutamate levels and OSA. Cortex Pharmaceuticals, Inc., Irvine, CA Phase IIa trial ongoing	CPAP Oral appliances Surgery	Increased glutamate activity Improved respiratory parameters Improved cognition Improved sleep quality Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
AttenueX IntraVesical System for treatment of stress urinary incontinence	Women in whom stress urinary incontinence has been diagnosed	Current treatment options for stress urinary incontinence include muscle retraining exercises and surgical options, both of which are of limited efficacy. The AttenueX® IntraVesical System is proposed as a non-surgical alternative for treatment of stress urinary incontinence; the system comprises a small balloon that is inserted into the bladder and is purported to act as a shock absorber to limit the effects of stressors (e.g., laughing, coughing) on the bladder wall muscles and prevent incontinence; balloon is inserted through the urethra and must be replaced every 3 months. Solace Therapeutics, Framingham, MA Phase III trial listed in national clinical trials database, but current status is listed as unknown; company website is live but not updated since 2009	Pelvic floor exercises Surgery (e.g., sling procedure)	Improved Stamey grade (measure of incontinence) Decreased incontinence frequency

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Autologous bone marrow progenitor cells for treatment of traumatic brain injury in children	Children aged 5 to 14 years in whom severe traumatic brain injury (TBI) (Glasgow coma score between 5 and 8) has been diagnosed	Children who survive severe TBI typically experience significant physical and cognitive disability; no effective treatments protect or promote repair of the brain in children who have experience traumatic brain injury. This procedure involves harvesting bone marrow from the hip very soon after hospital admission for acute TBI; collected bone marrow is taken to a specialized center to isolate the mononuclear fraction and process it; the bone marrow-derived mononuclear cells (BMMNCs) are then reinfused intravenously within 48 hours of the TBI injury; intention is to have these cells migrate to the site of brain injury and differentiate into neurons and cell-supporting elements to try to improve functional outcomes. University of Texas Health Science Center at Houston Medical School, Houston, TX Phase I trial completed with 10 patients; procedure performed under an investigational new drug (IND) process because of the manipulation of the cells. Researchers state: "Even autologous cell protocols used in a nonhomologous fashion must be performed under an IND through the Food and Drug Administration/CBER branch... . The auditing and verification of the data and adverse events, as well as the durable, legacy housing of research records must be considered in planning these trials. An external Data Safety and Monitoring Board must be established, convened, and meet after each patient enrollment with a full review of all adverse events, and attribution to the protocol must be determined. This is extraordinarily laborious for studies in critical care. After a safety review, a GO/NO GO decision must be made to move to the next enrollment. These board members must also be available for consultation for potential protocol deviations that could impact the patient."	There are no effective treatments to protect or promote repair of the brain in TBI-injured children	Reduced adverse neurologic events (seizures, change in Glasgow coma scale, cerebral vascular accident) Reduced disability Reduced infectious morbidity and secondary organ injury Improved cognitive function

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Autologous stem cell transplantation for facial reconstruction after osteoradionecrosis and other advanced craniofacial diseases	Patients in whom late stage osteoradionecrosis (ORN) has been diagnosed	ORN is defined as a condition of nonvital bone at a site of injury from radiotherapy; ORN can be spontaneous, but most often results from tissue injury; existing treatment options are palliative or limited in restorative capacity. In this therapy, bone marrow is harvested from the patient, cultured and incubated in a fibrin-rich and platelet-rich medium for 12 days; the mix of cultured bone marrow cells (stem and progenitor) is transplanted to the patient in an effort to regenerate damaged nerve, bone, skin, and vessels from maxillary and mandibular osteoradionecrosis (hard and soft tissue). POLUSA Hospital, Lugo, Spain Pilot trial completed	Other forms of craniofacial reconstruction Allografts Mechanical devices Vascularized and nonvascularized tissue transfers	Restored form and function (masticatory) Resolved fistulas, trismus, xerostomia Resolved chronic pain
Balloon angioplasty and/or stenting of azygos and internal jugular vein for treatment of multiple sclerosis	Patients in whom multiple sclerosis (MS) has been diagnosed and who exhibit evidence of chronic cerebrospinal venous insufficiency (CCSVI)	No effective treatments for MS exist; therapies providing relief of symptoms are needed; CCSVI, in particular stenotic and occlusive lesions in the azygos and internal jugular vein, is hypothesized to play a role in the etiology, disease progression, and/or pathogenesis of MS. Image-guided interventional endovascular management is a procedure in which an interventional radiologist performs percutaneous transluminal angioplasty using either an angioplasty balloon and/or stent to improve circulation/reduce hypoperfusion of brain parenchyma to relieve MS symptoms. Procedure uses existing technologies and is in early diffusion in Europe and U.S.; first reported by University of Ferrara, Italy Clinical trials underway to further assess validity	Corticosteroids Disease modifying drugs Fingolimod INFs	Improved cognitive and motor function Reduced relapse Reduced lesions on imaging Improved quality of life

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Bardoxolone methyl (RTA 402) for treatment of chronic kidney disease	Patients with T2DM in whom moderate to severe chronic kidney disease (CKD) has been diagnosed	Effective treatment options are needed for slowing or preventing progression of severe CKD in patients with diabetes. Bardoxolone methyl is an antioxidant inflammation modulator that activates Nrf2; Nrf2 induces transcription of genes that reduce oxidative stress levels and suppress inflammatory mediators; intended to improve kidney function and delay progression of CKD. Administered as an oral, once-daily pill. Reata Pharmaceuticals, Inc., Irving, TX Phase III trial ongoing	Management of diabetes or high blood pressure Human recombinant erythropoietin (rhEPO) to treat anemia Dialysis Kidney transplantation Palliative care	Prevention of kidney failure, dialysis or kidney transplantation Improved glomerular filtration rate Improved renal function Improved CKD stage
Beta-3 adrenoceptor agonist (Mirabegron) for treatment of overactive bladder	Patients in whom overactive bladder leading to urinary incontinence has been diagnosed	Current therapeutic approaches for overactive bladder have a poor side-effect profile and are generally not very effective. Mirabegron is a selective beta-3 adrenoceptor agonist that is purported to relax bladder smooth muscles, potentially allowing bladder filling and urine storage. Drug is administered orally. Astellas Pharma, Inc., Tokyo, Japan Phase III trials completed; new drug application (NDA) submitted to FDA in Aug 2011; Nov 2011, FDA accepted the NDA filing	Behavioral therapy in combination with bladder relaxing drugs (e.g., tolterodine, oxybutynin, oxybutynin skin patches, trospium, solifenacin, darifenacin) Onabotulinum toxin A Sacral nerve stimulation Surgical treatment (bladder enlargement, cystectomy)	Decreased urge to urinate Decreased urination episodes per week Improved International Consultation on Incontinence Questionnaire-Overactive Bladder score Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Beta blockers off-label for treatment of serious infantile hemangiomas	Infants in whom a hemangioma has been diagnosed	Superficial hemangiomas often are not treated and resolve on their own to leave normal-appearing skin. Sometimes, laser ablation is used to remove small vessels. Significant hemangiomas, however, can impair vital or sensory functions or cause disfigurement. They are treated with lasers and/or steroid injections. Oral pharmacologic options are desired. Propranolol is a nonselective beta blocker that works via vasoconstriction and could decrease expression of vascular endothelial growth factor 1(VEGF1) and basic fibroblast growth factor (bFGF) by downregulating the RAF-mitogen-activated-protein kinase pathway; this is believed to trigger apoptosis in endothelial capillary cells, thereby reducing size of hemangiomas. Hackensack University Medical Center, Hackensack, NJ, and various centers conducting trials Phase II and III trials ongoing	Corticosteroids Laser treatment	Reduced hemangiomas Improved functional ability Prevention of future complications Improved quality of life
Bevacizumab off-label for treatment of retinopathy of prematurity	Infants weighing 1,500 grams or less at birth and at 30 weeks' or less gestation in whom stage 3 retinopathy of prematurity (ROP) in zone I or posterior zone II has been diagnosed	ROP occurs in many infants who are born before 31 weeks' gestation; it can result in alternating episodes of tissue hyperoxia and hypoxia and induction of vascular endothelial growth factors (VEGFs), which can lead to development of abnormal retinal fibrovascular tissue and cause blindness; ROP in premature infants is an acute condition with a time frame measured in days and weeks. Current standard therapy (peripheral retinal ablation) for ROP is known to work, but does not prevent all vision loss and recurrence of VEGF can be as high as 40% in treated infants; off-label use of bevacizumab is injected into the infant's vitreous to reduce incidence of blindness by suppressing VEGF. BEAT-ROP cooperative is sponsoring trial; Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland, is the manufacturer but it is not pursuing labeled indication Postmarket trial of off-label use completed	Peripheral retinal ablation with lasers (e.g., xenon, argon, diode)	Prevented recurrence of neovascularization arising from the retinal vessels Improved visual acuity

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Bioabsorbable bupivacaine implant (Xaracoll) for postsurgical pain relief	Patients who undergo hysterectomy	Implant (Xaracoll®) intended to deliver localized pain relief after surgery; implant is biodegradable and bioabsorbable matrix of purified fibrillar collagen filled with local anesthetic bupivacaine. Innocoll, Inc., Ashburn, VA Phase II trials ongoing; several phase II trials completed	Postsurgical administration of intravenous and oral analgesics (opioids, nonsteroidal antiinflammatory drugs [NSAIDs])	Improved localized pain relief Fewer side effects (e.g., nausea, constipation, dependence) compared to systemic postsurgical pain relief modalities
Bioartificial liver system (Excorp Medical) for fulminant hepatic failure	Patients with fulminant hepatic failure (acute liver failure) awaiting a liver transplant	Extracorporeal bioartificial liver support systems are intended to replace lost liver function, such as the synthesis of metabolic enzymes and key proteins (e.g., blood clotting factors), while a transplant candidate awaits a donor liver; cell-based liver support systems add a "bioreactor" filter cartridge to standard liver dialysis systems that temporarily remove blood from the body to remove circulating toxins. For its bioreactor component, this bioartificial liver system uses porcine hepatocytes harvested from a controlled animal herd. Excorp Medical, Inc., St. Paul, MN Phase I/II trial ongoing; granted orphan product status by FDA	Standard care for acute liver failure, including antibiotics to treat infection and lactulose to treat hepatic encephalopathy	Improved survival
Bioartificial liver system (Extracorporeal Liver Assist Device) as bridge to liver transplantation	Patients in whom acute liver failure has been diagnosed	Extracorporeal bioartificial liver support system (Extracorporeal Liver Assist Device [ELAD®]) is intended to replace liver functions, such as synthesis of metabolic enzymes and key proteins; cell-based liver support systems add a "bioreactor" filter to standard liver dialysis systems that temporarily remove blood from the body to remove circulating toxins; ELAD incorporates cultured human hepatocytes in bioreactor cartridges as part of a dialysis-like system; functions as bridge while transplant candidate awaits donor liver. Vital Therapies, Inc., San Diego, CA Phase II/III trials ongoing	Standard care for acute liver failure, including antibiotics to treat infection and lactulose to treat hepatic encephalopathy	Improved rate of 30-day transplant-free survival

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Bioartificial liver system (Extracorporeal Liver Assist Device) for management of fulminant hepatic failure	Patients in whom fulminant hepatic failure (acute liver failure) has been diagnosed	Extracorporeal bioartificial liver support system (ELAD) is intended to replace lost liver functions, such as the synthesis of metabolic enzymes and key proteins; cell-based liver support systems add a "bioreactor" filter to standard liver dialysis systems that temporarily remove blood from the body to remove circulating toxins; ELAD incorporates cultured human hepatocytes in bioreactor cartridges as part of a dialysis-like system; functions as bridge while transplant candidate awaits donor liver. Vital Therapies, Inc., San Diego, CA Phase II trials completed	Standard care for acute liver failure, including antibiotics to treat infection and lactulose to treat hepatic encephalopathy	Improved survival for liver transplant patients awaiting a donor liver
Bioartificial liver (HepaMate™) for treatment fulminant hepatic failure	Patients with fulminant hepatic failure (acute liver failure)	Extracorporeal bioartificial liver support systems (BLSSs) are intended to replace lost liver function while a transplant candidate awaits a donor liver. Cell-based liver support systems add a "bioreactor" filter cartridge to standard liver dialysis systems that temporarily remove blood from the body to remove circulating toxins; HepaMate™ uses the company's PICM-19 porcine embryonic liver stem cell line in the bioreactor component and the HepaDrive blood perfusion system. Alliqua, Inc., New York, NY (Formerly HepaLife Technologies) Phase I trial completed; company stated in Sept 2011 that it "will require additional capital in order to execute the longer term aspects of its business plan, including additional research and development efforts related to HepaMate."	Standard care for acute liver failure (antibiotics to treat infection and lactulose to treat hepatic encephalopathy)	Increased survival while awaiting donor liver

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Borate glass nanofiber material (13-98B3) for treatment of venous stasis wounds	Patients with venous stasis wounds	Venous stasis wounds are caused by poor blood circulation in the lower extremities due to weakening of venous valves. Venous stasis ulcers are slow to heal and commonly recur after treatment, progressing to rapidly eroding and deep wounds. Borate glass nanofiber material is intended to mimic the structural properties of fibrin to form a clot and assist in the migration of epidermal cells to the wound site; this material has also been shown to fight against bacterial infection and is said to be easily absorbed by surrounding tissue; the cottony glass nanofiber material is 300 nanometers to 5 micrometers in diameter. Mo-Sci Corp., Rolla, MO Pilot trial completed on 12 participants in Aug 2010; larger trial was planned for mid-2011, but no additional information has been provided	Antibiotics Compression garments Growth factors Occlusive and nonocclusive wound dressing Skin grafts Wound debridement	Improved or resolved venous stasis wounds in shorter time frame
BreathID test to monitor liver function	Patients at risk of or in liver failure	Breath test (BreathID®) intended to monitor liver function; theory is that breath test could give additional liver function assessment not available with blood tests. Office-based test. Exalenz Bioscience, Inc., Modi'in, Israel Phase III trials ongoing in Israel; approved to detect *Helicobacter pylori* infection	Liver function blood tests	Improved patient comfort Increased compliance with liver function testing Earlier detection of liver function problems

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BioErodible MucoAdhesive (BEMA) delivery of buprenorphine for treatment of moderate to severe chronic pain	Patients in whom moderate to severe chronic pain has been diagnosed	Buprenorphine is an opioid that is used in current formulations for treatment of opioid addiction or management of moderate pain; BEMA™ (BioErodible MucoAdhesive) is drug delivery technology used to deliver opioids and other drugs by encapsulating the drug in a dissolvable polymer film used on the inside of the check for buccal delivery. The technology was FDA approved for use with fentanyl and is under development for delivery of buprenorphine. BioDelivery Sciences International, Raleigh, NC Phase III trials ongoing; company anticipates filing NDA in early 2012	Cyclooxygenase-2 (COX-2) inhibitors Current buprenorphine formulations: Buprenex (injectable) NSAIDs Opioids (oxycodone, hydrocodone, morphine)	Reduced pain Reduced risk of addiction
Bupivacaine extended-release liposome injection (Exparel) for treatment of postsurgical pain	Patients who have undergone soft-tissue or orthopedic procedures and require local anesthesia postsurgery	Local analgesics such as bupivacaine have been successfully used for many years in the management of postsurgical pain; however, their activity is of limited duration (about 7 hours); there is a need for a long-acting nonopioid postsurgical analgesic. Exparel™ is a formulation of bupivacaine that is an extended-release liposome injection that uses Pacira's DepoFoam® technology; it is intended to provide up to 72 hours of post-surgical analgesia. Pacira Pharmaceuticals, Inc., Parsippany, NJ Phase III trials completed; NDA submission accepted by FDA in Dec 2010; planned decision date extended from Jul 2011 to Oct 28, 2011; in Oct 2011, the manufacturer announced the FDA's approval of this therapy for the treatment of postsurgical pain	Conventional bupivacaine Opioids	Reduced pain on visual analog pain scale Reduced need for other pain medication

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Caspase-1 inhibitor (VX-765) for treatment of partial-onset epilepsy	Patients in whom treatment-resistant partial-onset epilepsy has been diagnosed	Some patients with partial-onset epilepsy are not responsive to current therapy; use of antiinflammatory medication is a novel approach to treat this condition. VX-765 is intended to inhibit caspase-1, which is an enzyme involved in the production of interleukin-1-beta (IL-1-beta); both induction of caspase-1 and activation of IL-1-beta occur in human epilepsy. In clinical trials, is being dosed orally at 900 mg three times per day, while patients continue to receive standard therapy. Vertex Pharmaceuticals, Inc., Cambridge, MA Phase II trial completed; phase IIb trial planned for 4Q2011	Tricyclics GABA derivatives Valproate Lamotrigine Levetiracetam Tiagabine	Reduced frequency of partial-onset seizures Improved quality of life
CF101 for treatment of moderate to severe dry-eye syndrome	Patients in whom moderate to severe dry-eye syndrome has been diagnosed	Immunomodulatory effect of adenosine receptor agonist (CF101) inhibits inflammatory cytokine production and auto-regulatory T-cell proliferation; CF-101 is intended to relieve symptoms and reduce intraocular pressure (IOP). Tablets were taken orally for 12 weeks as monotherapy in phase II trial. Can-Fite BioPharma, Ltd., Petah-Tikva, Israel Phase III trial ongoing	Dry-eye medications	Improved corneal fluorescein staining (a measure of ocular surface inflammation) Increased tear production Improved dry-eye symptom score

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ChemR23 inhibitor (CCX832) for treatment of psoriasis	Patients in whom autoimmune psoriasis has been diagnosed	Existing systemic treatments for psoriasis suppress the immune system to control symptoms and have significant side effects in some patients. CCX832 is an oral small molecule drug intended to reduce dermal inflammation by selectively inhibiting the ChemR23 receptor; selectively inhibiting the psoriasis immune response may reduce side effects from existing broad-spectrum immunosuppressants. ChemoCentryx, Inc., Mountain View, CA Phase I trial ongoing	Topical ointments to control itch (cortisone) and scaling (e.g., salicylic or lactic acid) Biologic immunosuppressors (adalimumab [Humira], alefacept [Amevive], etanercept [Enbrel], infliximab [Remicade]) Immunosuppressors (e.g., methotrexate or cyclosporine) Prescription retinoids (vitamin A, vitamin D) for skin lesions, exfoliation Antibiotics for secondary infections Phototherapy	Elimination or reduced severity of dermal inflammation Reduced need for symptom control with systemic immunosuppressors, thereby reducing side effects

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Clip-on smart phone device (Catra) for detection of cataracts	Patients at risk for developing cataracts	Cataracts are the leading cause of blindness, accounting for approximately 48% of cases of blindness. Late detection has resulted in cataract progression to the point of blindness, particularly in rural and more disadvantaged areas in the U.S. and globally. Current diagnostic tools are expensive and may not accurately detect cataracts, particularly in earlier stages of disease. The smart phone device (Catra) is a clip-on device intended for use by a clinician; it emits beams of light that sweep across the eye to detect cloudy patches formed in the eye as a result of cataracts. The beams of the device are focused to the same point on the fovea, also known as the maximum resolution area of the retina. Catra depends on light passing through the lens, as indicated by the patient, who notifies the doctor if the point of light remains steady, dims, or disappears. The device may also map the size, position, shape, and density of the cataract. It may also detect cataracts at earlier stages, particularly because it detects changes in the lens caused by cataracts that haven't yet become opaque. Massachusetts Institute of Technology, Cambridge, MA Pilot trial completed	Catatrac (hand-held device) Ocular tonometry Slit lamp exam Visual acuity exam	Reduced incidence of blindness from cataracts Improved daily activity functioning Reduced need for services required to support people with blindness Improved quality of life
PYM50028 (Cogane) for treatment of Parkinson's disease	Patients in whom early-stage PD has been diagnosed	PYM50028 (Cogane™) is a small molecule neurotrophic factor inducer that readily crosses the blood-brain barrier. In preclinical studies, Cogane stimulated release of neurotrophic factors and increased neurite outgrowth; importantly, also reversed the decrease of neurotrophic factors and reversed dopaminergic neuronal degeneration in vitro; intended to significantly reduce parkinsonian symptoms. Phytopharm, plc, Huntingdon, UK Phase II trial ongoing	Levodopa (L-DOPA) Deep brain stimulation (DBS)	Improved motor skill function and reduction in symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Collagenase clostridium histolyticum (Xiaflex) for treatment of Peyronie's disease	Men in whom Peyronie's disease has been diagnosed	Peyronie's disease is the development of a collagen plaque that causes the penis to curve while erect; treatments for Peyronie's disease are experimental or require surgical correction. Collagenase clostridium histolyticum (Xiaflex®) is a locally injected protein mixture that is intended to disrupt the collagen plaques. Xiaflex has been approved for treatment of the hand disorder Dupuytren's contracture. Auxilium Pharmaceuticals, Inc., Malvern, PA Phase III trial ongoing	Verapamil local injections INF local injections Surgical correction	Change in penile curvature from baseline Improved Peyronie's Disease Questionnaire (PDQ) score
Corneal collagen cross-linking for treatment of progressive keratoconus	Patients in whom progressive keratoconus has been diagnosed	Keratoconus is a degenerative disease of the eye and is the leading cause of corneal transplants in the U.S. Progressive keratoconus requires invasive interventions, such as corneal transplants and insertion of corneal rings; these invasive surgical interventions may present unfavorable complications, such as graft rejection, persistent visual problems, permanent vision loss, and prolonged surgical recovery. If accepted, corneal collagen-crosslinking (CCL) would provide a procedure that is less invasive, requires a shorter recovery time, and generates more optimal clinical outcomes to improve patient quality of life; CCL is a procedure performed by removing the corneal epithelium and applying riboflavin drops to the eye; the eye is then exposed to the ultraviolet light, interacting with the riboflavin; the interaction produces reactive oxygen molecules that cause the formation of chemical bonds between and within the corneal collagen fibrils, making them stiffer. Avedro, Inc., Waltham, MA Phase III trial completed; CE marked in European Union	Corneal ring segment inserts Corneal transplants/penetrating keratoplasty Epikeratophakia Radial keratotomy (under investigation)	Improved corneal structure Improved vision Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Daclizumab (Zenapax) for treatment of multiple sclerosis	Patients in whom MS has been diagnosed	Current treatments for MS may slow disease progression, but the disease has no cure. Effective treatments are needed. Daclizumab (Zenapax®) is a humanized monoclonal antibody against the CD25 alpha subunit of the high affinity interleukin-2 receptor; daclizumab is intended to bind the receptor and inhibit T-cell activation, thus slowing disease progression and degradation of the axon protective myelin sheath. Administered 150 mg, injected subcutaneously, once every 4 weeks Biogen Idec, Inc., Weston, MA Abbott Laboratories, Abbott Park, IL Phase III trials ongoing; data may be available late 2012; FDA granted fast track designation	Fingolimod Glatiramer Interferon beta (INFb)-1a Natalizumab	Delayed disease progression Decreased demyelination Fewer relapses Improved quality of life
Deferiprone (Ferriprox) for treatment of contrast-induced acute kidney injury	Patients in whom contrast-induced acute kidney injury (CI-AKI) has been diagnosed	The only current standard treatment for CI-AKI in high risk patients with CKD is hydration and avoidance of nephrotoxic drugs. Deferiprone (Ferriprox®) is an orally active hydroxypyridin-4-one (HPO) iron chelator that binds iron and removes excess iron from the body. If proven effective, deferiprone could become the first therapeutic drug to prevent CI-AKI in CKD. Deferiprone 900 mg is administered orally, one immediate release tablet and two extended-release tablets, 1 to 3 hours before angiography, and then every 12 hours for 8 days. CorMedix, Inc., Bridgewater, NJ Phase II trial completed Jun 2011; phase III trial planned for 2012	Cincor™ system (in development) Deferoxamine Hydration	Reduced occurrence and complications of CI-AKI Reduced incidence of CI-AKI in high risk patients with CKD

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Davunetide for treatment of progressive supranuclear palsy	Patients in whom progressive supranuclear palsy (PSP) has been diagnosed	No treatments exist for PSP, a rare condition; anticholinergic medications for PD are used to control symptoms. Davunetide is a first-in-class agent intended to target tau tangles and PSP is believed to have underlying tau-related pathology (abnormal clumps of tau); davunetide is an intranasal formulation of a microtubule-interacting peptide that is intended to prevent neuronal apoptosis (programmed cell death) by repairing the microtubular network and potentially restoring both axonal transport within nerve cells and chemical transmission between them; also intended to promote neurite growth and restore transmission between nerve cells; is derived from naturally occurring activity-dependent neuroprotective protein (ADNP); also known as AL-108. Administered intranasally, 30 mg twice a day. Allon Therapeutics, Inc., Vancouver, British Columbia, Canada Phase III trial ongoing; FDA granted orphan drug status in Jan 2010	Anticholinergic medications	Improved symptom control Delayed or halted disease progression Improved quality of life
Dimethyl fumarate (BG-12) for treatment of relapsing-remitting multiple sclerosis	Patients in whom relapsing-remitting RRMS has been diagnosed	BG-12 represents a novel mechanism of action for this disease state; available treatments provide unsatisfactory efficacy for many patients. Dimethyl fumarate (BG-12) is a fumaric acid ester (FAE); these drugs (from use in psoriasis) have been shown to reduce peripheral CD4+ and CD8+ T lymphocytes (because FAE can induce apoptosis [programmed cell death]); may have both immunomodulatory and neuroprotective qualities; safety profile may allow combination dosing. Dosed in oral form, three times daily. Biogen Idec, Inc., Weston, MA Phase III trials ongoing; received fast track status from FDA in 2008	Fingolimod Glatiramer acetate Interferon beta (INFb) INFb-1a (Avonex) Natalizumab	Reduced frequency of relapse Reduced symptom severity Slowed disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
DNA chip for detecting lipoprotein lipase gene mutations that cause lipoprotein lipase deficiency	Patients at risk of lipoprotein lipase (LL) deficiency and resulting acute pancreatitis	DNA chip (microarray) diagnostic tool to detect mutations in the (LL) gene from a blood sample to identify patients at risk for acute pancreatitis. Progenika Biopharma S.A., Vizcaya, Spain Amsterdam Molecular Therapeutics Holding N.V., Amsterdam, The Netherlands U.S. trial status unclear; CE marked Sept 2010	Standard lipid profile laboratory test Other laboratory exams	Increased definitive diagnosis of LL deficiency Identification of patients at risk for acute pancreatitis
Doxepin nasal solution (Dolorac) for migraine prophylaxis	Patients in whom chronic migraine headaches (more than 180 headache days per year) have been diagnosed	A nasal solution (Dolorac) formulation of the tricyclic antidepressant doxepin; tricyclic antidepressants have been used off label for some time for migraine prophylaxis. Winston Pharmaceuticals, Inc., Vernon Hills, IL Phase II trials completed Nov 2010; company announced plans to initiate two phase III pivotal trials for chronic migraine in the second quarter of 2011	Botox injection Off-label medications for this condition: beta blockers (propranolol, atenolol, metoprolol, nadolol, timolol), tricyclic antidepressants (amitriptyline, nortriptyline, doxepin), anti-epileptics (divalproex, valproic acid, topiramate)	Migraines prevented Reduced side effects
Droxidopa (Northera) for treatment of symptomatic neurogenic orthostatic hypotension	Patients who have received diagnosis of Parkinson's disease, multiple system atrophy, and/or pure autonomic failure who are at risk of neurogenic orthostatic hypotension	Droxidopa (Northera™) is a norepinephrine precursor; allows for reuptake of norepinephrine into peripheral nervous system neurons, stimulating receptors for vasoconstriction and providing physiological improvement in symptomatic neurogenic orthostatic hypotension. Administered orally up to three times daily. Chelsea Therapeutics, Inc., Charlotte, NC Phase IIIs ongoing; NDA submitted to FDA Sept 28, 2011; FDA granted orphan drug and fast track designations; approved for marketing in Japan	Midodrine hydrochloride (ProAmatine, Apo-Midodrine [Canada]), the only FDA-approved drug to treat orthostatic hypotension; midodrine is an alpha1-adrenoceptor agonist	Decreased orthostatic hypotension Decreased risk of falling Decreased confusion from reduced cerebral circulation

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Dual orexin receptor antagonists (MK-6096 and MK-4305) for treatment of primary insomnia	Patients in whom primary insomnia has been diagnosed	Insomnia is a common sleep problem that may stem from factors including stress, poor sleeping habits, depression, and chronic pain. Primary insomnia is known as the inability to sleep that is not attributed to any medical, psychological, or environmental factor. Current pharmacotherapies for this indication may come with unwanted adverse events and have limited efficacy. Dual orexin receptor antagonists act by inhibiting the binding of neuropeptide orexin to its receptor, known to regulate the sleep-wake cycle through control of downstream pathways that involve histaminergic, dopaminergic, and cholinergic activity. MK-6096 is administered orally, 2.5, 5, 10, or 20 mg per dose before bedtime; MK-4305 is administered orally, 15, 20, 30, or 40 mg per dose. Merck & Co., Inc., Whitehouse Station, NJ MK-6096: phase II trial completed MK-4305: phase III trial ongoing	Anticonvulsants Antihistamines Behavior modifications Benzodiazepines Hypnotics (Ambien, Sonata) Melatonin stimulants Muscle relaxants	Improved sleep cycle Improved quality of life
Ear implant for treatment of Ménière's disease	Patients with persistent, severe vertigo in whom Ménière's disease has been diagnosed	Inner ear implant modeled after cochlear implant and designed to quell vertigo attacks experienced by people with Ménière's disease; an electrode is inserted into each of three semicircular canals; external processor is worn behind the ear and communicates wirelessly with internal components; patient activates when vertigo episode begins; less invasive, permanent alternative to surgery, alternative to medications that address only symptoms and have many side effects. University of Washington, Seattle, WA Phase III trial ongoing	Medications Surgery	Cessation of vertigo

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Embryonic stem-cell therapy for spinal cord injury	Patients with subacute, functionally complete spinal cord injuries with a neurological level between T3 and T10	Stereotactic injection of stem cell product (GRNOPC1) into spinal cord at injury site. Geron Corp., Menlo Park, CA Phase I trials suspended because the manufacturer has ceased funding until a partner is found to continue development of this therapy collaboratively	Palliative care, rehabilitation for spinal-cord-injured patients Investigations of electrical spinal cord stimulation to restore function	Restoration of spinal neurological function Improved function Improved activities of daily living Increased independence Improved quality of life
Eprodisate disodium (Kiacta) for treatment of amyloid A amyloidosis	Patients at risk for amyloid A amyloidosis, especially those in whom rheumatoid arthritis or chronic infection is present	Eprodisate disodium (Kiacta™) is designed to interfere with the formation of amyloid A fibrils that can accumulate in organs and tissues. Orally administered capsules. Bellus Health, Inc. (formerly Neurochem), Laval, Quebec, Canada Celtic Therapeutics Management LLP, St Thomas, U.S. Virgin Islands Phase III trials; NDA submitted to FDA in 2006, but FDA requested more data before approval; company initiated phase III confirmatory trial in 2010 to address this concern	Standard treatment primarily targets symptomatic relief and reduction of amyloid production Immunosuppressive agents to reduce chronic inflammation, including: chlorambucil, cyclophosphamide, methotrexate, and biologics (tumor necrosis factor-alpha [TNF-alpha] inhibitors and IL-1-receptor antagonists) Surgical excision of infected tissue and antibiotics for chronic infection Kidney transplantation (for kidney failure) Colchicine for familial Mediterranean fever	Reduced risk of organ failure (especially kidneys, liver, spleen) Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Erythropoiesis-stimulating agent (peginesatide) for treatment of anemia of chronic renal failure	Patients with chronic renal failure on dialysis treatment in whom anemia has been diagnosed	Anemia is a common consequence of chronic renal failure, affecting more than 90% of patients with chronic renal failure stage 5. Erythropoiesis stimulating agents have been established as a treatment for anemia in chronic renal failure subjects, and have improved the management of anemia over alternatives such as transfusion. Peginesatide (Hematide™) is a long-acting, parenteral formulation being developed for the correction of anemia in patients with chronic renal failure; it binds to and activates the human erythropoietin receptor (on bone marrow cells) and stimulates erythropoiesis in human red cell precursors in a manner similar to other known erythropoiesis-stimulating agents. Peginesatide is administered subcutaneously or intravenously, 0.04 to 0.16 mg/kg of body weight per dose, once monthly. Affymax, Inc., Palo Alto, CA, in collaboration with Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trial completed; FDA advisory panel scheduled to meet Dec 7, 2011 to determine whether it recommends approval of this therapy	Ivy EPO Other ESAs Renal transplantation	Reduced frequency of drug administration Resolution of anemia Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Etanercept for treatment of dermatomyositis	Patients in whom dermatomyositis has been diagnosed	Dermatomyositis is a chronic inflammatory disease of skin and muscle that is associated with patches of slightly raised reddish or scaly rash accompanying, or more often, preceding muscle weakness, which can result in difficulty performing physical activities, and if untreated in adults, death may occur from severe and prolonged muscle weakness, malnutrition, pneumonia, or lung failure; the major causes of death from the disorder are cancer and lung disease; in some patients trouble with swallowing may occur, as well as fatigue and discomfort; some patients do not respond to current antiinflammatory therapy that may not be proven effective for dermatomyositis. Etanercept is a dimeric soluble form of the p75 TNF receptor purported to bind TNF alpha and beta molecules, thus inhibiting the binding of TNF molecules to cell surface receptors and preventing inflammation associated with dermatomyositis. Etanercept may be administered 50 mg, once weekly, by subcutaneous injection. Amgen, Inc., Thousand Oaks, CA Phase I trials completed; FDA approved in 1998 for moderate to severe rheumatoid arthritis and other inflammatory conditions	Azathioprine Intravenous immunoglobulin (IVIG) Methotrexate Prednisone	Symptom resolution as measured by International Myositis Assessment Clinical Study (IMACS) score Halted or slowed disease progression
Exon-skipping agent (Eteplirsen, AVI-4658) for treatment of Duchenne muscular dystrophy	Patients in whom DMD has been diagnosed	Current treatments for DMD address symptoms only; additionally, patients who receive available treatment still have a reduced lifespan and require additional support from devices. Eteplirsen is intended for patients in whom DMD has been diagnosed and who have a mutation in the dystrophin gene; Eteplirsen splice-switching oligomer is intended to skip exon 51 of the dystrophin (a protein that plays a key structural role in muscle fiber function) gene during translation, thereby restoring the gene's ability to make a shorter (i.e., not perfect, but functional) form of dystrophin. It is delivered once weekly in intravenous infusion. AVI BioPharma, Inc., Bothell, WA Phase II trial ongoing; phase III trial planned; FDA granted orphan drug status in 2007	Corticosteroids Beta-2 agonists Orthopedic devices Physical therapy Respiratory support devices	Delayed or halted muscle degeneration Reduced symptoms Increased survival Improved quality of life

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Ezogabine (Potiga) for treatment of epilepsy	Patients in whom epilepsy has been diagnosed	Ezogabine (Potiga™) is a drug with a new mechanism of action intended for treatment of epileptic seizures; as a potassium channel opener, it stabilizes neuronal potassium channels in the open position with the intention of modifying ion channels so they modify neuronal hyperexcitability, and thus reduce seizures. Valeant Pharmaceuticals International, Inc., Mississauga, Ontario, Canada GlaxoSmithKline, Middlesex, UK FDA approved Jun 2011	Anticonvulsant medications for partial seizures (e.g., tricyclics, GABA derivatives, valproate, lamotrigine, levetiracetam, tiagabine)	Reduced frequency of partial seizures Improved quality of life
Fentanyl iontophoretic transdermal system (Ionsys) for patient-controlled delivery of pain medication	Patients who would receive opioid treatment for pain (e.g., postsurgery patients)	The iontophoretic transdermal system delivers fentanyl (Ionsys™) for pain relief through a device about the size of a credit card that is affixed to the patient's upper arm or upper chest. The patient pushes a button on the patch, activating a battery and allowing iontophoretic (electrotransport) delivery of fentanyl HCl (40 mcg) over 10 minutes through intact skin. The device can be activated up to six times an hour and automatically shuts off after 24 hours. ALZA Corp. and Janssen Pharmaceuticals, Inc., both subsidiaries of Johnson & Johnson, Inc., New Brunswick, NJ Incline Therapeutics, Inc., Redwood City, CA Received FDA NDA approval May 2006, but product was not launched; in Jun 2010, Ionsys was acquired by Incline Therapeutics, which must reapply for FDA approval following introduction of new safety features. Approved in Europe but the marketing authorization was suspended by the European Medicines Agency in Nov 2008 after a recall because some devices had self-activated.	Non-patient-controlled fentanyl patches Patient-controlled analgesic pumps	Adequate postsurgery pain management Fewer side effects because of delivery mode

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Fingolimod (Gilenya) for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	Fingolimod (Gilenya™) is the first FDA-approved oral therapy for RMMS. Fingolimod is an agonist to sphingosine-1-phosphate receptors on the surface of thymocytes and lymphocytes; intended to reduce the number of circulating lymphocytes available to have an autoimmune reaction to the myelin sheath of axons. Taken once daily. Novartis AG, Basel, Switzerland FDA approved Sept 2010	Glatiramer acetate INFb INFb-1a (Avonex) Natalizumab	Reduced frequency of relapse Slowed disease progression Improved quality of life
Gene therapy NLX-P101 (AAV2-GAD) for treatment of Parkinson's disease	Patients in whom PD has been diagnosed	Current treatments for PD address symptoms rather than the underlying cause, and the patient eventually plateaus or ceases to respond to them; gene therapy is a novel treatment modality for this indication. Glutamic acid decarboxylase (GAD) is an enzyme that catalyzes production of GABA, an inhibitory neurotransmitter); in patients with PD, too little GABA is produced, resulting in overstimulation of the subthalamic nucleus; as a result of this overstimulation, neurons that produce dopamine (major role in movement control) are strained. NLX-P101 is administered in a neurosurgical procedure by injecting virus (which carries gene that codes for GAD) directly into the brain. Neurologix, Inc., Fort Lee, NJ Phase II trial ongoing	Dopamine agonists Levodopa MOA-B inhibitors	Improved motor skill functions/movement control Slowed disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gene therapy (CD34+ cells) for childhood severe combined immunodeficiency	Children in whom severe combined immunodeficiency has been diagnosed (also known as "bubble boy disease")	One form of severe combined immunodeficiency is caused by an enzyme deficiency, adenosine deaminase, known to compromise the immune system function; disease is often fatal and is typically treated with multiple weekly injections of enzyme replacement therapy. This intervention uses autologous (i.e., the cells came from the patients) adenosine deaminase vector-transduced CD34+ cells to reconstitute the immune system in an effort to cure the underlying immunodeficiency. The multi-center study was conducted by the San Raffaele Telethon Institute for Gene Therapy, Milan, Italy Small trial ongoing; expected completion date 2021; cells have received orphan drug designation from the European Medicines Agency	Bone marrow transplantation from unrelated donors or parents, which is not always possible	Improved survival Fewer infections Improved quality of life Freedom from weekly enzyme injections
Glucocerebrosi-dase (taliglucerase alfa) for treatment of Gaucher's disease	Patients in whom Gaucher's disease has been diagnosed who have not yet begun treatment or who are currently being treated with enzyme replacement therapy via imiglucerase (Cerezyme)	Gaucher's disease is caused by a hereditary deficiency of glucocerebrosidase, which leads to enlarged and malfunctioning organs, skeletal disorders, and painful neurologic complications. Taliglucerase alfa is a plant-cell expressed form of glucocerebrosidase; intended as a lower-cost enzyme replacement therapy; compound also known as recombinant active form of lysosomal enzyme, glucocerebrosidase. Administered via an infusion. Pfizer, Inc., New York NY Protalix BioTherapeutics, Inc., Carmiel, Israel Phase III trial completed; NDA submitted to FDA; complete response letter from FDA issued in Feb 2011; timeline for resubmission unclear pending meeting with FDA; granted orphan designation; available under "expanded access" protocol; marketing authorization application submitted to European Medicines Agency Nov 2010; granted orphan designation in Europe	Cerezyme enzyme replacement with intravenous recombinant glucocerebrosidase (imiglucerase) Blood transfusions Joint replacement surgery Splenectomy Bone marrow transplant (rarely done because of significant risk)	Decreased spleen volume as confirmed by magnetic resonance imaging Secondary endpoints including the following: Reduced liver volume Improved hemoglobin measurements Increased platelet counts Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Glutamate receptor antagonist (perampanel) for treatment of partial-onset epilepsy	Patients in whom partial-onset epilepsy has been diagnosed	Some patients with partial-onset epilepsy do not respond to current therapy. Perampanel represents a new mechanism of action/class of drugs for this disease state; a highly selective, noncompetitive AMPA-type glutamate receptor antagonist; AMPA receptors (located in excitatory neurons) transmit signals stimulated by glutamate and are believed to play a role in diseases characterized by excess neuroexcitatory signaling, such as epilepsy; drug also known as E2007. Eisai Co., Ltd., Tokyo, Japan Phase III trials completed; NDA and marketing authorization application submitted to FDA and to the European Medicines Agency, respectively, in May 2011; Jul 2011, FDA issued Refusal to File letter requesting that reformatting and reanalysis be done on submitted datasets before consideration for NDA acceptance	Tricyclics GABA derivatives Valproate Lamotrigine Levetiracetam Tiagabine	Reduced frequency of partial seizures Improved quality of life
Glycogen synthase kinase-3 enzyme inhibitor (tideglusib; Zentylor) for treatment of progressive supranuclear palsy	Patients in whom PSP has been diagnosed	Currently, no treatments exist for PSP. Tideglusib (Zentylor™) represents a novel drug class for this indication as a glycogen synthase kinase 3 (GSK-3) inhibitor for treatment of PSP. In patients with PSP, hyperphosphorylation of the tau protein occurs and contributes to microtubule destabilization and axonal transport dysfunction; GSK-3 is believed to be the major enzyme responsible for the abnormal hyperphosphorylation of tau; it may also be involved in the formation of the beta-amyloid peptide; it is a disease-modifying drug. Noscira, S.A., Madrid, Spain Phase II trial ongoing; FDA granted orphan drug and fast track status; has orphan drug status in EU	Anticholinergic medications Davunetide (in development)	Improved symptom control Delayed or halted disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gracilis muscle transplant for treatment of facial paralysis in pediatric population	Pediatric patients in whom facial paralysis has been diagnosed	Current surgical measures may have higher failure rates and less optimal outcomes in the event of successful muscle transfer. Gracilis muscle implantation involves transferring a segment of the gracilis muscle into the cheek, allowing for blood vessel and nerve regeneration and consequent facial reanimation. Massachusetts Eye and Ear Infirmary, Boston, MA Pilot study completed as of Jul 2011	Facial slings (masseter, temporalis, or anterior belly of digastric muscle) Nerve graft	Improved surgery success rate Improved facial reanimation Improved quality of life
GSK-2402968 (PRO-051) for treatment of Duchenne muscular dystrophy	Ambulatory patients 5 years and older who have been given a diagnosis of DMD who have a dystrophin gene mutation including deletions of exon 50, exon 52, exons 45-50, exons 48-50, and exons 49-50	Current treatments for DMD are limited to reducing symptoms without addressing their underlying cause. Patients experience a shortened lifespan and require additional support from devices. GSK2402968 is an antisense oligonucleotide which induces exon skipping of exon 51; technology uses small pieces of DNA called antisense oligonucleotides to skip a defective exon (small sequences of genetic code that codes for sections of protein) to correct the reading frame and allow a normal protein to be produced. This RNA therapeutic is given by injection. GlaxoSmithKline, Middlesex, UK, in partnership with Prosensa, Leiden, The Netherlands Phase III trial ongoing; FDA granted orphan drug status	Symptom control using corticosteroids and beta-2 agonists Physical therapy Orthopedics Respiratory support (respirator/ventilators)	Decreased muscle degeneration Improved symptoms Decreased need for supportive devices Improved quality of life Increased survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Heterologous liver cell infusion as bridge to liver transplant for treatment of urea cycle disorders	Patients in whom a genetic-based urea cycle disorder has been diagnosed	Urea cycle disorders are a family of genetic disorders in which patients lack one of the enzymes required for conversion of ammonia to urea; ammonia builds up, causing significant morbidity and possible mortality; patients with urea cycle disorders have a 10-year survival rate of less than 50% using current pharmaceutical and dietary treatments; patients receiving successful liver transplants have a survival rate of more than 90%; however, liver transplantation in patients 5 years of age or younger is technically difficult; there is a need for effective treatments that would allow control of disease symptoms in young patients until transplantation is possible. This treatment is intended for patients between birth and 5 years of age as a bridge to a definitive liver transplantation, which in many cases resolves the disorder; heterologous liver cell infusion is intended to temporarily populate the liver with cells that can provide a sufficient level of enzymatic activity to reduce ammonia levels to manageable levels; cells would be isolated from livers from the transplant pool that were determined to be unsuitable for whole liver transplant, and cells would be infused over the course of 6 days. Cytonet GmbH & Co., KG, Weinheim, Germany Phase II trials ongoing in U.S. and Europe	Dietary management Ammonia scavengers (sodium phenylbutyrate, sodium benzoate) Urea cycle enzyme catalysts (L-citrulline, L-arginine)	Changes in 13C urea formation Reduced frequency and severity of metabolic crises
High-intensity focused ultrasound for treatment of primary hyper-parathyroidism	Patients in whom primary hyperparathyroid-ism has been diagnosed who either decline or are not candidates for parathyroidectomy	High-intensity focused ultrasound technique with TH-One under sonographic guidance is intended to ablate the gland while the patient is under conscious sedation. Theraclion, Paris, France Pilot trial completed in Bulgaria; phase I trial ongoing in France	Parathyroidectomy Percutaneous ethanol injection	Decreased serum parathyroid hormone levels Decreased serum calcium levels Reduced size of benign parathyroid tumors Reduced blurred vision, back pain, depression, fatigue Improved quality of life Adverse events

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Hormone stimulation drug (FG-2216) for treatment of anemia from dialysis	Patients needing dialysis who are at risk for anemia	First oral drug (FG-2216) intended to stimulate production of the hormone erythropoietin in dialysis patients who are at risk for anemia; erythropoietin stimulates production of oxygen-carrying red blood cells. Astellas Pharma, Inc., Tokyo, Japan Fibrogen Inc., San Francisco, CA Phase II trial completed	Erythropoietin replacement therapy with erythropoiesis-stimulating agents	Resolution of anemia Improved quality of life
Human spinal-cord-derived neural stem cells (NSI-566RSC) for treatment of amyotrophic lateral sclerosis	Patients who have received a diagnosis of ALS	The only available pharmacologic option, Riluzole, may slow, not stop, disease progression. Stem cell therapy may potentially repair neurologic damage. NSI-566RSC was developed from human spinal-cord-derived neural stem cells; this neural stem cell product is injected into the lumbar spinal cord. Neuralstem, Inc., Rockville, MD Phase I trial ongoing; FDA has granted orphan drug designation for treatment of ALS	Riluzole (Rilutek) Physical therapy and speech therapy to improve daily functioning Medications for symptom management (muscle cramps, constipation, fatigue, excessive salivation, excessive phlegm, pain, depression)	Slowing or halting progression of ALS Reduced symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Hypoglossal nerve stimulation (HGNS) for treatment of obstructive sleep apnea	Patients in whom obstructive sleep apnea (OSA) has been diagnosed	OSA affects about 18 million Americans, with fewer than 10% of affected people having received a diagnosis. It is associated with diseases such as hypertension, diabetes, cardiovascular disease, stroke, depression, and sudden cardiac death. Current treatments (e.g., lifestyle changes, use of CPAP) depend on patient compliance, which is known to be low. The Apnex Hypoglossal Nerve Stimulation (HGNS) System is a surgically-implanted investigational device that activates the upper airway muscles to ensure opening of the airways during sleep. Mild stimulation of the hypoglossal nerve via the neuromodulator and stimulation lead complex occurs while the system monitors a patient's breathing patterns (using respiration leads). Stimulation of the hypoglossal nerve is a key factor for preventing the muscles of the tongue from blocking the patient's airway. This investigational device is used only while a patient is asleep and also contains a manual option for the patient to turn on and off as needed. Apnex Medical, Inc., St. Paul, MN Phase II/III trial ongoing	Aura6000 (under development) CPAP Inspire upper airway system (under development) Lifestyle changes (dietary, weight loss, alcohol reduction, etc.) OSA drugs (under development) Surgery Tongue suspension systems	Prevention of complications of OSA, including cardiovascular disease and sudden cardiac death Improved airway compliance Improved airway muscle tone Improved long-term cardiovascular outcomes Improved sleep quality Improved quality of life
Implantable miniature telescope for treatment of end-stage age-related macular degeneration	Patients in whom end-stage age-related macular degeneration (ARMD) has been diagnosed and who have severe vision loss	A small telescope replaces the natural lens and is intended to enable recipients to see an image that is magnified more than two times; surgically implanted in one eye; other eye is used for peripheral vision. VisionCare Ophthalmic Technologies, Inc., Saratoga, CA FDA approved with conditions in 2010; two postapproval studies required; in Nov 2011, first patient received the new device	Laser surgery Photodynamic therapy Anti-VEGF injections	Improved vision Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Inhaled apomorphine (VR040) for fluctuating idiopathic Parkinson's disease	Patients in whom fluctuating idiopathic PD has been diagnosed	VR040 is a proprietary formulation of apomorphine using proprietary delivery technology delivered to the bloodstream by inhalation through the lungs using proprietary dry powder inhalation technology. Vectura Group, plc, Chippenham, UK Phase II trials completed; European Medicines Agency granted orphan drug designation 2006; Vectura is seeking to license	L-dopa with and without inhaled VR040	Improved ability to control movement Slowed disease progression
Keratin gel for nerve regeneration of traumatically injured peripheral nerves	Patients who have experienced traumatic injury to peripheral nerves	Treatments for nerve gaps (severed nerves) include grafts or conduits, but neither is highly effective with nerve gaps greater than 5 mm. Keratin gel applied inside a nerve guidance conduit during nerve-repair surgery is proposed as a treatment to promote nerve regeneration that bridges that gap. Wake Forest University, Winston-Salem, NC, received $2.4 million grant from U.S. military to study university-developed keratin gel for peripheral nerve repair Phase I/II trials planned pending FDA authorization to proceed; Keretec Ltd., Canterbury, New Zealand, received marketing clearance in 2009 for a keratin-based wound dressing (Keretec Keragel)	Autologous grafts of healthy nerve tissue Implantation of nerve guidance conduits (tubes) between severed nerve endings	Improved efficacy of nerve repair with nerve grafts or guidance conduits Absence of reduced nerve function in healthy nerves, which may happen with graft harvesting
Kidney growth factor peptide (NX-001) for prevention of delayed graft function in renal transplantation	Patients who have received a kidney transplant	NX001 is a kidney growth factor peptide; growth factors are proteins that bind to receptors on the cell surface and activate cellular proliferation and/or differentiation. Several kidney-specific growth factors are known and could stimulate dormant cells to initiate DNA synthesis to promote repair and regeneration of kidney cells to try to speed and improve function of transplanted kidneys. NephRx Corp., Kalamazoo, MI Phase I trial ongoing; phase II trial planned for late 2011; FDA granted orphan drug status in 2010	No other treatment for delayed graft function	Faster graft function Improved graft function Improved graft survival Improved patient survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Lasmiditan (COL-144) for treatment of migraine headaches	Patients in whom migraine headaches have been diagnosed	Small-molecule, serotonin receptor agonist (Lasmiditan) that binds to the 5-HT^1F receptor; intended to have a reduced vasoconstrictive effect compared with other drugs; oral and intravenous formulations studied. CoLucid Pharmaceuticals, Inc., Research Triangle Park, NC Phase IIb trial completed (outside U.S.); FDA accepted IND in Aug 2011; phase III trial planned	Triptans (e.g., Axert, Frova, Maxalt, Imitrex, Zomig) Dihydroergotamine injection, intramuscular, intravenous, subcutaneous Dihydroergotamine intravenous plus antiemetic Acetaminophen plus aspirin plus caffeine oral Aspirin oral Butorphanol injection Ibuprofen oral Naproxen sodium oral Naratriptan oral Prochlorperazine intravenous Rizatriptan oral Sumatriptan injection, oral, subcutaneous Zolmitriptan oral	Quicker reduction in pain and light/noise sensitivity Reduced recurrence of symptoms Reduced side effects

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Laquinimod for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	Results seen with current RRMS therapies are unsatisfactory. Laquinimod represents a new mechanism of action for this disease state. Laquinimod is a synthetic immunomodulator with anti-inflammatory properties; exact mechanism of action has not yet been elucidated, but may exert its effect by modulating the immune system from a proinflammatory to an antiinflammatory response, and by preventing damaging immune system cells from entering central nervous system (CNS). Dosed once daily, orally. Teva Pharmaceutical Industries Ltd., Petach Tikva, Israel Active Biotech, Lund, Sweden Phase III trials completed; additional phase III trial ongoing; manufacturer expected to file NDA in early 2012; received fast track status from FDA in 2009	Fingolimod Glatiramer acetate INF INFb-1a (Avonex) Natalizumab	Reduced brain tissue loss/atrophy Reduced frequency of relapse Slowed disease progression Improved quality of life
Laser surgery for treatment of epilepsy	Patients in whom epilepsy has been diagnosed	An estimated 3 million people in the U.S. have some form of epilepsy, with approximately 1 million cases resistant to medical therapy. Pharmacological therapies have helped treat epilepsy, but recurrence may commonly occur. Surgical procedures such as craniotomy may be performed, but may leave the brain susceptible to unintended injury and resultant neurological complications. If accepted, laser therapy would provide a minimally invasive, potentially curative therapy for patients receiving a diagnosis of epilepsy. Laser surgery involves use of MRI-guided laser technology to ablate lesions in specific and nearly inaccessible regions of the brain. The laser probe is inserted through a hole (diameter of a pen) created in the skull to map the brain and then ablate the confirmed affected area. To protect surrounding neurological tissue, an automatic system shuts the laser down when approaching such areas. Laser therapy is for patients in whom definable lesions causing epilepsy have been detected by MRI. Texas Children's Hospital, Houston, TX Pilot trial completed	Antiseizure medications Craniotomy DBS	Reduction or elimination of seizures

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Levadex (MAP-0004) orally inhaled treatment for treatment of migraine headaches	Patients in whom migraine headaches have been diagnosed	A derivative (Levadex™ [MAP-0004]) of the currently available dihydroergotamine; intended to alleviate migraine headache symptoms quickly through oral inhalation. MAP Pharmaceuticals, Inc., Mountain View, CA Positive phase III results reported; in Jan 2011, company partnered with Allergan for Levadex commercialization; NDA accepted by FDA in Aug 2011 with a decision expected in Mar 2012	Triptans (e.g., Axert, Frova, Maxalt, Imitrex, Zomig) Dihydroergotamine, intramuscular, intravenous, subcutaneous Dihydroergotamine, intravenous, plus antiemetic Acetaminophen plus aspirin plus caffeine oral Aspirin oral Butorphanol injection Ibuprofen oral Naproxen sodium oral Naratriptan oral Prochlorperazine intravenous Rizatriptan oral Sumatriptan injection Zolmitriptan oral	Quicker reduction in pain and light/noise sensitivity Reduced recurrence of symptoms Reduced side effects

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Levetiracetam (Keppra) for treatment of chronic poststroke aphasia	Patients who have experienced stroke and in whom chronic aphasia (speech difficulty) has been diagnosed	The main treatment for aphasia is conventional speech and language therapy. However, it does not achieve adequate effectiveness for many stroke patients with speech and language deficits poststroke. Of all the drugs used in an attempt to improve aphasia, only piracetam, donepezil, and amphetamine have shown some limited efficacy in some patients. Levetiracetam (Keppra®) is an S-enantiomer derived from piracetam, and both levetiracetam and piracetam derive from gamma-aminobutyric acid. Levetiracetam was initially studied in animal models of cognitive impairment to try to find a drug more effective than piracetam. In trials of stroke patients with poststroke aphasia, levetiracetam (250 mg orally twice daily for 7 days, 500, 750, 1000 mg) is being tested. Kessler Foundation, West Orange, New Jersey Phase I trial ongoing	Speech-language therapy Piracetam Donepezil Amphetamine	Improved comprehension Improved memory Improved speech capability Improved capacity to read and write
Macrophage regulator (NP001) for treatment of amyotrophic lateral sclerosis	Patients in whom ALS has been diagnosed	NP001 is a small-molecule regulator of macrophage activation; aberrant macrophage activation believed to be a primary contributor to the pathology underlying ALS and other neurodegenerative diseases; intended to restore normal functioning of macrophages in CNS, reducing inflammation and normalizing the cellular environment. Administered intravenously. Neuraltus Pharmaceuticals, Inc., Palo Alto, CA Phase II trial ongoing; FDA granted fast track and orphan drug status Aug 2011	Drugs that address symptoms but do not address biomarkers	Improved biomarker levels Restoration of macrophages to their neuroprotective state Improved activities of daily living Delayed disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Magnetic tongue-piercing aid for directing mobile wheel chair	Patients with spinal cord paralysis, particularly from the neck down	The magnetic pierced-tongue aid is a magnetic device in the mode of a ball-shaped tongue ring that is intended to mobilize a wheelchair by sending signals to a headset containing sensors. Sensors in the user's headset respond to the tongue ring's magnetic signals based on the direction in which the user moves the tongue (e.g., tongue moves to the mouth's upper left corner, prompting wheelchair to move forward). The tongue was targeted for device implant because it does not tire easily and is generally unaffected by spinal cord injuries. Current technologies, including the "sip and puff" wheelchair, may be less flexible, more difficult to use, and less aesthetically pleasing. The magnetic pierced-tongue aid for wheelchair users may provide more flexibility, better accuracy, and greater quality of life for patients who have severe muscle weakness (e.g., paraplegia, quadriplegia, MS, stroke, muscular dystrophy). Georgia Institute of Technology, Atlanta, GA Pilot trial completed	Comparators depend on severity of spinal cord paralysis Chin control wheelchair Head control wheelchair "Sip and puff" wheelchair Speech control wheelchair Tongue keyboard controller wheelchair	Improved wheelchair function and control Improved aesthetics of device Improved mobility Improved quality of life
Menerba (MF-101) for treatment of hot flashes in postmenopausal women	Postmenopausal women experiencing hot flashes	The experience of hot flashes is a highly common symptom of menopause, affecting approximately 80% of women at some point at the end of reproductive lives. Hormone replacement therapy (HRT) has been used to treat postmenopausal women suffering from hot flashes, but has associated risks, including breast cancer, endometrial cancer, stroke, and heart disease. MF-101 is a selective estrogen receptor beta (ERB) agonist that stimulates estrogen activity while not stimulating the estrogen alpha receptors known to be in association with the development of breast and endometrial cancer; MF-101 contains liquiritigenin, purported to be a highly active estrogen (specifically ERB) compound derived from the root of *Glycyrrhizae uralensis* Fisch. MF-101 is administered orally, 5, 10, or 15 g, daily. Bionovo, Inc., Emeryville, CA Phase III trial ongoing	Antidepressants Estrogen therapy (pill or cream form) Hormone therapy Ibuprofen Neurontin Phytoestrogens Progesterone/pro-gestin-estrogen Raloxifene Tamoxifen Vitamin B complex Vitamin E	Decreased incidence of hot flashes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mapracorat ophthalmic suspension for treatment of postcataract-surgery inflammation	Patients who have undergone cataract surgery	Selective glucocorticoid receptor agonist (Mapracorat; BOL-303242-X) exhibits glucocorticoid-like antiinflammatory activities; intended for use to reduce inflammation and adverse effects of classic steroids used to treat ophthalmic inflammation. Bausch & Lomb, Inc., Rochester, NY Phase III trial ongoing; one phase III trial terminated	Antibiotics Corticosteroids NSAIDs Tobradex (tobramycin 3 mg/mL, dexamethasone 1 mg/mL)	Reduced inflammation-related complications Reduced side effects
Mecobalamin (E-0302) for treatment of amyotrophic lateral sclerosis	Patients in whom ALS has been diagnosed	Only one drug (Riluzole) is currently approved for treatment of ALS. Mecobalamin (E-0302) is a methylated form of vitamin B_{12} proposed for parenteral therapy for ALS. Eisai Co., Ltd., Tokyo, Japan Phase II/III clinical trials ongoing in Japan	Riluzole Supportive care	Increased survival rate Improved functional rating scale Increased safety Improved quality of life
Mesenchymal stem cell transplantation for treatment of multiple sclerosis	Patients in whom MS has been diagnosed	Current MS therapies are intended to minimize immune-system damage to the CNS and slow disease progression; however, there are no therapies designed to prevent and reverse damage to the CNS by the immune system. Mesenchymal stem cells (MSCs) injected into the blood are purported to have a wide range of effects that decrease the reactivity of immune cells and encourage tissue repair, which may be beneficial to patients with MS. MSCs injected into the blood are purported to migrate into areas of inflammation or injury in the CNS and mediate protective effects. Cleveland Clinic, Cleveland, OH University Hospitals Seidman Cancer Center, Cleveland, OH Case Western Reserve University, Cleveland, OH Phase I trial ongoing	Fingolimod Glatiramer acetate INFb INFb-1a (Avonex) Laquinimod Natalizumab	Improved motor/cognitive function Reduced brain tissue loss/atrophy Reduced frequency of relapse Slowed rate of disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Metabotropic glutamate receptor 5 antagonist dipraglurant (ADX48621) for treatment of Parkinson's disease	Patients in whom PD has been diagnosed	Current PD therapies are associated with poor tolerability including development of levodopa-induced dyskinesia (PD-LID), which occurs in about half of patients receiving treatment. While dystonia is a significant problem for PD patients; currently no products are specifically licensed for treatment of dystonias. New therapies with better efficacy and tolerability are needed. Dipraglurant is a negative allosteric modulator of metabotropic glutamate receptor 5 (mGluR5), which is purported to be found in regions of the brain that serve as key control points in the neuronal motor circuits responsible for abnormal glutamate signaling. Perturbations in glutamate signaling (along with disruptions in dopaminergic signaling) are believed to be an underlying cause of PD. By inhibiting mGluR5, dipraglurant is intended to restore normal movement via a nondopaminergic mechanism, thereby offering a dopamine sparing therapy. Additionally, preclinical findings suggest that mGluR5 inhibitors may be neuroprotective and may hold potential to treat PD progression. Dipraglurant is purported to reduce both of the major PD-LID symptoms, chorea (rapid uncontrolled movements) and dystonia (writhing and cramping movements). Administered orally 50 mg once daily up to 100 mg three times daily. Addex Pharmaceuticals, Geneva, Switzerland Phase IIa trial ongoing	Dopamine agonists Levodopa/carbidopa Mavoglurant MOA-B inhibitors, etc.	Improved motor skill functions Reduced disease progression Sustained effect of treatment over time Reduced incidence/severity of levodopa-induced dyskinesia Reduced symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Metabotropic glutamate receptor 5 antagonist mavoglurant (AFQ056) for treatment of Parkinson's disease	Patients in whom PD has been diagnosed	Current therapies for PD are associated with poor tolerability including the development of PD-LID, which occurs in about half of all PD patients. New therapies with better efficacy and tolerability are needed. Mavoglurant is an antagonist of metabotropic glutamate receptor 5 (mGluR5), which is purported to be found in regions of the brain that serve as key control points in the neuronal motor circuits responsible for abnormal glutamate signaling. Perturbations in glutamate signaling (along with disruptions in dopaminergic signaling) are believed to be an underlying cause of PD. By inhibiting mGluR5, mavoglurant is intended to restore normal movement via a nondopaminergic mechanism, thereby offering a dopamine sparing therapy. Additionally, preclinical findings suggest that mGluR5 inhibitors may be neuroprotective and may hold potential to slow PD progression. Mavoglurant is purported to reduce both of the major PD-LID symptoms, chorea (rapid uncontrolled movements), and dystonia (writhing and cramping movements). Drug is administered 100 mg, daily. Novartis AG, Basel, Switzerland Phase IIb trials ongoing	Dipraglurant Dopamine agonists Levodopa/carbidopa MOA-B inhibitors, etc. NP002	Improved motor skill functions Slowed disease progression Sustained effect of treatment over time Reduced incidence/severity of levodopa-induced dyskinesia Reduced symptoms Improved quality of life
Micro-bypass implant (iStent) for treatment of glaucoma	Patients undergoing cataract surgery who are also at risk of developing glaucoma due to uncontrolled elevated IOP	IStent is intended for implantation during cataract surgery in patients with or at risk for open-angle glaucoma; iStent is designed to increase aqueous outflow by shunting aqueous humor from the anterior chamber to the Schlemm's canal, bypassing the trabecular meshwork; procedure avoids having to move the iris, conjunctiva, or sclera and preserves other surgical and medical options for treatment of glaucoma. Glaukos Corp., Laguna Hills, CA Phase I U.S. trial ongoing; in Aug 2010, FDA advisory panel recommended approval; FDA is reviewing.CE marked in select countries in Europe; approved in Canada	Trabectome (device) Trabeculotomy Surgery Medications Combination of medications and surgery	Preserved vision Reduced elevated or uncontrolled IOP

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Migalastat hydrochloride (AT1001) for treatment of Fabry disease	Patients in whom Fabry disease has been diagnosed who have either migalastat-responsive mutations in alpha-galactosidase A or who are receiving enzyme replacement therapy	Current enzyme replacement therapies for Fabry disease are expensive to produce and have been subject to recent shortages. AT1001 is a small molecule drug that acts as a molecular chaperone that enhances the activity of alpha-galactosidase A, the enzyme that is deficient in Fabry disease; could be used to enhance the activity of exogenously provided enzyme replacement therapy or used to enhance the endogenous activity of certain alpha-galactosidase mutant isoforms that have been shown to be responsive to it; in trials, testing as monotherapy and in combination with enzyme replacement therapy. Amicus Therapeutics, Inc., Cranbury, NJ Phase III trial ongoing	Enzyme replacement therapy Palliative treatment of secondary symptoms	Increased GL-3 levels (urine, kidney biopsy) Improved renal function (e.g., glomerular filtration rate) Improved quality of life
Nabiximols oromucosal spray (Sativex) for treatment of multiple sclerosis spasticity and neuropathic pain	Patients in whom MS has been diagnosed	Few effective treatment options are available for patients with MS. Sativex® is a whole plant medicinal cannabis extract that contains Tetranabinex® and Nabidiolex® (cannabidiol) as its main component; delta-9-tetrahydrocannabinol (THC) in the extract acts as a partial agonist at both cannabinoid receptors, CB1 and CB2, mimicking the effects of the endocannabinoids, which may modulate the effects of neurotransmitters (e.g., reduce effects of excitatory neurotransmitters such as glutamate) to improve symptoms. Sativex is sprayed under the tongue, 100 mcL/dose, which contains 2.5 mg cannabidiol and 2.7 mg THC; Sativex is intended to be an add-on treatment to current MS therapies. GW Pharmaceuticals, plc, Salisbury, UK Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan Phase III trials ongoing; approved in New Zealand and Canada for treatment of spasticity due to MS; approved in Canada for relief of MS-related neuropathic pain	Opioids	Reduced pain Reduced spasticity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
N-acetylgalactos-amine 6-sulfatase (GALNS) for treatment of Morquio syndrome	Patients in whom the genetic disorder Morquio syndrome type A has been diagnosed	Morquio syndrome type A is a rare autosomal recessive genetic disorder resulting from a deficiency in N-acetylgalactosamine-6-sulfate sulfatase activity, which leads to the accumulation of keratan sulfate and various developmental defects; no treatments are available to address the underlying cause of the disease; only palliative treatments are available. N-acetylgalactosamine 6-sulfatase (BMN-110) is an enzyme replacement therapy intended to treat the underlying disorder. BioMarin Pharmaceutical, Inc., Novato, CA Phase III trial ongoing	No current treatments are available to resolve the underlying disease.	Disease regression Improved bone growth as measured by radiograph Improved activities of daily living Increased physical endurance (6-minute walk test) Improved respiratory function Reduced urine keratan sulfate levels
NBI-98854 for treatment of tardive dyskinesia	Patients with schizophrenia who have been given a diagnosis of tardive dyskinesia	Only one treatment is approved for treating this condition, and the development of the disease is not yet well understood. More and better treatment is needed. NBI-98854 is a vesicular monoamine transporter type 2 (VMAT2) inhibitor that regulates the levels of dopamine release during nerve communication while reducing the likelihood of "off-target" side effects. This compound provides sustained plasma and brain concentrations of the active drug to minimize side effects associated with excessive dopamine depletion. Neurocrine Biosciences, Inc., San Diego, CA Phase II trial ongoing	Tetrabenazine Parkinson's medications (Mirapex, etc.) Benzodiazepines Tarvil Omega-3 fatty acids Cogentin	Reduced abnormal involuntary movements
Neural stem cell therapy (ReN001) for stroke recovery	Patients in whom a stroke has been diagnosed	Stem cell therapy with ReN001, a clonal human neural stem cell line generated in the laboratory; stem cells are injected into the brain under local anesthetic and intended to assist in recovery from stroke. ReNeuron Group, Inc., Guildford, UK Phase I trial ongoing in UK; investigational new drug (IND) application on hold with FDA in U.S.	Current rehabilitative treatment for disabled stroke survivors	Resolution of functional deficits

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Neuron transplantation (MotorGraft) for patients with spinal muscular atrophy type 1	Patients in whom spinal muscular atrophy (SMA) type I has been diagnosed	A stem cell-derived motor neuron transplantation therapy, MotorGraft™ is intended for treatment of SMA type I; cells are delivered surgically into the spinal cord of these patients. California Stem Cell, Inc., Irvine, CA Phase I trial placed on clinical hold (delayed) per FDA official response to company's IND	No treatment exists	Improved function in muscles that control crawling, walking, swallowing and breathing
Nicotinic receptor agonist NP002 for treatment of Parkinson's disease	Patients in whom PD has been diagnosed	Current PD therapies are associated with poor tolerability, including the development of PD-LID which occurs in about half of all PD patients receiving treatment. New therapies with better efficacy and tolerability are needed. Patients with PD have been found to have fewer nicotinic receptors in their brains, and smoking has been shown to have a neuroprotective effect against PD; NP002 is a small molecule, orally available nicotinic receptor agonist which is purported reduce PD-LID without negatively affecting PD symptoms. Administered 1 to 6 mg, four times daily. Neuraltus Pharmaceuticals, Inc., Palo Alto, CA Completed phase I/II trial	Dipraglurant Dopamine agonists Levodopa/carbidopa Mavoglurant MOA-B inhibitors, etc.	Improved motor skill functions Reduced disease progression Sustained effect of treatment over time Reduced incidence/severity of levodopa-induced dyskinesia Reduced symptoms Improved quality of life
Nitroglycerin for prevention of osteoporosis	Postmenopausal women who have normal bone density or osteopenia	Currently available treatments for osteoporosis either prevent bone resorption or promote bone formation, but no compound performs both functions, which nitroglycerin is purported to do. Nitroglycerin leads to the production of nitric oxide, which has been demonstrated in vitro to cause decreased bone resorption, increased osteoblast cell proliferation, increased osteocalcin synthesis, and increased osteoblastic cell mineralization; these processes could all prevent bone loss. National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD Phase III trial ongoing at University of Toronto	Antibone resorptive drugs (bisphosphonates, selective estrogen receptor modulators, estrogen, calcitonin, anti-RANKL antibodies). Bone formation stimulators (teriparatide)	Increased lumbar vertebrae and hip bone mineral density Improved serum osteocalcin levels Improved bone-specific alkaline phosphatase levels Reduced hip and spine fractures

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Nonsurgical, removable dental hearing device (SoundBite) for treatment of single-sided deafness	Patients in whom single-sided deafness has been diagnosed	Hearing loss affects more than 28 million people in the U.S., prompting use of hearing devices. Available hearing aids may not provide optimal quality for patients, and surgical interventions or bone anchored implants may be too invasive and expensive. The nonsurgical, removable dental hearing device (SoundBite™) consists of a behind-the-ear (BTE) microphone unit which houses the receiver, a wireless transmitter, an attached microphone, and a discreet, removable in-the-mouth (ITM) hearing device. The BTE unit transmits sound to the ITM device, which then is intended to produce imperceptible sound vibrations via the teeth through bones and to both cochleae. The ITM device is custom molded to the teeth without surgery or alterations to tooth structure. Sonitus Medical, Inc., San Mateo, CA FDA 510(k) clearance granted 2011	Bone anchored implants Hearing aid devices (BTE, in-the-ear devices, canal aids)	Improved hearing Improved quality of life
NX-1207 for treatment of benign prostatic hyperplasia	Patients in whom benign prostatic hyperplasia (BPH) has been diagnosed	Current therapies for BPH address only secondary symptoms (muscle relaxation by alpha blockers) and can have adverse effects (impotence, decreased libido by 5-alpha reductase inhibitors). NX-1207 is a small molecule drug administered by ultrasound-guided transrectal intraprostatic injection that is intended to shrink the size of an enlarged prostate. While its exact mechanism of action is unknown, it is thought that NX-1207 has pro-apoptotic properties. Nymox Pharmaceutical Corp., Hasbrouck Heights, NJ Phase III trials ongoing	Alpha blockers: terazosin, doxazosin, tamsulosin, alfuzosin, silodosin 5-Alpha reductase inhibitors: finasteride, dutasteride Surgery (transurethral resection of the prostate) Minimally invasive surgery (laser ablation, transurethral microwave therapy)	Improved International Prostate Symptom Score or improved American Urological Association Symptom Index Increased urine flow rate Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Obeticholic acid (INT-747) for treatment of nonalcoholic steatohepatitis	Patients in whom nonalcoholic steatohepatitis has been diagnosed	Obeticholic acid (INT-747) is a farnesoid X receptor agonist derived from human bile intended for administration to decrease liver tissue scarring and fibrosis. Intercept Pharmaceuticals, Inc., New York, NY Phase II trial completed in type II diabetes patients with non-alcoholic fatty liver disease; study of 280 patients with NASH to be initiated in collaboration with the National Institute of Diabetes and Digestive and Kidney Diseases	Currently, no other treatment exists	Reduced tissue scarring Slowed progression of fibrosis Improved liver function Improved quality of life Reduced need for liver transplantation
Ocrelizumab for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	Current therapy for RRMS provides unsatisfactory results for many patients. Ocrelizumab represents a novel mechanism of action for this disease state; is a human monoclonal antibody (mAb) intended to target CD20-positive B-cells (believed to play a role in MS), then interact with immune system to eliminate these CD20-positive B-cells. Administered via infusion, once every 6 months. F. Hoffman-La Roche, Ltd., Basel, Switzerland Biogen Idec, Inc., Weston, MA Phase III trials ongoing	Fingolimod Glatiramer acetate INFb INFb-1a (Avonex) Natalizumab	Decreased frequency of relapse Slowed disease progression Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label etanercept for treatment of Kawasaki disease	Patients in whom Kawasaki disease (KD) has been diagnosed	KD is the most common cause of acquired heart disease in U.S. children, and many patients are refractory to current standard of care; new treatment options are needed for patients whose disease is refractory to treatment. Etanercept is a dimeric soluble form of the p75 TNF receptor purported to bind TNF alpha and beta molecules, thus inhibiting the binding of TNF molecules to cell surface receptors and preventing inflammation associated with KD. Etanercept may be administered immediately after intravenous immunoglobulin (IVIG) infusion, 0.8 mg/kg/dose, two times weekly. Amgen, Inc., Thousand Oaks, CA Phase II trial ongoing; FDA approved in 1998 for moderate to severe rheumatoid arthritis and other inflammatory conditions	High-dose aspirin IVIG	Improved survival Prevented increase in coronary artery diameter Prevented new coronary artery dilation/cardiac dysfunction Reduced fever
Olesoxime (TRO19622) for treatment of amyotrophic lateral sclerosis	Patients who have been given a diagnosis of sporadic, familial, or probable ALS	Only one drug is available for treatment of ALS; it is of limited efficacy and does not reverse the damage done by ALS. Olesoxime is a potentially disease-modifying drug intended to promote neuroaxonal repair and remyelination, and the function and survival of neurons and other cell types under disease-relevant stress conditions through interactions with the mitochondrial permeability transition pore (mPTP). Olesoxime is an oral compound. Trophos SA, Marseille, France Phase II/III trials ongoing	Riluzole Supportive care	Improved survival Survival without need of tracheostomy or IV Improved scores on the 48-point ALS Functional Rating Scale (Revised) Improved vital capacity Improved score on manual muscle test Improved quality of life
Olesoxime (TRO19622) for treatment of spinal muscular atrophy	Patients who have been given a diagnosis of spinal muscular atrophy (SMA)	No drugs are currently approved to treat SMA. Olesoxime potentially promotes neuroaxonal repair and remyelination and the function and survival of neurons and other cell types under disease-relevant stress conditions through interactions with the mitochondrial mPTP; this oral compound potentially promotes remyelination and provides neuroprotection. Trophos SA, Marseille, France Phase II trial ongoing	Butyrates Valproic acid Hydroxyurea Riluzole Quinazoline495 Assistive technology	Increased survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral calcitonin (Ostora) for prevention and treatment of postmenopausal osteoporosis	Women at risk for or in whom postmenopausal osteoporosis has been diagnosed	No oral formulation of (salmon) calcitonin is available; oral formulation has the potential to increase compliance and prescription habits compared with injection and nasal formulations. Salmon calcitonin (Ostora™) is a naturally occurring hormone involved in calcium regulation; binds to osteoclasts to slow the rate of bone breakdown and resulting bone loss; approved and widely used in other forms. Tarsa Therapeutics, Philadelphia, PA Phase III trial completed; company plans to file new drug application in late 2011	Capsitonin oral calcitonin (in development) Injectable calcitonin Intranasal calcitonin	Slowed rate of bone breakdown Decreased bone loss Decreased numbers of hip and spine fractures Improved quality of life
Oral opioid antagonist (ALKS-37) for treatment of opioid-induced bowel dysfunction	Patients in whom opioid-induced bowel dysfunction (OBD) has been diagnosed	No oral pharmaceuticals are available to treat the bowel dysfunction often induced by opioid treatment. ALKS 37 is an orally active, peripherally restricted opioid antagonist intended to improve gastrointestinal (GI) motility and the frequency of bowel movements while preserving the analgesic effects of the opioid for pain management; ALKS 37 is intended to be a metabolically stable molecule that targets the GI tract with limited systemic exposure; also known as RDC-1036. Alkermes, Inc., Waltham, MA Phase II trial completed	Laxatives Injectable opioid antagonists (methylnaltrexone)	Reduced bowel dysfunction Increased frequency of bowel movements Compliance with opioid treatment

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral opioid antagonist (NKTR-118) for treatment of opioid-induced bowel dysfunction	Patients in whom opioid-induced constipation (OIC) or other manifestations of opioid bowel dysfunction (OBD) have been diagnosed	No oral pharmaceuticals are available to treat the bowel dysfunction often induced by opioid treatment, and bowel dysfunction is a common reason for not using opioids for pain management. NKTR-118 combines AstraZeneca's polymer conjugate technology platform with nalaxol, a derivative of naloxone (opioid antagonist) to make an orally active, peripherally restricted opioid antagonist intended to improve GI motility and the frequency of bowel movements while preserving the analgesic effects of the opioid for pain management; targets peripheral opioid receptors to alleviate constipation while limiting the penetration across the blood-brain barrier which would reduce analgesic effects. AstraZeneca, London, UK Nektar Therapeutics, San Francisco, CA Phase III trials ongoing	Laxatives Injectable opioid antagonists (methylnaltrexone)	Reduced bowel dysfunction while on opioid therapy Increased frequency of bowel movements Improved compliance with opioid therapy
Osseointegrated implants for lower-limb prostheses	Patients who have had amputation of a lower limb	Prosthetic legs typically attach over a stump of the remaining limb. Osseointegrated implants feature a body-prosthesis interface that is fused into bone of the residual limb to potentially improve mobility and comfort of prostheses; the prosthetic limb connects to the fused metal implant that protrudes through the skin. Specific device manufacturer(s) unclear In early use in Europe; FDA has not yet approved any trials	Conventional prosthetic legs that attach over stump of residual lower limb	Improved gait, mobility and comfort Reduced pain Improved fit
Oxybutynin intravaginally (FP 1097) for treatment of urinary urge incontinence	Women in whom urinary urge incontinence has been diagnosed	FP 1097 is an intravaginal delivery method for the anticholinergic drug oxybutynin and is of interest because of its potential to avoid systemic side effects of oral drugs (e.g., dry mouth, constipation, blurry vision, confusion) used to treat the condition. FemmePharma Global Healthcare, Inc., Wayne, PA Phase II trials completed; phase III trial planned for 2011; FDA has agreed to grant FP 1097 505(b)(1) filing status (lower evidence requirement)	Systemic anticholinergic drugs: oxybutynin, tolterodine, solifenacin, darifenacin, fesoterodine fumarate	Reduced micturition and incontinence episodes Reduced systemic side effects (dry mouth, constipation, blurry vision, confusion)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pegylated human interferon beta-1a (BIIB017) for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	Standard-of-care INF treatments for RRMS are characterized by limitations such as frequent dosing (once or twice weekly), injection site reactions, and flulike symptoms. Long-acting INF beta (INFb) could address some of these limitations because no long-acting forms of INFb are available. BIIB017 is pegylated (PEG) human INFb-1a (Avonex, first-line immunomodulator); early trials suggest PEG INFb-1a is stable in the blood stream for up to 7 days. Designed to be dosed once or twice monthly, which may improve compliance and relieve frequency of injection site reactions/flu symptoms. Delivered via injection. Biogen Idec, Inc., Weston, MA Phase III trials ongoing; received fast track status from FDA in 2009	Nonpegylated INFb 1-a Nonpegylated INFb 1-b AZ-01 (in development)	Improved treatment compliance Reduced RRMS symptoms Reduced injection site reactions Reduced flulike symptoms associated with injection Slowed disease progression Improved quality of life
Pegylated human interferon beta-1b (AZ-01) for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	Standard-of-care INF treatments for RRMS are characterized by limitations such as frequent dosing (once or twice weekly), injection site reactions, flulike symptoms, and limited efficacy for some patients. Long-acting INFb might address these limitations; no long-acting forms of INFb are available. AZ-01 is a pegylated (PEG) form of human INFb-1b (first-line immunomodulator; early trials suggest PEG INFb-1b is stable in the blood stream for up to 14 days. Designed to be dosed once monthly, which may improve compliance and relieve frequency of injection site reactions/flulike symptoms. Delivered via injection. Allozyne, Inc., Seattle, WA Phase Ia trial completed	Nonpegylated INFb 1-a Nonpegylated INFb 1-b BIIB017 (in development)	Reduced MS symptoms Slowed or halted disease progression Improved compliance with treatment Decreased side effects from treatment Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pegylated recombinant phenylalanine ammonia lyase (PEG-PAL) enzyme replacement therapy for treatment of phenylketonuria	Individuals in whom phenylketonuria has been diagnosed	Pegylated recombinant phenylalanine ammonia lyase (PEG-PAL); phenylketonuria is an inherited disorder in which an enzyme that is needed to break down essential amino acid phenylalanine is missing; drug is intended to reduce levels of phenylalanine in patients unresponsive to Kuvan®. Administered by injection, one to three times a week. BioMarin Pharma, Inc., Novato, CA Phase II trials ongoing; FDA granted orphan drug status	Kuvan (tetrahydrobiopterin or BH4)	Decreased phenylalanine levels Fewer diet restrictions Improved quality of life Injection site inflammation is most common adverse event (43 percent)
Personalized T-cell immunotherapy (Tovaxin) for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	There is no cure for MS. Current treatments do not sustain long-term remission, and some have severe secondary effects. Tovaxin® is a personalized cellular immunotherapy derived from T cells isolated from peripheral blood, expanded ex vivo, and reintroduced into the patients via subcutaneous injections; process triggers a potentially potent immune response against specific subsets of autoreactive T cells known to attack myelin and reduces the risk of relapse over time. Opexa Therapeutics, Inc., The Woodlands, TX Phase II trials completed	INFb-1a (Avonex®, CinnoVex™, ReciGen® and Rebif®) INFb-1b (Betaseron®) Glatiramer acetate (Copaxone®) Mitoxantrone Natalizumab (Tysabri®)	Decreased annualized relapse rate Improvement in disability score Improved safety Improved long-term management of disease
PET/MRI integrated imaging system (Biograph mMR) for diagnosis of neurologic conditions	Patients who require morphologic, functional, and metabolic imaging exams for neurologic indications	Imaging exams (Biograph mMR™) that combine positron emission tomography (PET) with MRI; intended to provide simultaneous acquisition of morphologic, functional, and metabolic imaging data; exam intended to take 30 minutes compared with 1 hour or more for sequential positron emission tomography and magnetic resonance imaging exams. Siemens Healthcare, Malvern, PA FDA 510(k) clearance granted June 2011	Stand-alone positron emission tomography and magnetic resonance imaging exams	More efficient imaging for patient Improved diagnosis from combined morphologic, functional, and metabolic imaging Improved treatment planning

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Phentermine/topiramate (Qnexa) for treatment of obstructive sleep apnea	Patients in whom OSA has been diagnosed	OSA affects about 18 million Americans, and less than 10% of affected people have the condition diagnosed. OSA is associated with hypertension, diabetes, cardiovascular disease, stroke, depression, and sudden cardiac death. Current treatment efficacy (e.g., lifestyle changes, use of CPAP) depends on patient compliance, which is known to be low. No pharmacologic therapy is approved for OSA. Phentermine/topiramate (Qnexa®) is a combination drug under investigation for treatment of OSA, obesity, and T2DM. Phentermine is believed to work on the hypothalamus portion of the brain to stimulate the adrenal glands to release norepinephrine, which is purported to reduce hunger, and topiramate is an anticonvulsant that blocks sodium (Na) channels and is purported to affect weight loss; if approved, the phentermine/topiramate combination would become the first approved drug for treatment of OSA. The drug has been administered orally in trials at a dose of 15 mg of phentermine instant release and 92 mg of topiramate controlled release. Vivus, Inc., Mountain View, CA Phase II trial (OB-204) completed Sept 2009; no further information available as of Nov 2011	CPAP Hypoglossal neurostimulation Lifestyle changes (dietary, weight loss, alcohol reduction, etc.)	Decreased OSA Weight loss Prevention of complications of OSA, including cardiovascular disease and sudden cardiac death
Phrenic nerve stimulation (Remedē system) for central sleep apnea associated with heart failure	Patients in whom central sleep apnea associated with HF has been diagnosed	Remedē™ system is a device that is implanted in chest (similar to pacemaker). It is attached to two insulated wires inserted into veins; stimulation wire placed in vein near one of patient's phrenic nerves sends communication between diaphragm and the brain, which stimulates phrenic nerve and returns patient to normal breathing. Respicardia, Inc., Minneapolis, MN Pilot trial expected to be completed by end of 2011; phase II trial ongoing	Adaptive servo ventilator Oxygen therapy	Slowed progression of HF Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Poloxamer compound (ANX-188) for treatment of sickle cell crisis	Patients in whom sickle cell crisis has been diagnosed	ANX-188 is a surfactant-containing, hydrophilic poloxamer that limits adhesion of sickled cells to each other and vascular endothelium, actions responsible for vaso-occlusive pain crisis. ANX-188 may shorten duration of painful vaso-occlusive crises (VOC) and may not present adverse effects associated with current treatments for sickle cell disease (SCD). Administered as an intravenous infusion for 48 hours. Adventrx Pharmaceuticals, Inc., San Diego, CA Phase III trial completed in 1999 by another company; rights bought by Adventrix, which is seeking FDA approval for new phase III trial; has orphan drug designation	Allogeneic stem cell transplant Gene therapy Azacitidine, hydroxyurea, butyrate decitabine, lenalidomide, polamidomide KCl cotransporter and Gardos channel inhibition Nitrous oxide Sildenafil Statins Antioxidant therapy	Reduced severity and duration of VOCs Reduced health disparities (African Americans) Improved quality of life
PPAR-gamma agonist (ATx08-001) for treatment of postherpetic neuralgia	Patients who have ongoing neuropathic pain after an outbreak of shingles (postherpetic neuralgia [PHN])	PHN affects a significant proportion of adults older than age 65 who have a bout of shingles, and severe PHN can require hospitalization; current treatments for PHN have variable efficacy in different patients and often require trial and error to achieve optimal relief. ATx08-001 is a novel oral peroxisome proliferator-activated receptor (PPAR)-gamma agonist that is purported to have a safety and toxicology profile distinct from current PPAR-gamma agonists; preclinical studies and preliminary human trials have demonstrated that modulation of PPAR-gamma activity is able to modify pain sensation. Aesthus Therapeutics, Inc., North Brunswick, NJ Phase II trial completed	Lidocaine skin patches Tricyclic antidepressants: Nortriptyline Amitriptyline Anticonvulsants: Gabapentin Pregabalin Opioids: Tramadol Oxycodone Morphine	Reduced pain on visual analog scale Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Preladenant for treatment of moderate to severe Parkinson's disease	Patients in whom moderate to severe PD has been diagnosed	Preladenant acts as a potent and selective antagonist at the adenosine A2A receptor; unlike L-dopa, effects do not appear to decrease over time and it appears to have fewer side effects. Merck & Co., Inc. (Schering-Plough), Whitehouse Station, NJ Phase III trials ongoing	L-dopa and carbidopa Rasagiline (Azilect) as monotherapy or adjunct therapy in advanced cases	Improved symptoms (motor function) Slowed disease progression Preserved independence Delayed need for assisted care
Prosthetic arm to restore natural function	Patients with trauma-induced amputations of the upper limbs	Advanced prosthetic arm technology comprises two major components, a prosthetic arm and body-machine interfaces; the prosthetic arm is intended to produce near-normal movement, dexterity and function; provide effortless and intuitive function via simple thoughts; and restore tactile sensation; body-machine interfaces are designed to improve the number of control sites available to manipulate the arms. Techniques under clinical evaluation include implantable myoelectric sensors, peripheral nerve interface electrodes, and targeted muscle reinnervation (surgery). Research commissioned and funded by U.S. Defense Advanced Research Projects Agency (DARPA), Arlington, VA; U.S. Department of Defense, Washington, DC, and U.S. Department of Veterans Affairs, Washington, DC, conducting clinical testing. Several U.S. and international research partners participating Early phase trials ongoing; FDA is piloting a new regulatory pathway for this technology: the Innovative Device pathway, which is intended to get innovative devices to market within 4 years	Conventional prosthetic arms	Significant restoration of limb function compared with current prosthetic devices

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PTH(1-84) for treatment of hypo-parathyroidism	Patients in whom hypo-parathyroidism has been diagnosed	Hypoparathyroidism is a rare disorder in which parathyroid hormone is markedly decreased or absent from the circulation: the hormone regulates and maintains a balance of calcium and phosphorus; low levels of parathyroid hormone may lead to low calcium levels in blood and bones and an increased amount of phosphorus. Therapy to replace missing hormone has been unavailable up to this point; treatment has consisted of daily supplementation of calcium; PTH(1-84) is hormone replacement therapy intended to provide long-term control of serum calcium and urinary calcium excretion. Columbia University, New York, NY Phase III trial ongoing	High-dose calcium High-dose vitamin D	Controlled serum and urinary calcium Improved quality of life Improved safety
Real-time functional magnetic resonance imaging (fMRI) with cognitive training to treat chronic pain	Patients in whom chronic pain has been diagnosed	Chronic pain is often unresponsive to conventional treatment over time. Well-defined regions of the brain (i.e., rostral anterior cingulate cortex) are believed to be responsible for pain perception; real-time functional MRI (fMRI) is under study to determine whether patients in pain who are able to view their brain activity during an MRI can use that information to learn how to control pain; until recently, fMRI data had to be analyzed off-line, but now software developed at Stanford University is enabling researchers to analyze imaging data in near real time to show patients their brain activity moment by moment; fMRI is being used over a 6-month period consisting of 12 visits that include six sessions in an MRI scanner and cognitive training to try to control the brain activity triggering the pain signals. Omneuron, Inc., Menlo Park, CA National Institute of Neurological Disorders and Stroke (NINDS), Bethesda, MD Phase II trial ongoing	Standard therapies with and without fMRI Combination therapies Management with tricyclic antidepressants, anticonvulsants, or opioid analgesics Physical therapy Spinal cord stimulation Transcutaneous electrical nerve stimulation	Ability to perform activities of daily living Decreased pain Improved quality of life Return to work

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ranibizumab (Lucentis) for treatment of diabetic macular edema	Patients who have been given a diagnosis of clinically significant diabetic macular edema	Laser-based treatments stabilize but do not improve vision and are associated with additional loss of clarity, color, and peripheral vision. Ranibizumab (Lucentis®) is a monoclonal antibody fragment (Fab) derived from the same parent murine antibody as bevacizumab (Avastin). It is an anti-angiogenic that has been FDA approved to treat the "wet" type of age-related macular degeneration, a common form of age-related vision loss. Ranibizumab is currently in being studied for diabetic macular edema (a new indication). Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Novartis AG, Basel, Switzerland Positive results reported from two phase III trials; biologics license application (BLA) submission is expected within 2011	Intravitreal triamcinolone acetonide (steroid) Laser photocoagulation Panretinal photocoagulation Vitrectomy Experimental treatments: C-peptide Oligomeric proanthocyanidin (pine bark extract)	Improved vision Stabilized vision Improved quality of life Reduced side effects of existing treatment
Reciprocating gait orthosis (ReWalk) for spinal cord injuries	Patients in whom spinal cord injury has been diagnosed who must use wheelchairs	Robotic exoskeleton technology (ReWalk™) to restore walking ability to immobilized patients; system features wearable leg braces and a backpack that powers and controls the system. Argo Medical Technologies, Ltd., Yokneam Illit, Israel Phase I trial ongoing; As of Nov 2011, ReWalk-I system was FDA-listed for institutional use only. The company expects to register ReWalk-P, for personal use for those who qualify for its use upon medical examination and rehabilitation training, by the end of 2011	Wheelchairs	Improved mobility Improved independence Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Recombinant human microplasmin injection (Ocriplasmin) for treatment of focal vitromacular adhesion of the eye	Patients in whom focal vitromacular adhesion (VMA) of the eye has been diagnosed	Focal VMA is a condition in which the vitreous gel, in the center of the eye, has an unusually strong adhesion to the macula, the center of the retina at the back of the eye. VMA is believed to play a key role in several back-of-the-eye conditions, such as macular hole and some forms of macular edema. A microplasmin molecule similar to human plasmin is thought to have potential to break down fibrin clots (fibrinolysis) that adhere the vitreous gel to the macula; intravitreal injection of microplasmin (Ocriplasmin) is thus a potential nonsurgical treatment for VMA. ThromboGenics NV, Heverlee, Belgium Phase III trial ongoing; company expects to file NDA by end of 2011	Pegaptanib sodium (Macugen) injection Surgery	Preserved vision Reduced complications associated with surgical treatment Improved quality of life
Recombinant porcine factor VIII (OBI-1) for treatment of acquired hemophilia	Individuals in whom acquired hemophilia A has been diagnosed and who develop immune reaction to human Factor VIII	About 15% to 30% of patients with acquired hemophilia develop immune reaction to recombinant human Factor VIII; recombinant porcine Factor VIII (OBI-1) is considered to be a physiologic replacement therapy that activates the natural hemostatic pathway. Administered as intravenous infusion every 2 to 3 hours for the first 24 hours of treatment. Inspiration Biopharmaceuticals, Inc., Laguna Niguel, CA Phase II, III trial ongoing	Human Factor VIIa	Adequate control of bleeding episodes
Retargeted endopeptidase (AGN-214868) for treatment of overactive bladder and urinary incontinence	Patients in whom overactive bladder leading to urinary incontinence has been diagnosed	Current therapeutic approaches for overactive bladder have a poor side-effect profile and are generally not very effective. AGN-214868 is a recombinant protein that is based on the botulinum toxin; in AGN-214868, the neuron binding domain of the botulinum neurotoxin has been replaced with a peptide that targets the endopeptidase activity of the toxin to peripheral neurons involved in the overactivity of bladder muscles leading to urinary incontinence. Syntaxin Ltd., Oxford, UK, in collaboration with Allergan, Inc., Irvine, CA Phase II trial ongoing	Behavioral therapy in combination with bladder relaxing drugs (e.g., tolterodine, oxybutynin, oxybutynin skin patches, trospium, solifenacin, darifenacin) Onabotulinum toxin A Sacral nerve stimulation Surgical treatment (bladder enlargement, cystectomy)	Decrease in urge to urinate Decrease in urination episodes per week Improved International Consultation on Incontinence Questionnaire-Overactive Bladder score Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Retargeted endopeptidase (AGN-214868) for treatment of postherpetic neuralgia	Patients in whom postherpetic neuralgia has been diagnosed	Postherpetic neuralgia can be very painful and debilitating; current treatments have variable efficacy for different patients and often require trial and error to determine optimal treatment; even then treatment can be suboptimal and the syndrome can persist long-term. AGN-214868 is a recombinant protein that is based on botulinum toxin; in AGN-214868, the neuron-binding domain of the botulinum neurotoxin has been replaced with a peptide that targets the endopeptidase activity of the toxin to peripheral neurons involved in transmission of postherpetic neuralgia pain. Syntaxin Ltd., Oxford, UK, in collaboration with Allergan, Inc., Irvine, CA Phase II trial ongoing	Lidocaine skin patches Tricyclic antidepressants (nortriptyline, amitriptyline) Anticonvulsants (gabapentin, pregabalin) Opioids (tramadol, oxycodone, morphine)	Reduced pain score on visual analog pain scale Improved quality of life
Retinal pigment cells (Spheramine) for treatment of Parkinson's disease	Patients in whom PD has been diagnosed	Spheramine® uses cultured human retinal pigment epithelial (hRPE) cells attached to microscopic carrier beads in an effort to help transplanted cells survive in the brain; hRPE cells, which are normally found at the back of the eye in the retina's inner layer, produce levodopa, a precursor of dopamine; PD is characterized by decreased production of the neurotransmitter dopamine; in Spheramine therapy, cells are implanted into the most affected brain regions by injection during a single stereotactic surgical procedure performed under magnetic resonance imaging guidance. Titan Pharmaceuticals, Inc., South San Francisco, CA Phase II trials ongoing	Other drug therapies Stem cell transplantation	Improved motor skills Improved mood and intellectual ability Decreased complications Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Retinal prosthesis system (Argus II) for treatment of retinitis pigmentosa	Patients with retinitis pigmentosa (RP) and a functioning optic nerve	Currently no medications or devices are available to restore lost vision or halt progression of vision loss that occurs with the inherited disorder RP. The Argus™ II implant consists of an array of electrodes that is surgically inserted into the retina of one eye and used in conjunction with an external camera and video processing system to provide a rudimentary form of sight; by electrically stimulating the retina, visual perception is enabled for blind persons with severe to profound RP; intended to restore a level of vision that is sufficient to improve patients' ability to function more independently. Second Sight, Inc., Sylmar, CA Phase II trial ongoing under FDA investigational device exemption (IDE) status, CE marked in 2011	Other retinal prostheses in development: On the retina: Intelligent Implants, Bonn, Germany Under the retina: Optobionics, Chicago, IL Retinal Implant (Germany) subretinal location of implant and no glasses Gene therapy delivered to retinal cells	Improved visual acuity Improved quality of life and independence
Robotic navigation aid (Guide Vest) to assist visually impaired persons	Patients with visual impairment	Current assistive devices and measures, such as long canes and guide dogs, have limitations that subject patients to injuries that affect quality of life. The guide vest robotic navigation aid is a head-mounted camera/vest combination that allows the head camera to capture images wirelessly through the Simultaneous Localization and Mapping (SLAM) software to build maps of the patient's environment. This allows the technology to accurately identify a safety path devoid of obstacles. The safety route is communicated to the patient through vibratory micro motors in the shoulder and waist that vibrate in the event that the route is obstructed. Vibrations to the shoulders are intended to indicate a higher object (i.e. left shoulder vibration for higher left obstacle) and vibrations to the waist indicate a lower object. If adopted, the guide vest may serve as a first-line assistive technology device for individuals in whom visual impairment has been identified. University of Southern California Keck School of Medicine's Doheny Eye Institute, Los Angeles, CA Pilot study completed at Braille Institute	Long canes Spectacles with stereoscopic cameras (undergoing study) Remote Infrared Audible Signage (RIAS) "Sighted" wheelchair	Decreased risk of falls and injury Improved mobility Increased independence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Sclerostin neutralizing monoclonal antibody (AMG 785) for treatment of postmenopausal osteoporosis	Patients in whom postmenopausal osteoporosis (PMO) has been diagnosed	Sclerostin antibodies represent a new class of anabolic therapy for PMO. AMG 785/CDP7851 is a humanized monoclonal antibody (MAb) that binds to and inhibits sclerostin, a protein secreted by osteocytes that inhibits bone formation by reducing osteoblastogenesis; AMG 785 is intended to allow the body to add more bone to the skeleton though osteoblastogenesis. Delivered via subcutaneous injection in four doses. Amgen, Inc., Thousand Oaks, CA Phase II trials ongoing	Estrogen therapy Selective estrogen receptor modulators Calcitonin Bisphosphonates Parathyroid hormone Strontium ranelate Cathepsin K inhibitors Glucagon like peptide 2 Denosumab Osteoprotegerin AvB3 integrin antagonists	Higher bone density Reduced fracture rate Improved quality of life Increased survival
Selective phosphodiesterase 4 inhibitor (AN2728) for treatment of psoriasis	Patients in whom mild to moderate plaque psoriasis has been diagnosed	Current immunomodulatory treatments for psoriasis have significant shortcomings; topical corticosteroids can cause thinning of the skin and systemic immune modulators can have immunosuppressive effects. Like corticosteroids, AN2728 is applied topically and inhibits NF-kappa B thereby reducing inflammation; however, AN2728 has a novel target for psoriasis treatment (phosphodiesterase 4); this novel antiinflammatory mechanism of action may allow longer topical treatment and/or combination treatment with existing therapies. Anacor Pharmaceuticals, Inc., Palo Alto, CA Phase II trials completed	Topical ointments: Corticosteroids Calcineurin inhibitors Salicylic acid Coal tar Phototherapy Systemic medications: Retinoids Methotrexate Cyclosporin Hydroxyurea Immunomodulators Thioguanine	Improved psoriasis area severity index scale Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
SOLX gold shunt for treatment-refractory glaucoma	Patients in whom treatment-refractory glaucoma has been diagnosed	There is no cure for glaucoma and untreated or if refractory to treatment, it leads to blindness. The SOLX® Gold Shunt is gold implant uses the eye's natural pressure differential to reduce IOP. The device is a flat, perforated, rectangular-shaped implant inserted between choroid layer and sclera in the trabecular meshwork area; differentiated from other surgical glaucoma options, because it is purported to reduce IOP without creating a bleb, which is a source of serious complications. SOLX, Inc., Waltham, MA Phase III trial ongoing; approved in Canada and parts of Europe	Trabectome (device) - Trabeculotomy Laser surgery Medications to reduce IOP Glaucoma drainage device (GDD) Ahmed glaucoma valve (AGV) - sheet valve Krupin implant - slit valve Molteno implant Baerveldt implant	Reduced IOP Preserved vision
Somatostatin analog (pasireotide) for treatment of Cushing's disease	Patients in whom Cushing's disease caused by an adrenocorticotropic hormone (ACTH)-secreting pituitary tumor has been diagnosed	The majority of Cushing's disease cases are caused by benign pituitary tumors that generate elevated levels of ACTH; ACTH stimulates the production and release of the stress hormone cortisol; too much ACTH results in too much cortisol, which controls the body's use of carbohydrates, fats, and proteins and helps reduce inflammatory responses. No medical treatments directly targeting ACTH-secreting pituitary tumors are available and not all patients respond to surgical or radiotherapy treatment. Pasireotide is a subcutaneously administered, somatostatin analog that activates a wide range of somatostatin receptors and has demonstrated the ability to inhibit ACTH secretion. Novartis AG, Basel, Switzerland Phase III trial ongoing	Surgical resection Radiation therapy Ketoconazole Mitotane Metyrapone	Reduced ACTH levels Reduced morbidity from excess cortisol Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Subretinal micro-electrode for treatment of blindness	Patients in whom hereditary retinal degeneration has been diagnosed and who are going blind	Device (chip) with 1,500 individual light-sensitive elements is surgically implanted into the eye under the retina; light-sensitive elements are designed to pass electrical impulses to the nerve cells in the eye. Retina Implant AG, Reutlingen, Germany Pilot trial completed; early unphased clinical trial ongoing	Epiretinal implants with external camera and processor unit	Vision restoration Improved activities of daily living Improved quality of life
Subretinal transplantation of retinal pigment epithelial cells to treat Stargardt macular dystrophy	Children and young adults in whom Stargardt macular dystrophy has been diagnosed	Study to determine the safety and tolerability of subretinal transplantation of retinal pigment epithelial cells derived from human embryonic stem cells. Advanced Cell Technology, Inc., Santa Monica, CA Phase I/II trials ongoing; FDA and EU granted orphan drug status	Currently, no treatment exists	Significantly improved visual performance Reversed loss of central vision Improved functional status
Sumatriptan iontophoretic patch (Zelrix) for treatment of acute migraine	Patients who are having an acute migraine episode	The Zelrix patch is new formulation of sumatriptan; a single-use transdermal patch that delivers low, controlled levels of migraine drug sumatriptan; patch is based on SmartRelief patch technology. NuPathe, Inc., Conshohocken, PA Phase III trials completed; NDA submitted to and accepted by FDA Jan 2011; company received complete response letter from FDA in Aug 2011 and plans to resubmit the NDA in early 2012	Currently available oral drugs: NSAIDs (oral) Combination analgesics containing caffeine Isometheptene combinations Migraine-specific drugs (i.e., triptans [naratriptan, rizatriptan, sumatriptan, zolmitriptan], dihydroergotamine) Combination drug therapy (e.g., aspirin plus acetaminophen plus caffeine) Ergotamine	Fast pain relief Reduced side effects compared with high level oral dose

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Teriflunomide for treatment of relapsing-remitting multiple sclerosis	Patients in whom RRMS has been diagnosed	No cure is available for MS and more effective treatments with fewer serious side effects are needed. Teriflunomide blocks new synthesis of pyrimidines, reduces T- and B-cell proliferation. Given in trials as once-daily, oral teriflunomide monotherapy, 7 or 14 mg. Sanofi-Aventis, Bridgewater, NJ Phase III trials ongoing	Glatiramer acetate (Copaxone) INFb (Betaseron) INFb-1a (Avonex) Fingolimod (Gilenya) Natalizumab	Longer remission time Reduced relapse rate Improved quality of life
Teriparatide (Forteo) for hard-to-heal fractures	Patients in whom unhealed bone fractures of the pelvis have been diagnosed	Teriparatide (Forteo®) subcutaneous injection intended to promote fracture healing in Jones, pelvic, and shoulder fractures. Eli Lilly & Co., Indianapolis, IN Clinical trial ongoing (non-phased); already approved as treatment for osteoporosis	Fracture healing rate without teriparatide Growth factors Electrical stimulation	Faster and more complete healing time Improved function Improved mobility Improved quality of life
Terlipressin for reversal of hepatorenal syndrome type 1	Patients in whom hepatorenal syndrome (HRS) type 1 has been diagnosed	HRS is a rapid, progressive renal impairment with poor prognosis with more than 80% mortality within 3 months. Terlipressin is a synthetic vasopressin analog that acts as a systemic vasoconstrictor, mainly in abdominal circulation, which may improve renal blood flow and renal function in patients with HRS; no U.S. approved drugs for HRS currently available. Given intravenously in combination with albumin. Ikaria Holdings, Inc., Clinton, NJ Phase III and II/III trials ongoing	Standard care with and without terlipressin Liver transplantation (i.e., the treatment for HRS type 1 and underlying end-stage cirrhosis; however, because of long waiting lists, many patients die before transplantation)	Confirmed HRS reversal Increased survival to time of transplantation Transplant-free survival up to 90 days

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Thermal pulsation system (LipiFlow) for treatment of meibomian gland dysfunction	Patients in whom meibomian gland dysfunction (MGD) has been diagnosed	MGD occurs when the oil produced by the meibomian glands in eyelids becomes slightly thicker than normal, which can block the narrow duct that through which the oil travels from the gland to the tear film. Oil production continues and fills and swells the glands, causing dry eye because of the blockage; severe blockage can create enlarged glands (a cyst) or even infection. MGD may be the leading cause of dry eye and is often misdiagnosed for classic dry eye. LipiFlow® is a single-use eyepiece that applies directed energy (48 degrees Celsius) to warm and massage the eyelids and heat the obstructive material to enable it to pass through the duct without damaging glands or other delicate structures of the eye; 25 ducts are present on each eyelid. A 12-minute per eye procedure is performed in a doctor's office. TearScience, Inc., Morrisville, NC Received FDA 510(k) clearance Jul 2011	Eyelid heat treatment (warm compresses) Fluoroquinolones Macrolide antibiotics (topical azithromycin) Omega 3 supplementation Tetracyclines	Decreased symptoms and complications
Tissue bulking agent (NASHA/Dx; Solesta) for treatment of fecal incontinence	Patients in whom fecal incontinence has been diagnosed	Current pharmaceutical, diet, and nerve-stimulation therapies for fecal incontinence may not lead to effective improvement, and surgical treatments may be too invasive, costly, and result in unfavorable outcomes. Solesta is a biocompatible tissue bulking agent, comprised of dextranomer microspheres and stabilized sodium hyaluronate; this gel may allow for narrowing of the anal canal and increased sphincter control. Treatment may serve as a first-line therapy that provides optimal outcomes in a less invasive and less costly manner for this indication. NASH/Dx (Solesta®) is administered via injection (dextranomer microspheres, 50 mg/mL, and stabilized sodium hyaluronate, 15 mg/mL, in a phosphate buffered 0.9 % sodium chloride solution) in the deep submucosal layer in the proximal anal canal. Oceana Therapeutics, Inc., Edison, NJ FDA approved Apr 2011	Antidiarrhea drugs Bowel training mechanisms Dietary changes Enemas/laxatives Sacral nerve stimulation Surgeries (sphincter repair, sphincter replacement, sphincteroplasty, colostomy, rectal prolapse correction)	Improved sphincter control Decreased fecal incontinence Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Topical XEN402 for treatment of postherpetic neuralgia	Patients in whom postherpetic neuralgia has been diagnosed	XEN402 blocks sodium channel sub-type Nav1.7 (sodium channels regulate electrical conductivity in the neurons) and is intended to alleviate pain from postherpetic neuralgia, which develops after shingles in a large proportion of elderly patients. Applied topically. Xenon Pharmaceuticals, Inc., Burnaby, British Columbia, Canada Phase II trial ongoing	Anticonvulsants (Gabapentin [Neurontin], pregabalin [Lyrica]) Lidocaine skin patches Opioid painkillers (Tramadol [Ultram, Ryzolt], oxycodone [Percocet] or morphine) Tricyclic antidepressants	Reduced or eliminated pain Reduced time to pain reduction Shorter recovery time
Traditional Chinese herbal remedies for treatment of chronic childhood immune thrombocytopenia	Children (<18 years) in whom chronic immune thrombocytopenia (ITP) has been diagnosed	ITP is an autoimmune disorder manifested as isolated low platelet counts that result in spontaneous internal bleeding episodes. Traditional Chinese herbalist will prescribe the herbal remedies (Bu Zhong Yi Qi Tang, Zhi Xue Tang, Chuan xin lian kang yan pian mod, and Tian Wang Bu xin Dan) according to traditional Chinese medicine principles from one of four formulations. Phase II, III trial ongoing	Corticosteroids Intravenous immunoglobulin	Decrease bleeding episodes Resolution of ITP Reduced side effects compared to drug therapy
TrkA kinase inhibitor (CT327) for treatment of psoriasis	Patients in whom mild to moderate psoriasis vulgaris has been diagnosed	Current psoriasis treatments address symptoms or the inflammatory pathway in psoriasis. Keratinocyte homeostasis may underlie the pathophysiology of psoriasis; therefore, therapies targeting keratinocyte proliferation may represent novel therapeutic options. CT327 is a TrkA kinase inhibitor that is administered in a topical ointment; drug is modified with the manufacturer's "low systemic exposure" technology intended to allow local levels of the drug without systemic spread; the TrkA receptor is activated by nerve growth factor, which has been implicated in keratinocyte homeostasis and the pathophysiology of psoriasis. Creabilis SA, Luxembourg City, Luxembourg Phase II trial complete	Topical ointments: Corticosteroids Calcineurin inhibitors Salicylic acid Coal tar Phototherapy Systemic medications: Retinoids Methotrexate Cyclosporin Hydroxyurea Immunomodulators Thioguanine	Improved psoriasis area severity index scale Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Troponin activator (CK-2017357) for treatment of myasthenia gravis	Patients in whom generalized myasthenia gravis (MG) has been diagnosed	The drugs used to control MG either diminish in effectiveness over time (cholinesterase inhibitors) or cause severe side effects of their own (immunosuppressants). Most patients need treatment for the remainder of their lives, and more effective options are needed. Oral CK-2017357 is a fast skeletal muscle troponin activator; selectively activates the fast skeletal muscle troponin complex and increases its sensitivity to calcium, which increases skeletal muscle force in response to neuronal input and delays onset and reduces degree of muscle fatigue. Cytokinetics, Inc., South San Francisco, CA Phase II trial ongoing	Cholinesterase inhibitors Immunosuppressant drugs Thymectomy Emergency plasmapheresis or IVIG	Improved muscle function Delayed onset and reduced magnitude of muscle fatigue Reduced need for therapeutic thymectomy (nonthymoma) Fewer side effects
UroLift system for treatment of benign prostatic hyperplasia	Patients in whom BPH is causing lower urinary tract symptoms (e.g., difficulty urinating, recurrent bladder infections, frequent urge to urinate)	BPH is currently treated either with drugs that address only secondary symptoms or have significant side effects or with minimally invasive or invasive surgery, which involves significant recovery time. The UroLift® system is a set of minimally invasive devices intended to expand the urethral lumen through the use of sutures to retract the expanded lobes of the prostate; the treatment is performed under local anesthesia and recovery time may be as short as 2 weeks. NeoTract, Inc., Pleasanton, CA Phase III trial ongoing	Alpha blockers 5-Alpha reductase inhibitors Surgical treatments (e.g., transurethral resection of prostate, transurethral microwave therapy, open prostatectomy) Minimally invasive surgical treatment (e.g., laser ablation, transurethral needle ablation, transurethral microwave therapy)	Improved International Prostate Symptom Score (IPSS) Increased urine flow rate Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vagus nerve stimulation for treatment of fibromyalgia	Patients in whom treatment refractory fibromyalgia has been diagnosed	Fibromyalgia remains poorly understood and there remains a lack of effective treatment options for many patients. The vagus nerve stimulation (VNS) stimulator device is implanted in patients with fibromyalgia and is adjusted to the highest current that can be comfortably tolerated. The device is intended to alter nerve centers in the brain, which may inappropriately mediate pain responses in patients; VNS is intended to be used as an adjunctive therapy. Under study at the University of Medicine and Dentistry of New Jersey's New Jersey Medical School, Newark, NJ, and Pain and Fatigue Study Center, Beth Israel Medical Center, New York, NY Various manufacturers make VNS systems Phase I/II trial completed	Duloxetine Fluoxetine Gabapentin Lorazepam Milnacipran Pregabalin Stress reduction Tricyclic antidepressants	Minimal clinically important difference (MCID+; pain, overall wellness, and physical function)
Vascular endothelial growth factor (Eyelea, aflibercept) for treatment of wet age-related macular degeneration	Patients in whom the neovascular form of ARMD (wet) has been diagnosed	VEGF Trap-Eye (Eylea™, aflibercept) is a recombinant fusion protein consisting of human VEGF receptors 1 and 2 extracellular domains that are fused to the Fc portion of human IgG1. The drug is formulated as a solution for intravitreal injection. It is intended to inhibit the binding and activation of VEGF receptors. Aflibercept is "indicated for the treatment of patients with neovascular age-related macular degeneration (wet AMD)." It is "contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients" in the drug. The recommended dose is 2 mg by injection once a month for the first 3 months, followed by 2 mg 2 months. Regeneron Pharmaceuticals, Inc., Tarrytown, NY Phase III trials completed; FDA approved Nov 2011	Ranibizumab (Lucentis)	Improved visual acuity Improved treatment compliance because of reduced number of eye injections

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
VEN-309 (iferanserin) for treatment of symptomatic internal hemorrhoids	Patients in whom internal symptomatic hemorrhoids have been diagnosed	According to the National Institute of Diabetes and Digestive and Kidney Diseases, an estimated 12.5 million adults in the U.S. have symptomatic hemorrhoids; internal hemorrhoids can cause bleeding, pain, or pruritus with topical therapies such as witch hazel, hydrocortisone cream, and topical anesthetics used to treat these symptoms. These agents are not disease-modifying (i.e., they do not treat the actual pathogenesis). Surgical intervention may also be used in the treatment of therapy. VEN-309 has highly selective, antagonistic properties against peripheral 5-HT2A (serotonin family) receptors involved in clotting and the contraction of arteries and veins, leading to hemorrhoid formation. Through this mechanism of action, VEN-309 is said to improve the flow of blood out of the dilated veins that comprise the hemorrhoid, thereby reducing bleeding, itchiness, and pain. VEN-309 is administered topically intra-anally, twice a day, at 0.5% ointment (containing 10 mg VEN-309). Ventrus Biosciences, Inc., New York, NY Phase III trial ongoing; expected primary completion Feb 2012	Cryotherapy Surgical interventions Topical treatments (for symptoms)	Halted progression of hemorrhoids Reduced bleeding Reduced itchiness and pain associated with internal hemorrhoids Improved quality of life
Video game therapy for stroke rehabilitation	Patients who are recovering from mild to moderate ischemic or hemorrhagic strokes	Wii is a video gaming system. A motion-detection system allows patients to see their actions on a television screen with real-time sensory feedback; Wii tennis and Wii Cooking Mama, which uses movements that simulate cutting a potato, peeling an onion, and shredding cheese, are being used in stroke rehabilitation intended to improve motor skills and speed. Heart and Stroke Foundation, Ottawa, Ontario, Canada Ontario Stroke System, Toronto, Ontario, Canada Phase I trial completed	Standard physical therapy Standard occupational therapy Robot-assisted rehabilitative therapy	Improved motor function Improved quality of life Improved strength

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Viral delivery of nerve growth factor (CERE-120; AAV2-neurturin) for treatment of Parkinson's disease	Patients in whom PD has been diagnosed	Current treatments for PD address symptoms rather than underlying cause, and the patient eventually plateaus or ceases to respond to them. CERE-120 is an adeno-associated virus (AAV) vector carrying the gene for neurturin, a naturally occurring protein that repairs damaged and dying dopamine-secreting neurons, keeping them alive and restoring normal function. Degeneration of these neurons is responsible for the major motor impairments of PD. CERE-120 has been delivered by stereotactic injection into the brain. Ceregene, Inc., San Diego, CA Phase I/II trial ongoing	No treatments currently exist, just symptom relief (levodopa, dopamine agonists, MOA-B inhibitors, etc.)	Reduced symptoms Increased motor skill functions Slowed disease progression Continued effect of treatment over time Improved quality of life
Wearable artificial kidney (WAKs) for end-stage kidney failure	Patients with advanced kidney failure	In current peritoneal dialysis (dialysate) is infused into the abdomen through a permanent indwelling catheter to remove toxins. Peritoneal lining acts as a filter. Spent dialysate solution is drained from peritoneal cavity. With WAKs, dialysate is cleaned and reinfused through external pumps and filtration components that are attached to the front of a vest or waist belt worn by the patient. AWAK Technologies, Inc., Burbank, CA Clinical trials scheduled to start the end of 2011	Conventional home dialysis systems	Adequate filtration of toxins from kidneys Improved quality of life Improved mobility

Table 9. AHRQ Priority Condition: 09 Infectious Disease including HIV-AIDS: 82 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ACH-1625 for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	Current standard of care (pegylated interferon [INF] and ribavirin) for HCV infection is not effective for more than half of infected patients seeking treatment and is poorly tolerated in many patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. ACH-1625 is a NS3 protease inhibitor intended to block the activity of HCV protease, preventing the cleavage and maturation of functional viral particles; ACH-1625 is purported to be highly potent and to induce high rates of rapid virologic responses irrespective of interleukin-28 genotype; intended to be used in combination with pegylated INF and ribavirin. Administered orally, 200 to 800 mg, once per day. Achillion Pharmaceuticals, Inc., New Haven, CT Phase II trial ongoing	Boceprevir Pegylated INF Ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
AGS-004 for treatment of HIV infection	Patients in whom HIV infection has been diagnosed	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy present opportunities for the development of novel and effective HIV therapies. AGS-004 is a personalized dendritic cell vaccine loaded with HIV RNA derived specifically from the patient; intended to generate a relevant immune response to the HIV strain actively infecting the patient, thus controlling viral load after cessation of therapy. Administered in a series of four injections. Argos Therapeutics, Inc., Durham, NC Phase II trials ongoing	Antiretroviral therapy	Improved CD4+ T-cell counts Improved CD8+ T-cell responses Sustained control of viral load after cessation of therapy Time to viral load reduction Reduced morbidity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ALN-RSV01/RNAi for treatment of respiratory syncytial virus	Patients (children and adults) who have been given a diagnosis of respiratory syncytial virus (RSV) infection, including lung transplant recipients	Currently, no pharmacologic interventions are available for RSV infection; the only treatment is supportive care. ALN-RSV01 is an inhaled (nebulized) RNAi therapeutic that targets the nucleocapsid *N* gene of the RSV genome, a gene required for replication of RSV; ALN-RSV01 is intended to silence the *N* gene, thereby reducing the virus' ability to reproduce. Alnylam Pharmaceuticals, Cambridge, MA Phase II trial ongoing	Supportive care (e.g., oxygen support, hydration, etc.) Salbutamol Hypertonic saline	Reduced infection rate Improved lung function Reduced progression of bronchiolitis obliterans syndrome (BOS) Shorter hospital stay for treating RSV infection
Amikacin Inhale for the treatment of gram-negative pneumonia	Critically ill patients who are on ventilators in intensive care units (ICUs)	Amikacin Inhale (NKTR-061, BAY41-6551) is a drug-device combination that combines a special liquid formulation of the aminoglycoside antibiotic amikacin with proprietary liquid pulmonary technology; intended to deliver amikacin deep into the infected lungs of patients in the ICU with gram-negative pneumonia. Nektar Therapeutics, San Francisco, CA Bayer AG, Leverkusen, Germany Phase III trial registered	Intravenous antibacterial therapy	Resolution of infection Reduced treatment failures Increased survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Setrobuvir (ANA598; nonnucleoside NS5B polymerase inhibitor) for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients. Effective treatments are needed. Setrobuvir is a HCV nonnucleoside, NS5B polymerase inhibitor intended to limit viral replication when used in combination with pegylated INF and ribavirin for both treatment-naive patients and patients whose HCV infection has failed to respond to a prior course of therapy with INF and ribavirin. Administered orally, 200 to 400 mg. Anadys Pharmaceuticals, Inc., San Diego, CA Phase IIb trials ongoing; FDA granted fast track designation	NS5B inhibitors (in phase II trials) Pegylated INF Ribavirin Telaprevir Boceprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Autologous dendritic cell vaccine for treatment of HIV infection	Patients in whom chronic HIV infection has been diagnosed	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments. HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy present opportunities for the development of novel and effective HIV therapies. Autologous dendritic cells (DC) are the most efficient antigen presenting cells in the immune system; priming DC with antigen can lead to the generation of adaptive immune responses (B cell and T cell); the vaccine consists of DC generated with granulocyte-macrophage colony-stimulating factor (GM-CSF) and INF; the cells are also pulsed with lipopeptides encoding HIV-1 antigens; these cells are then readministered into the patient in four injections over 6 months; the vaccine is intended to induce CD8+ T-cell responses against HIV-1 infected cells, capable of controlling the infection and reducing the need for medication. Baylor College of Medicine, Houston, TX Phase I trial completed as of Jul 2011; phase II trial to be planned after examination of efficacy by HIV-1 genotype in patients	AGS-004 Antiretroviral therapy Off-the-shelf therapeutic vaccines in development	Reduced morbidity Reduced time to viral load reduction Reduced use of antiretroviral therapy (ART) Sustained control of viral load after cessation of therapy Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BAL30072 for treatment of serious gram-negative infections	Patients in whom serious gram-negative infection has been diagnosed	Beta-lactam antibiotics are a mainstay of antimicrobial therapy, but their use is increasingly compromised by acquired resistance, especially in gram-negative bacteria. A recent survey of thousands of patients from hospitals globally revealed gram-negative bacteria in 60% of clinical isolates in ICUs. A need exists for novel gram-negative antibiotics with broad coverage against clinically relevant pathogens; purportedly no compounds are currently in late-stage development in this space. BAL30072 is a novel siderophore (iron-binding) sulfactam antibiotic with a unique mode of action; BAL30072 is purported to have potent bactericidal activity against gram-negative pathogens including *Pseudomonas aeruginosa*, *Acinetobacter* spp., *Klebsiella* spp. and *Enterobacter* spp.; BAL30072 is purported to exploit natural nutrient uptake systems of pathogens to gain access to its intracellular target; BAL30072 is stable towards many types of beta-lactamase enzymes, and metallo-beta-lactamases, which can deactivate most of the currently marketed beta-lactam antibiotics, such as cephalosporins and carbapenems; may be used for the treatment of hospital-acquired pneumonia (including ventilator-associated pneumonia), complicated intra-abdominal infections, or complicated urinary tract infections. Basilea Pharmaceutica, Ltd., Basel, Switzerland Phase I trial initiated mid-2011	Aminoglycosides Carbapenems	Improved clinical response Improved microbiologic response Shorter hospital stays Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bavituximab for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Many patients treated with the current standard of care remain chronically infected with HCV. Bavituximab is a monoclonal antibody directed against phosphatidylserine (PS) exposed on the surface of cells infected by HCV; PS expression is believed to be immunosuppressive; bavituximab is thought to bind to PS and block the immunosuppressive signals, improving immune responses to HCV; it could potentially effectively treat HCV irrespective of the viral genotype or drug resistance; bavituximab is being administered in various dose regimens of 0.3 to 6 mg/kg of body weight, weekly, for 8 or 12 weeks in clinical trials as a monotherapy and combination therapy with ribavirin. Peregrine Pharmaceuticals, Inc., Tustin, CA Phase I/II trial ongoing; also under study in patients with both HCV and HIV infection.	NS5B polymerase inhibitors (in phase II trials) Pegylated INF Ribavirin Telaprevir Boceprevir Combination therapy	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
BC-3781 for treatment of acute bacterial skin and skin structure infections	Patients in whom an acute bacterial skin and skin structure infection (ABSSSI) has been diagnosed	Antibacterial resistance has made some of the current treatment options for ABSSSI ineffective; new antibacterials are needed to effectively treat serious infections. BC-3781 may be the first pleuromutilin antibiotic for systemic use; BC-3781 targets the bacterial 50s ribosomal subunit inhibiting protein synthesis. Can be administered orally and intravenously, 100 to 150 mg. Nabriva Therapeutics AG, Vienna, Austria Phase II trial completed	Clindamycin Linezolid Minocycline Trimethoprim/sulfa-methoxazole Vancomycin	Increased resolution of infection/cure Decrease in time to early clinical response (cessation of spread of erythema with a lack of fever)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bedaquiline (TMC207) for treatment of drug-resistant tuberculosis	Patients in whom drug-resistant tuberculosis (TB) is inspected	Bedaquiline (TMC207) is an experimental diarylquinoline antituberculosis drug; intended to achieve clinical response rates twice as fast as standard treatment. Tibotec BVBA, Beerse, Belgium Phase III trial ongoing	Ethionamide (Trecator) Kanamycin Ofloxacin (Floxin) Pyrazinamide	Resolution of active TB infection Reduced time to clinical response Improved patient compliance with therapy Reduced spread of infection Improved quality of life
BI-201335 (NS3/4 protease inhibitor) for treatment of chronic hepatitis C infection	Patients in whom chronic infection with HCV has been diagnosed	Current standard of care for HCV infection is ineffective in more than half of infected patients; effective treatments that improve clinical outcome in a shorter period of time are needed. BI-201335 is a NS3/4 protease inhibitor intended to block the activity of HCV protease preventing the cleavage and maturation of functional viral particles. Administered orally, 120 or 240 mg, once daily in combination with pegylated INF and ribavirin (standard of care); may also be administered in an INF-free regimen with BI-207127 (polymerase inhibitor). Boehringer Ingelheim, Ingelheim, Germany Phase III trials ongoing; granted FDA fast track status in combination with standard of care and in INF-free combination with BI-207127	Boceprevir Pegylated INF Ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BI-207127 (non-nucleoside NS5B polymerase inhibitor) for treatment of chronic hepatitis C infection	Patients in whom chronic infection with HCV has been diagnosed	Current standard of care for HCV infection is ineffective in more than half of infected patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. BI-207127 is a non-nucleoside NS5B polymerase inhibitor intended to allosterically bind HCV RNA-dependent RNA polymerase and inhibit replication of the viral genome. Dosed 100, 200, 400, 800, and 1,200 mg three times a day. Boehringer Ingelheim, Ingelheim, Germany Phase II trial completed; granted FDA fast track status in combination with BI-201335 (NS3/4 protease inhibitor) in INF-free combination	Boceprevir Pegylated INF PSI-7977 Ribavirin Telaprevir VX-222	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Bioabsorbable gentamicin surgical implant (CollaRx) for postsurgical infection control	Surgical patients at risk for localized, deep-tissue infection	CollaRx® implant is a biodegradable and bioabsorbable matrix of purified fibrillar collagen filled with antibiotic gentamicin intended for local delivery of antibiotic to prevent postsurgical infections. Innocoll, Inc., Ashburn, VA Phase III trials planned	Intravenous and oral antibiotic administration	Reduced surgical site infections and subsequent treatment

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BIT225 (viroporin inhibitor) for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C infection (HCV) has been diagnosed	Existing HCV drugs have limited effectiveness and can be toxic; fewer than half of infected patients do not respond to current therapies, demonstrating the need for new treatments that directly target and halt replication and reproduction of the virus. BIT225 is a first-in-class drug candidate designed to specifically target the p7 membrane polypeptide of HCV; part of a new group of small molecular compounds that inhibit a new class of antiviral targets known as viroporins. By blocking the ion channel activity of viroporins, these compounds are able to inhibit viral budding and replication; BIT225 is being investigated in combination with INF and ribavirin; preclinical studies have shown BIT225 to be highly synergistic with INF and ribavirin as with NS5B (polymerase) inhibitors. Currently administered orally, 200 or 400 mg. Biotron Ltd., Sydney, Australia Phase II trial ongoing	Boceprevir INF Polymerase inhibitors (in clinical development) Other protease inhibitors (in clinical development) Ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
BMS-650032 (NS3 protease inhibitor) for treatment of chronic hepatitis C infection	Patients in whom chronic infection with HCV has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients and is poorly tolerated in many patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. BMS-650032is a NS3 protease inhibitor intended to block the activity of HCV protease preventing the cleavage and maturation of functional viral particles. Administered orally, 200 mg, twice daily, in combination with BMS-914143 (NS5A inhibitor) with or without pegylated INF and ribavirin (standard of care). Bristol-Myers Squibb, New York, NY Phase II trials ongoing	Boceprevir Pegylated INF Ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BMS-790052 (NS5A protease inhibitor) for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C infection (HCV) has been diagnosed	Current standard of care for HCV infection is ineffective in more than half of infected patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. BMS-790052 is a first-in-class inhibitor of HCV NS5A; NS5A is a multifunctional, nonenzymatic endoplasmic reticulum (ER) membrane-associated phosphoprotein, which regulates multiple steps of the HCV life cycle, including viral RNA replication and virion maturation; although the role of the protein is poorly understood, NS5A is required for viral replication; it is proposed that BMS-790052 destabilizes the association of NS5A with the ER membrane, thus inhibiting the formation of functional virions. It may be used in combination with standard of care and other investigational agents including pegylated INF lambda. Administered orally, 60 mg, once daily. Bristol-Myers Squibb, New York, NY Phase III trials planned	Boceprevir Pegylated INF PSI-7977 Ribavirin Telaprevir VX-222	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
BMS-914143 (pegylated interferon lambda) for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is ineffective in more than half of infected patients and the presence of pegylated INFa-2a results in poor treatment tolerability in many patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. BMS-914143 (pegylated INF lambda) is a recombinant, pegylated form of INF lambda, a type III INF, which binds to a unique receptor on cells with a restricted cellular distribution and may improve tolerability when compared with treatment with type I INFs/INFa-2a. Administered as a subcutaneous injection, 180 mcg/mL, once weekly, for 24 or 48 weeks depending on response. Bristol-Myers Squibb, New York, NY Phase III trial planned	INFa-2a INF-free HCV drug combinations	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CB-183,315 for treatment of recurrent *Clostridium difficile* infection	Patients in whom recurrent *C. difficile* (CDI) infection has been diagnosed	Recurrent CDI is responsible for significant morbidity, mortality, and costs; recurrent CDI can be extremely resistant to treatment; up to 60% of patients previously treated for recurrent CDI with antibiotics develop further recurrence after therapy is stopped, which suggests that other therapeutic options are needed. CB-183,315 is a novel cyclic lipopeptide, which is purported to disrupt bacterial membrane potential, inhibiting bacterial metabolism. Administered orally, 125 to 250 mg, twice daily, for 10 days. Cubist Pharmaceuticals, Inc., Lexington, MA Phase II trial completed	Metronidazole Fidaxomicin Vancomycin	Reduced CDI recurrence rate Shorter hospitalization time Faster time to resolution of diarrhea
Clostridium difficile vaccine (ACAM-CDIFF) for prevention of infection in patients expecting treatment in a health care facility	At-risk individuals, including adults facing imminent hospitalization or current or impending residence in a long-term care or rehabilitation facility	*C. difficile* is a common hospital acquired infection the can lead to significant morbidity, mortality, lengthened hospital stays and cost methods to prevent *C. difficile* infection are needed. *C. difficile* vaccine (ACAM-CDIFF™) consists of a toxoid from the bacterium intended to induce protective antibody responses. Sanofi-Aventis, Bridgewater, NJ Phase II trials ongoing	Hospital infection control programs	Reduced *C. difficile* infection rates Reduced use of antibacterial drugs Reduced hospitalization time Reduced isolation

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CMX001 for treatment of adenovirus infection in patients who have received a hematopoietic stem cell transplant	Patients who recently received a hematopoietic stem cell transplant (HSCT)	In immunocompromised patients, such as those who have undergone HSCT, adenovirus infections are recognized as a significant cause of morbidity and mortality; immunocompromised pediatric HSCT patients are particularly susceptible to serious and/or fatal adenovirus infections, for which there are currently no approved treatment options. CMX001 is purported to be a broad spectrum, oral antiviral for the treatment or prevention of life-threatening double-stranded DNA (dsDNA) viral diseases; CMX001 combines Chimerix's PIM (phospholipid intramembrane microfluidization) conjugate technology with cidofovir, a selective inhibitor of viral DNA polymerase and an approved antiviral agent for the treatment of cytomegalovirus infection; PIM technology covalently modifies the cidofovir molecule so that it mimics a naturally occurring phospholipid metabolite that can utilize natural uptake pathways to achieve oral availability; additionally, CMX001 is purported to be significantly more potent in inhibiting viral DNA synthesis than cidofovir. Administered orally, twice weekly, for up to 3 months not to exceed 4 mg/kg of body weight in pediatric or adult patients. Chimerix, Inc., Durham, NC Phase II trials ongoing; FDA granted fast track designation	Cidofovir (off label)	Reduced morbidity from adenovirus infection Reduced mortality from adenovirus infection

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Collaborative care model (HITIDES) for treatment of depression secondary to HIV	Patients in whom depression secondary to HIV has been diagnosed	HIV Translating Initiatives for Depression Into Effective Solutions (HITIDES) is a collaborative care model to support HIV and mental health clinicians in delivering evidence-based depression treatment. Depression care team (registered nurse depression care manager, a clinical pharmacist, and a psychiatrist) works with treating (for HIV) clinicians, delivering the following components: participant education and activation, assessment of treatment barriers and possible resolutions, depression symptom and treatment monitoring, substance abuse monitoring, and instruction in self-management (e.g., encouraging patients to exercise and participate in social activities). Veterans Affairs Medical Centers Trial completed	Usual HIV care without depression care team	Depression improvement Improved care implementation process Improved quality of care Improved health status Improved health-related quality of life Decreased HIV symptom severity Improved HIV medication compliance Improved antidepressant compliance Improved patient satisfaction
Copper surfaces in the intensive care unit for prevention of hospital-acquired infections	Patients admitted to an ICU	Hospital-acquired infections (HAIs) are the fourth leading cause of death in the U.S. behind heart disease, stroke, and cancer; nearly 1 in every 20 hospitalized U.S. patients acquires an HAI, resulting in 100,000 deaths each year; bacteria on surfaces in ICUs are said to be responsible for 35% to 80% of patient infections. Replacing the most heavily contaminated touch surfaces in ICUs with antimicrobial copper is purported to control bacterial growth and lower the rates of infections acquired in the ICU; bacterial reduction rates are intended to achieve the same outcome as current "terminal cleaning" practices. International Copper Association Commercially available; studies at hospitals ongoing	Terminal cleaning of standard surfaces	Reduced infection rates Reduced bacteria isolated from surfaces Reduced morbidity and mortality from HAIs

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cyclophilin inhibitor alisporivir for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Current HCV treatment options are not effective in all patients, even with the newly approved agents of telaprevir and boceprevir; treatment options are also associated with frequent adverse events and a long duration of therapy; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. Cyclophilin A is a host cell protein involved in protein folding and transport, and it has been shown to be essential in HCV replication; cyclosporine A inhibits cyclophilin activity but is immunosuppressive; alisporivir (Debio-025) is an oral modified form of cyclosporin A, that is purported to act as a host-targeted antiviral with enhanced cyclophilin binding but no immunosuppressive activity, which is purported to be due to the inability of the alisporivir-cyclophilin complex to bind calcineurin which modulates proinflammatory lymphocyte signaling. Debiopharm, S.A., Lausanne, Switzerland Novartis AG, Basel, Switzerland Phase III trials ongoing; FDA granted fast track designation	Boceprevir Pegylated INF Ribavirin SCY-635 (in development) Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Cytosine nucleoside analog mericitabine (RG7128) for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C infection has been diagnosed	Current HCV treatment options are not effective in all patients, even with the newly approved agents of telaprevir and boceprevir; treatment options are also associated with frequent adverse events and a long duration of therapy; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. Mericitabine is a ccytosine nucleoside analog purported to inhibit virus genome replication. May or may not be used in combination with pegylated INF plus ribavirin. Pharmasset, Inc., Princeton, NJ F. Hoffmann-La Roche Ltd., Basel, Switzerland Phase IIb trials ongoing	Pegylated INF plus ribavirin	Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Danoprevir (protease inhibitor) for treatment of chronic hepatitis C infection	People chronically infected with HCV	Danoprevir is a protease inhibitor intended for treatment of chronic HCV infection. F. Hoffmann-La Roche Ltd., Basel, Switzerland Phase II trials ongoing	Ribavirin Pegylated INF	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Dapivirine gel for prevention of HIV infection	Females at risk for HIV infection	Dapivirine (TMC 120), a diarylpyrimidine inhibitor of HIV reverse transcriptase, has been put into vaginal microbicide gel formulation designed to protect women engaging in vaginal sex from HIV infection. Tibotec BVBA, Beerse, Belgium Johnson & Johnson, New Brunswick, NJ Phase I/II trials ongoing	Condoms	Reduced HIV transmission rates from unprotected sex

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
DAS181 (Fludase) for treatment and prevention of influenza-like illness	Patients at high risk for influenza-like illness (ILI)	Resistance to current neuraminidase inhibitors may leave patients at risk for ILI; treatments with new mechanisms of action may help treat existing and emerging mutant strains of the virus. ILI is caused by all types and strains of influenza and parainfluenza viruses; DAS181 (Fludase®) is a recombinant protein purported to be a broad spectrum agent against ILI; DAS818 targets host cell receptors and is purported to prevent the entry of influenza and parainfluenza viruses into host cells by binding to and inactivating sialic acid of the surface of cells lining the respiratory tract; DAS181 consists of two parts, a sialidase and a cell-surface anchoring domain, that are designed to attach to the respiratory epithelium and increase retention time and potency. Agent is administered via oral inhalation as a single 10 mg dose or 10 mg once daily for three days. NexBio, Inc., San Diego, CA Phase II trials ongoing	Laninamivir (In phase III trials) Oseltamivir Peramivir Zanamivir	Reduced viral loads in respiratory secretions Shorter time to achieve a sustained reduction in viral shedding Reduced transmission and incidence of influenza Reduced incidence of ILI
DNA vaccine (INO-3510) for prevention of H1N1 and H5N1 influenza	Patients at risk for H1N1 and H5N1 influenza	Influenza continues to cause significant morbidity and mortality in susceptible populations; improper strain selection and viral mutations continue to challenge vaccine developers. INO-3510 is a SynCon DNA vaccine intended to prevent H1N1 influenza and avian H5N1 influenza; administered using intradermal electroporation; SynCon vaccines are designed through a proprietary method with the intention of achieving cross-strain protection against the natural and frequent mutations of influenza strains within subtypes; vaccine product is intended to eventually be broadly protective and induce effective antibody and T-cell responses against influenza infection. Inovio Pharmaceuticals, Inc., Blue Bell, PA Phase I trial ongoing	Pandemic influenza vaccines Seasonal inactivated flu vaccines Seasonal live flu vaccines	Protection against influenza Reduced morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Duct tape Red Box safe zone for prevention of transmission of hospital infections and improve care	Patients with infections requiring isolation	Patients with infections requiring isolation sometimes have simple communication needs, yet, hospital infection control procedures require that personnel gown-up to enter the patient's room prior to communicating, thus introducing a barrier to communication. A duct tape Red Box safe zone can be applied to the floor extending 3 feet outside of the patient's room signifying the barrier to entry of an isolated room and providing a clear boundary where a health care provider can communicate with a patient regarding simple requests such as getting a glass of water; this intervention is intended to decrease the need for excessive gowning, and to increase the frequency with which health care providers check on patients in isolation. Trinity Medical Center, Rock Island and Moline, IL, and Bettendorf and Muscatine, IA	Standard infection control procedures	Improved frequency of communication Improved patient experience/satisfaction Reduced staff hours/costs spent gowning
Fecal transplantation for treatment of recurrent *Clostridium difficile* infection	Patients with recurrent CDI	Because of antibiotic resistance, new options are needed that can improve clinical cure rates and reduce CDI recurrence. Fecal matter from a healthy donor is collected and mixed with a saline solution and transplanted into the recipient via colonoscopy with the intended purpose of introducing healthy flora to the intestinal tract to prevent recurrence of CDI infection.	Probiotics Antibiotics	Reduced diarrhea Reduced dehydration Reduced reinfection
Fidaxomicin for treatment of *Clostridium difficile* infection	Patients in whom CDI has been diagnosed	Because of antibiotic resistance, new antibacterials that can improve clinical cure rates and reduce CDI recurrence are needed. Fidaxomicin is an antibiotic that is first in a new class called macrocyclics, which inhibit bacterial RNA polymerase, resulting in rapid killing; fidaxomicin has a narrow spectrum and selectively eradicates CDI with minimal disruption to the normal intestinal flora, which may lower recurrence rates. Administered orally, 200 mg, twice a day. Optimer Pharmaceuticals, Inc., San Diego, CA FDA approved May 27, 2011	Metronidazole (off-label) Oral vancomycin	Increased clinical cure rates Reduced *C. difficile* infection recurrence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Genetically altered strain of *Streptococcus mutans* (SMaRT) for prevention of tooth decay	Children and adults who are at risk for dental caries	Current therapies (preventive and corrective) have not been able to control and reduce the incidence and prevalence of tooth decay in young children; benefit would be greatest in patients of low socioeconomic background who have limited access to dental services. Vertical transmission of bacteria (*Streptococcus mutans*) usually from caregiver to infant (sharing utensils, food) and its subsequent colonization in the oral cavity is one of components of the infectious disease triad (host, agent and environment) involved in tooth decay; by replacing the native S. mutans with a genetically modified *S. mutans* (SMaRT) that is capable of killing native *S. mutans* and also not able to produce pH-lowering acid, both the demineralization of enamel and tooth decay are averted; intended to permanently replace native *S. mutans*; SMaRT is topically applied to the teeth by a dentist, pediatrician or primary care physician using a cotton-tipped swab during a single 5-minute treatment. Oragenics, Inc., Tampa, FL Phase I, started Apr 2005, concluded early due to lack of subjects; FDA issued clinical hold letter Jun 2007, clinical hold was removed Oct 2007 and phase I trial with attenuated strain is now ongoing	Antiseptic mouth rinses Fluoride Oral care hygiene program Sealants	Reduced incidence and prevalence of dental caries in pediatric populations Reduced health care costs Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
GSK2251052 for treatment of complicated intra-abdominal infections	Patients in whom complicated intra-abdominal infections have been diagnosed	Increasing resistance to existing antibiotics has created a critical need for novel therapies for the treatment of complicated urinary tract infections caused by gram-negative bacteria. GSK-2251052 (GSK ’052) is a novel boron-based, systemic antibiotic that specifically targets the bacterial enzyme leucyl-tRNA synthetase, or LeuRS, which is required for bacterial protein synthesis; inhibition of protein synthesis leads to termination of cell growth and cell death; GSK ’052, if it reaches market, could be the first commercially available antibiotic to target LeuRS; Preclinical and phase I results suggest that GSK ’052 may have efficacy against a broad range of gram-negative bacteria, including *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter* species (spp.), *Serratia marcescens*, *Proteus vulgaris*, *Providentia* spp., *Pseudomonas aeruginosa*, and *Enterobacter* spp., as well as other pathogens. In trials GSK ’052 was administered in doses of 750 to 1,500 mg twice daily as intravenous infusion. Anacor Pharmaceuticals, Inc., Palo Alto, CA; GlaxoSmithKline, Middlesex, UK Phase IIb trials ongoing	Aminoglycosides Meropenem Fluoroquinolones Tigecycline	Clinical response Microbiologic response Reduced morbidity and mortality from infection Resolution of infection

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GSK2251052 for treatment of complicated urinary tract infections	Patients in whom complicated urinary tract infections have been diagnosed	Increasing resistance to existing antibiotics has created a critical need for novel therapies for the treatment of complicated urinary tract infections caused by gram-negative bacteria. GSK-2251052 (GSK ’052) is a novel boron-based, systemic antibiotic that specifically targets the bacterial enzyme leucyl-tRNA synthetase, or LeuRS, which is required for bacterial protein synthesis; inhibition of protein synthesis leads to termination of cell growth and apoptosis (programmed cell death); GSK ’052, if it reaches market, could be the first commercially available antibiotic to target LeuRS; preclinical and phase I results suggest that GSK ’052 may have efficacy against a broad range of gram-negative bacteria, including *E. coli*, *K. pneumoniae*, *Citrobacter* species (spp.), *S. marcescens*, *P. vulgaris*, *Providentia* spp., *P. aeruginosa* and *Enterobacter* spp., as well as other pathogens. In trials GSK ’052 was administered in doses of 750 to 1,500 mg, twice daily, by intravenous infusion. Anacor Pharmaceuticals Inc., Palo Alto, CA; GlaxoSmithKline, Middlesex, UK Phase IIb trials ongoing	Aminoglycosides with or without ampicillin Cephalosporins (third generation) Fluoroquinolones Imipenem-cilastatin	Clinical response Microbiologic response Reduced morbidity and mortality from infection Resolution of infection
Hemopurifier blood filter for pandemics and bioterrorism	Patients affected by pandemic disease or bioterrorism agents	Hemopurifier blood filter works with conventional dialysis systems or other blood pumping technology using a broad-spectrum approach to attract and capture infectious agents from the bloodstream during pandemics or bioterrorism events; in vitro studies have shown that Hemopurifier effectively captures Dengue hemorrhagic virus, Ebola hemorrhagic virus, Lassa hemorrhagic virus, West Nile virus, H5N1 avian influenza virus, 2009 H1N1 influenza virus, the reconstructed Spanish flu of 1918 virus, and monkeypox virus, which serves as a model for human smallpox infection. Aethlon Medical, Inc., San Diego, CA In initial clinical trials; commercialization planned for India	Standard public health measures for containing and treating pandemic disease and/or biological weapon threats	Reduced severity of pandemic disease

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Hemopurifier blood filter for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C infection has been diagnosed	Hemopurifier blood filter works with standard hemodialysis or other conventional blood pump technology to capture and remove hepatitis C particles from general circulation; intended as an adjunct therapy to accelerate viral load reduction at the outset of standard of care drug regimens. Aethlon Medical, Inc., San Diego In initial trials; commercialization planned for India	Standard drug therapy	Reduced viral load Improved efficacy of drug therapy Resolution of chronic infection Improved quality of life
Hemopurifier blood filter for treatment of HIV infection	Patients in whom HIV infection has been diagnosed	Hemopurifier blood filter works with standard hemodialysis or other blood pumping devices to remove viral particles from circulating blood. Intended as a potential therapeutic option for HIV-infected individuals to manage disease progression once they become resistant to antiviral drug regimens. Aethlon Medical, Inc., San Diego, CA In initial clinical trials; commercialization planned for India	Standard antiviral therapy for HIV	Reduced viral load Improved efficacy of drug therapy Improved symptoms Improved quality of life
Lenalidomide for treatment of immune system decline in elderly patients	Patients in whom immunosenescence (decline in immune function due to aging) is suspected	Aging is frequently associated with a decline in immune function known as immunosenescence; treatments to prevent or reverse this process could help improve quality of life and increase lifespan. Lenalidomide is a thalidomide derivative used to treat blood malignancies; low doses of lenalidomide are hypothesized to rebalance cytokine levels to reflect those of younger healthy individuals (higher interleukin-2 and INF-gamma, lower interleukin-17), thus restoring immune function and improving quality of life. Celgene Corp., Summit, NJ Early phase trials ongoing	Healthy lifestyle interventions	Health maintenance Reduced frequency and duration of serious infections Reduced incidence of cancer Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Matrix metalloproteinase inhibitor CTS-1027 for treatment of chronic hepatitis C virus infection	Patients in whom chronic HCV infection has been diagnosed	Patients with HCV infection that is treatment resistant with ribavirin and pegylated INF remain more difficult to treat; new therapies with novel mechanisms of action that can reduce the length of infection and adverse events associated with effective HCV infection treatment are needed. CTS-1027 is an oral small molecule that inhibits matrix metalloproteinases, which are believed to be involved in sustained HCV replication and the inhibition of viral clearance by the immune system; CTS-1027 was designed not to inhibit matrix metalloproteinase-1 (MMP-1), because inhibition of MMP-1 has been associated with musculoskeletal side effects. Administered 60 mg, twice daily. Conatus Pharmaceuticals, Inc., San Diego, CA Phase II trial halted due to safety concerns, safety analysis ongoing	Alisporivir Bavituximab Pegylated INFa-2a Ribavirin	Earlier virologic response Reduced need for liver transplant Slowed or halted disease progression Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Improved quality of life
NB-1008 intranasal vaccine for prevention of respiratory syncytial virus	Infants and children, especially 2 to 3 years of age and the elderly in whom RSV has been diagnosed	The number one cause of childhood hospitalization both in the U.S. and around the world is RSV infection. There are no approved vaccines to prevent it. RSVNB-1008 is being developed as an intranasal vaccine for RSV. NanoBio Corporation, Ann Arbor, MI Phase I trial ongoing	Oxygen Suctioning of mucus from the airways Intubation with mechanical ventilation	Improved compliance with vaccination (no needles) Reduced incidence of bronchiolitis and pneumonia Reduced hospitalizations from RSV infection Reduced mortality from RSV infection

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Nitazoxanide and therapeutic hepatitis C virus vaccine (IC41) for chronic hepatitis C infection	Patients in whom HCV infection has been diagnosed	HCV infection in many infected patients is resistant to treatment or has a suboptimal response to available treatments. Nitazoxanide is a thiazolide with a broad spectrum of antiinfective activity. It may interfere with protease activity and the maturation and intracellular transport of the viral hemagglutinin protein (other drugs inhibit neuraminidase), leading to a reduction in viral replication; oral nitazoxanide will be combined with IC41 (Transvax™), a therapeutic HCV vaccine containing five HCV-derived peptides adjuvanted with synthetic poly-L-arginine (IC-30). The vaccine is administered intradermally. Romark Laboratories, L.C., Tampa, FL; Intercell AG, Vienna, Austria Phase II/III trials ongoing completed	Pegylated INF and ribavirin Protease inhibitors (in clinical development) Polymerase inhibitors (in clinical development)	Rapid virologic response Sustained virologic response Improved quality of life Slow or halt disease progression to liver failure
Nitazoxanide for treatment of viral influenza	Patients in whom viral influenza has been diagnosed	New influenza treatments are needed because of the development of resistance to existing agents. Nitazoxanide is a thiazolide with a broad spectrum of antiinfective activity. It may interfere with protease activity and the maturation and intracellular transport of the viral hemagglutinin protein (other drugs inhibit neuraminidase), leading to a reduction in viral replication. In trials administered orally, 300 mg, twice a day. Romark Laboratories, L.C., Tampa, FL Phase II/III trial completed	Oseltamivir (Tamiflu) Zanamivir (Relenza)	Reduced complications of influenza infection Shorter duration of symptoms
Nitroimidazole (PA-824) for treatment of pulmonary tuberculosis	Patients in whom multidrug-resistant/drug susceptible TB has been diagnosed	PA-824 is a nitroimidazole, a class of antibacterial agents, which has activity in vitro against all tested drug-resistant clinical isolates; intended to shorten treatment time and simplify treatment. Given orally. Novartis AG, Basel, Switzerland Bayer AG, Leverkusen, Germany Phase II trial ongoing	Rifampicin Isoniazid	Shorter duration of therapy Simpler dosing Improved compliance Safer method of action Lower cost of overall treatment

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
NS5A inhibitor PPI-461 for treatment of chronic hepatitis C virus infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. PPI-461 is an HCV NS5A inhibitor; NS5A is a multifunctional, nonenzymatic ER membrane-associated phosphoprotein, which regulates multiple steps of the HCV life cycle, including viral RNA replication and virion maturation; although the role of the protein is poorly understood, NS5A is required for viral replication; it is proposed that PPI-461 destabilizes N5A interactions thus inhibiting the formation of functional virions; it may be used in combination with other HCV treatment options. Administered orally, 50 to 100 mg, once daily. Presidio Pharmaceuticals, Inc., San Francisco, CA Phase I trial completed	Daclatasvir	Early virologic response Rapid virologic response (HCV RNA undetectable at week 4) Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Slowed or halted disease progression Reduced need for liver transplant Improved quality of life
Nucleoside polymerase inhibitor (TMC649128) for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients and the presence of pegylated INFa-2a results in poor treatment tolerability in many patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. TMC649128 is an oral nucleoside analog polymerase inhibitor; HCV polymerase is a virally encoded enzyme necessary for replication of the viral genome; TMC649128 is purported to have a high genetic barrier to resistance and antiviral activity across multiple HCV genotypes. Administered 1,000 mg, once daily. Medivir AB, Huddinge, Sweden Phase I trials ongoing	Boceprevir Nucleoside polymerase inhibitors Pegylated INF Ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Reduced need for liver transplant Slowed or halted disease progression Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
OraQuick Rapid HCV Antibody Test using an oral swab specimen for detection of hepatitis C virus infection	Patients with unknown HCV infection status	The current OraQuick® HCV Rapid Antibody Test requires blood from a finger prick, deterring some patients from being tested and some care settings from performing the test; a testing method using an oral swab may remove barriers for many patients with unknown HCV status to be tested in community health centers and primary care practices. OraQuick HCV Rapid Antibody Test is currently being validated for use with an oral swab sample that would contain antibodies to HCV, which can be detected by the kit; the OraQuick HCV Rapid Antibody Test uses an indirect lateral flow immunoassay method to detect antibodies to synthetic peptides and recombinant antigens from the core, NS3, and NS4 regions of the HCV genome, immobilized as a single test line on the assay strip. OraSure Technologies, Inc., Bethlehem, PA FDA approved OraQuick HCV Rapid Antibody Test that uses a finger stick under premarket approval process Jun 2010	OraQuick HCV Rapid Antibody test using venipuncture Other HCV tests	Increased rate of HCV detection Earlier treatment of HCV infection Reduced transmission Reduced morbidity Reduced mortality
Peramivir for treatment of influenza	Patients in whom H1N1 influenza has been diagnosed or is suspected	Because of resistance to existing antiviral agents used for flu, new antiviral therapies are needed. Additionally, therapies that provide broad coverage against different strains of influenza virus are needed. Peramivir is a cyclopentane neuraminidase inhibitor, which is intended to bind the active site of the protein and inhibit viral budding; peramivir has activity against influenza A and B viruses as well as in patients refractory to oseltamivir. Administered as an intravenous drug, 600 mg, once daily, for 5 to 10 days. BioCryst Pharmaceuticals, Inc., Research Triangle Park, NC Phase III trial ongoing; approved for emergency use in patients with confirmed or suspected H1N1 influenza	Laninamivir (in phase III trials) Oseltamivir Zanamivir	Decreased length of hospitalization Reduction in virus titers Relief of symptoms

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pharmacist-provided medication therapy management for patients with HIV/AIDS	Patients in whom HIV infection/AIDS has been diagnosed	A significant correlation between improved ART adherence and reduced viral load and therapeutic outcomes has been demonstrated; ART regimens comprise multiple classes of medications; treatment options are limited once resistance occurs, which can be associated with poor treatment adherence; programs to optimize treatment adherence are needed to optimize outcomes. Pharmacist-provided medication therapy management (MTM) services are being provided to California residents with HIV/AIDS as part of a Medi-Cal pilot program; participating pharmacies and pharmacists select various services offered above and beyond standard counseling, such as: evaluation of patients' ability to adhere to medications, in consultation with doctors and case managers; identifying and managing adverse drug reactions; tailoring drug regimens to fit patient lifestyle or special needs; individual appointments with pharmacists to discuss medication therapy; adherence packaging beyond any provided by manufacturer (e.g., personalized blister packs for all ART medications); identification of peer advocates to assist in medication adherence; and weekly telephone call or home visit after initiation of therapy. School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, CA	MTM in another care setting Nurse care coordinator	Decreased cost of care Decreased incidence of opportunistic infections Reduced need for inpatient services Reduced need to change treatment regimen Improved treatment adherence Reduced viral load

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PMX-30063 for treatment of acute bacterial skin infections	Patients in whom acute bacterial skin and skin structure infections (ABSSSIs) have been diagnosed	Drug resistant bacteria and the shrinking clinical pipeline of new agents to treat serious skin infections will continue to pose issues for effectively managing patients. Antibiotics with new mechanisms of action are needed. PMX-30063 is a novel, synthetic defensin-mimetic antibiotic; defensins are proteins that are part of the human innate immune system that target and disrupt bacterial cell membranes, leading to lysis; by targeting bacterial membranes, PMX-30063 is purported to avoid current resistance mechanisms and is less likely to develop future resistance; PMX-30063 is composed of biomimetic compounds that mimic key biological properties of proteins, but are purported to be more stable and inexpensive to produce than natural proteins; PMX-30063 is purported to have broad-spectrum activity; PMX-30063 has been shown to kill *Staphylococcus aureus* in human blood samples in vitro. Administered intravenously. PolyMedix, Inc., Radnor, PA Phase II trial ongoing	Linezolid Vancomycin	Complete clinical response Complete microbiologic response Infection resolution/cure
Point-of-care testing systems for methicillin-resistant *Staphylococcus aureus* screening	Patients who may be infected by methicillin-resistant *Staphylococcus aureus* (MRSA)	Current MRSA screening tests are time-intensive and typically require highly trained laboratory workers to perform the test. Testing systems and assays are being developed that could be used by non-clinical laboratory staff in the point-of-care setting and provide results in 10 to 15 minutes. Multiple manufacturers: Blaze Venture Technologies, Ltd., Ware, UK Enigma Diagnostics, Ltd., Salisbury, UK InstantLabs Medical Diagnostics Corp., Reston, VA QuantaLife, Inc., Pleasantville, CA Smiths Group, plc, London, UK TwistDx, Ltd., Cambridge, UK Early trials ongoing. Devices and test kits expected to be cleared through 510(k) pathway with no requirement for clinical evidence of efficacy	MRSA Culture Conventional first generation PCR second generation quantitative PCR	Reduced transmission of MRSA Increased sensitivity of MRSA detection Increased specificity of MRSA detection Increased speed of MRSA detection

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Polymerase inhibitor (GS-9190, tegobuvir) for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients; effective treatments that improve clinical outcome in a shorter period of time are needed. Tegobuvir is a nonnucleoside NS5B polymerase inhibitor intended to block the activity of HCV polymerase, preventing replication of the viral genome. Administered orally, 40 mg, twice daily in various combinations with GS-9256 (protease inhibitor), pegylated INF, and ribavirin. Gilead Sciences, Inc., Foster City, CA Phase IIb trials ongoing	Boceprevir Nonnucleoside polymerase inhibitors Nucleoside polymerase inhibitors Pegylated INF Ribavirin Telaprevir	Early virologic response Reduced need for liver transplant Slowed or halted disease progression Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Improved quality of life
Polymerase inhibitor (PSI-938) for treatment of chronic hepatitis C infection	Patients in whom hepatitis C infection has been diagnosed	PSI-938 is an unpartnered guanosine nucleotide analog polymerase inhibitor of HCV; expected to be used in conjunction with pegylated INF plus ribavirin, and in combination with another Pharmasset drug in development, PSI-7977. According to the developer, the drug candidates "use different prodrug strategies, but are metabolized to the same active purine triphosphate in human hepatocytes Pharmasset, Inc., Princeton, NJ Phase II trial ongoing; FDA granted fast track status Aug 24, 2011	Pegylated INF plus ribavirin	Cured infection (sustained virologic response with no detectable virus) Reduction of symptoms Improved quality of life Delay or halt progression to end-stage liver disease
Polymerase inhibitor (PSI-7977) for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C infection has been diagnosed	Uridine nucleotide analog polymerase inhibitor (PSI-7977) of HCV is expected to be used in conjunction with pegylated INF plus ribavirin, and possible in conjunction with PSI-938. Administered orally. Pharmasset, Inc., Princeton, NJ Phase III trials planned; received FDA fast track designation	Pegylated INF plus ribavirin	Cured infection (sustained virologic response with no detectable virus) Reduction of symptoms Improved quality of life Delay or halt progression to end-stage liver disease

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Polymerase inhibitor (VX-222) for treatment of chronic hepatitis C	Patients in whom chronic hepatitis C infection has been diagnosed	Polymerase inhibitor (VX-222) acts on HCV; likely to be used in combination with telaprevir and ribavirin. Vertex Pharmaceuticals, Inc., Cambridge, MA Phase II trials ongoing	Boceprevir Pegylated INF plus ribavirin Telaprevir	Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Preventive vaccine PENNVAX-B (VGX-3300) for HIV infection	Patients at high risk for chronic HIV-1 infection	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy continue to suggest that prophylactic HIV measures be pursued for individuals who are not infected with the virus, but are at high risk. PENNVAX™-B is a SynCon DNA vaccine that encodes sequences from the gag, pol, and env proteins of HIV-1; the DNA vaccine is administered with Inovio's Cellectra electroporation device; the vaccine is intended to be then taken up by local antigen presenting cells, which express the antigens and induce antibody and T-cell responses to the HIV-1 proteins and may provide protection against infection. Inovio Pharmaceuticals, Inc., Blue Bell, PA ChronTech Pharma AB, Huddinge, Sweden Phase I trials ongoing	Pre-exposure prophylaxis (tenofovir/emtricitabine) Prime-boost vaccination with DNA and modified vaccinia virus Ankara Vaginal gels dapivirine, tenofovir	Lower incidence of HIV-1 infection Improved B-cell and T-cell responses to HIV antigens

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Prime-boost vaccination with DNA and modified vaccinia virus Ankara for prevention of HIV infection	Persons who are at risk for HIV infection	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy continue to suggest that prophylactic HIV vaccination be pursued for individuals whom are not infected with the virus. This vaccine protocol consists of prime-boost strategy where two doses of a DNA vaccine (pGA2/JS7) are administered followed by two doses of a recombinant modified vaccinia virus Ankara (MVA) vector expressing HIV clade B Gag, Pol, and Env proteins (MVA/HIV62); the expressed proteins form onco-infectious virus-like particles with the intention of generating protective antibody and cellular responses; clade B is the most common clade in North America. GeoVax Labs, Inc., Smyrna, GA Phase IIa trial ongoing	Dapivirine gel Pre-exposure prophylaxis with antiretroviral Personalized vaccination Therapeutic vaccination	Improved antibody and T-cell responses Decreased incidence of infection
Pro 140 monoclonal antibody for treatment of HIV infection	Patients chronically infected with HIV	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy present opportunities for the development of novel and effective HIV therapies. Pro 140 is a monoclonal antibody directed against the CCR5 chemokine receptor that serves as the coreceptor for HIV infection; by binding to CCR5, Pro 140 is purported to reduce the rate of viral replication, increasing the efficacy of current antiretrovirals; expected to have better tolerability than current antiretrovirals (not metabolized in the liver); purported to not affect normal CCR5 function. Administered by subcutaneous injection on days 1, 8, and 15. Progenics Pharmaceuticals, Inc., Tarrytown, NY Phase II trial ongoing	Antiretroviral therapy Personalized vaccination Therapeutic vaccination (investigational)	Decreased viral load Decreased morbidity Increased survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Prophylactic vaccine recombinant vesicular stomatitis virus expressing HIV-1 Gag protein (VSV_{IN} HIV-1 gag) for HIV-1	Patients at risk for HIV-1 infection	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy continue to suggest that prophylactic HIV measures be pursued for individuals who are not infected with the virus. Recombinant vesicular stomatitis virus HIV-1 gag vaccine ($rVSV_{IN}$ HIV-1 gag) uses the negative-strand, nonsegmented RNA virus vector to deliver the HIV gag immunogen; this vector was selected for immunogenicity (naturally activating toll-like receptor-7 signaling), safety (cytoplasmic replication, incapable of integration within the host's genome), and a lack of previously existing natural immunity; intended to be used in combination with plasmid vaccines under investigation by Profectus. Profectus BioSciences, Inc., Baltimore, MD Phase I trials ongoing	Pre-exposure prophylaxis (tenofovir/emtricitabine) Prime-boost vaccination with DNA and modified vaccinia virus Ankara Vaginal gels dapivirine, tenofovir	Lower incidence of HIV-1 infection Improved T-cell responses to Gag
Protease inhibitor (ABT-450/r) for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	ABT-450/r is a HCV protease inhibitor Abbott Laboratories, Abbott Park, IL Phase II trials ongoing	Boceprevir INF and ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Protease inhibitor (boceprevir) for treatment of hepatitis C infection	Patients in whom hepatitis C infection has been diagnosed	Protease inhibitor (boceprevir) intended to cut treatment time to 6 months from 9 months; intended to "cure" active infection (sustained virologic response) in most patients. Merck and Vertex Pharmaceuticals, Inc., Cambridge, MA, are in competition to be first to market with their protease inhibitors. Merck & Co., Inc., Whitehouse Station, NJ FDA approved May 2011	INF and ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Protease inhibitor GS-9256 for treatment of chronic hepatitis C virus infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients; effective treatments that improve clinical outcome in a shorter period of time are needed. GS-9256 is a NS3 protease inhibitor intended to block the activity of HCV protease, preventing the cleavage and maturation of functional viral particles. Administered orally, 75 mg, twice daily, in various combinations with tegobuvir (polymerase inhibitor), pegylated INF, and ribavirin. Gilead Sciences, Inc., Foster City, CA Phase IIb trials ongoing	Boceprevir INF and ribavirin Telaprevir	Early virologic response Reduced need for liver transplant Slowed or halted disease progression Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Protease inhibitor MK-5172 for treatment of chronic hepatitis C virus infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care for HCV infection is generally ineffective in more than half of infected patients; effective treatments that improve clinical outcome in a shorter period of time are needed. MK-5172 is an NS3/4a protease inhibitor intended to block the activity of HCV protease from genotypes 1b, 2a, 2b, and 3a, preventing the cleavage and maturation of functional viral particles. Administered orally, 100 to 800 mg, once daily; may be used in combination with pegylated INF and ribavirin. Merck & Co., Inc., Whitehouse Station, NJ Phase II trial ongoing	Boceprevir INF and ribavirin Telaprevir	Early virologic response Reduced need for liver transplant Slowed or halted disease progression Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Improved quality of life
Protease inhibitor (telaprevir) for treatment of hepatitis C infection	Patients in whom hepatitis C infection has been diagnosed	Protease inhibitor (telaprevir) is intended to cut treatment time to 6 months from 12 months for two-thirds of patients and to "cure" active infection. Merck & Co., Inc., Whitehouse Station, NJ, and Vertex are in competition to be first to market with their protease inhibitors. Vertex Pharmaceuticals, Inc., Cambridge, MA FDA approved May 2011	INF and ribavirin Boceprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Protease inhibitor (vaniprevir, (MK7009) for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Vaniprevir (MK7009) is a next-generation HCV protease inhibitor. Merck & Co., Inc., Whitehouse Station, NJ Phase III trials ongoing	Boceprevir INF and ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Rapid molecular detection test (Xpert MTB/RIF) for *Mycobacterium tuberculosis* infection with rifampin resistance	Patients suspected of having *M. tuberculosis* infection	Automated molecular test (Xpert® MTB/RIF) for *M. tuberculosis* infection that also simultaneously tests for resistance to rifampin Cepheid, Sunnyvale, CA Expected to become available in the U.S. in 2012 or 2013; CE marked	Ziehl-Neelsen microscopy Tuberculin skin test (Mantoux test) Microscopy	Less training time Rapid detection Improved treatment Better control of antibacterial resistance
Recombinant interleukin-7 (CYT107) for immune reconstitution in treatment of HIV infection	HIV immune nonresponding patients whose tests show CD4 counts remaining between 101 and 350 cells after at least 2 years of highly active antiretroviral (HAART) therapy	CYT107 is a recombinant form of human interleukin-7; treatment is expected improve and prolong immune reconstitution and stabilize patient CD4+ T-cell counts of less than 500; intended to decrease activation/inflammation markers. Cytheris SA, Issy-les-Moulineaux, France Phase II trials ongoing	Standard HIV therapy HAART therapy	Improved immune response Reduced need for other medications Increased survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Routine anal Pap smear screening at HIV clinics to prevent anal cancer	Patients in whom HIV infection has been diagnosed	Patients with HIV have a higher risk of developing anal cancer, yet there are no national or international guidelines for anal dysplasia screening. Anal Pap screening can be incorporated into routine visits when patients attend HIV clinics for treatment and monitoring, and some clinicians recommend screening regardless of history of anal intercourse. University of Miami Miller School of Medicine, Miami, FL	Anal Pap screening or anoscopy by other physician during regular intervals (after 50 years of age)	Earlier detection of suspicious polyps Reduced anal cancer incidence in patients with HIV Reduced anal cancer mortality in patients with HIV
SB-728 for treatment of HIV infection	Patients in whom chronic HIV infection has been diagnosed	Many patients (30%) infected with HIV who have controlled their infection with ART still have low T-cell counts; therapies to increase T-cell counts in these patients are needed to prevent HIV-related morbidity. CR5 is a major coreceptor required for HIV to infect CD4+ cells; a naturally occurring mutation of the CCR5 gene, CCR5-delta32 has been shown to provide protection against HIV infection; SB-728 is an autologous T-cell product that uses zinc finger nuclease technology to generate CCR5-permanently modified T cells that are resistant to HIV infection and are capable of replicating in the gut mucosa, which serves as a reservoir for HIV. An apheresis is taken from patients, cells are modified in vitro, and readministered into patients once. Sangamo BioSciences, Inc., Richmond, CA Phase I/II trial ongoing	Antiretroviral therapy CYT-107 Pro 140	Improved CD4:CD8 ratio Persistence of modified T-cells in the circulation Increased T-cell counts Reduced viral load Reduced HIV/AIDS morbidity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
SCY-635 for treatment of chronic hepatitis C virus infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care (pegylated INF and ribavirin) for HCV infection is not effective for more than half of infected patients seeking treatment and is poorly tolerated in many patients; effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. Cyclophilin A is a host cell protein involved in protein folding and transport, it has also been shown to be essential in HCV replication; cyclosporine A inhibits cyclophilin activity but is immunosuppressive; SCY-635 is a novel cyclosporine analog that was developed to be nonimmunosuppressive and, like other inhibitors in this class, is not associated with an increased risk of hyperbilirubinemia; SCY-635 may also have an antifibrotic effect independent of demonstrated anti-HCV activity. Administered 300 to 400 mg, twice a day, for 28 days with pegylated INF and ribavirin. SCYNEXIS, Inc., Durham, NC Phase II trial ongoing	Bavituximab Boceprevir Direct acting antivirals Pegylated INF alpha-2a and lambda Ribavirin Telaprevir Combination therapy	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life
Taribavirin hydrochloride (AVS-000206) for treatment of chronic hepatitis C virus infection	Patients in whom HCV infection has been diagnosed	Effective treatment is needed for treatment resistant HCV infection. Taribavirin, a liver-targeted prodrug of ribavirin, is an antiviral designed to block the enzyme inosine monophosphate dehydrogenase (IMPDH) to inhibit the proliferation of certain cell types. Valeant Pharmaceuticals, Inc., Mississauga, Ontario, Canada Phase III trials completed	Pegylated INF and ribavirin Protease inhibitors (in clinical development) Polymerase inhibitors (in clinical development) TBI-301 (preclinical IMPDH)	Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Talactoferrin for treatment of severe sepsis	Patients in whom severe sepsis has been diagnosed	Each year, approximately 750,000 people in the U.S. develop severe sepsis, resulting in approximately 30% mortality; sepsis is one of the top 10 leading causes of death in the U.S. Few therapies are available for severe sepsis and have significant adverse events. An urgent need exists for effective and well tolerated therapies for severe sepsis. Talactoferrin is a recombinant protein intended to be an immunomodulator, dampening the overactive immune response associated with severe sepsis; talactoferrin is also purported to have antibacterial properties; administered as 15 mL of oral solution, three times daily, for up to 28 days or until discharge from the ICU. Agennix AG, Heidelberg, Germany Phase II/III trial ongoing	Antibiotics Blood pressure mediation Corticosteroid therapy to treat the inflammatory process Drotrecogin alfa activated (Xigris) Intravenous fluids Mechanical ventilation Oxygen	Reduced mortality
Tenofovir and emtricitabine (Truvada) for prevention of HIV infection	People at risk for HIV infection	Truvada® is a combination of two reverse transcriptase inhibitors Viread® (tenofovir disoproxil fumarate) and Emtriva® (emtricitabine) given as pre-exposure prophylaxis for people at high risk of HIV infection. Preliminary studies have shown that daily prophylactic use of tenofovir and emtricitabine may prevent the acquisition of HIV in men who have sex with men and heterosexual men. Data for prophylactic use in women have been confounding due to lack of efficacy. The two drugs are combined into one oral tablet taken daily. Already FDA approved for treatment; may currently be used off-label prophylactically for males and females at high-risk for HIV-1 infection. Gilead Sciences, Inc., Foster City, CA Phase II-IV trials ongoing to determine appropriateness of preventive therapy based on efficacy in different male (heterosexual males and males who have sex with males) and female (heterosexual) populations; already marketed for HIV treatment; prevention of HIV infection would be new indication.	Condoms Harm reduction campaigns Safe needle exchange programs	Reduced transmission and incidence of HIV

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tenofovir gel 1% for prevention of HIV transmission	Women who are sexually active	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy continue to suggest that prophylactic HIV measures be pursued for individuals who are not infected with the virus. Tenofovir 1% gel is a topical formulation of the nucleotide reverse transcriptase inhibitor tenofovir that is intended to inhibit reverse transcription, an essential part of the viral life cycle; women apply the gel vaginally 12 hours or less prior to sexual intercourse and within 12 hours after sexual intercourse. International Partnership for Microbicides, Silver Spring, MD Gilead Sciences, Inc., Foster City, CA Phase III trial ongoing; FDA fast track designation	Dapivirine gel Pre-exposure prophylaxis with antiretroviral Prophylactic vaccination	Prevention of HIV infection women at risk
Therapeutic vaccine (DermaVir) for HIV infection	Patients in whom chronic HIV infection has been diagnosed	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments; HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy continue to suggest that improved therapeutic options be pursued to treat patients. DermaVir therapeutic vaccine is designed to induce T-cell responses against HIV-1 capable of controlling viral load; the vaccine is comprised of "pathogen-like" nanomedicine particles formulated using a novel synthetic polymer, mannosylated linear polyethyleneimine (PEIm), a synthetic polymer, purported to have the size and the shape of infectious virus particles capable of delivering nucleic acids to antigen presenting dendritic cells (APCs), without the risk of actual infection; the vaccine is administered topically using a patch placed by a health care practitioner; once applied to the skin and taken up by APCs, the single DNA plasmid immunogen, expresses 15 HIV antigens and up to 3,000 T-cell epitopes, which are purported to safely self-assemble into virus-like particle immunogens that are targeted to generate immunity. Genetic Immunity, LLC, McLean, VA Phase II trials ongoing	Highly active antiretroviral HAART) therapy Personalized vaccination Therapeutic vaccination	T cell precursors with high proliferative capacity Reduced viral load Reduction of medication regimen Reduced HIV-related morbidity

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Therapeutic vaccine (HerpV) for treatment of genital herpes infection	Patients infected with herpes simplex virus 2 (HSV-2)	One in six people from age 14 to 49 years are infected with HSV-2, greatly affecting quality of life; additionally, there is some evidence to suggest that resistance to existing herpes treatments is increasing. HerpV is a recombinant, off-the-shelf, therapeutic vaccine for the treatment of genital herpes that is caused by HSV-2; HerpV is comprised of recombinant heat shock protein-70 complexed with 32 distinct 35-mer synthetic peptides from the HSV-2 proteome; intended to allow for more accurate immune targeting and surveillance, reducing the likelihood of immune escape, and providing adequate epitope diversity in diverse genetic populations; the addition of heat shock protein-70 is intended to increase antigen presentation and immunogenicity of the peptides; the vaccine also contains Agenus' proprietary adjuvant QS-21 Stimulon. Agenus, Inc., Lexington, MA Phase I trial completed	Acyclovir Valacyclovir	Reduced duration of outbreaks Reduced frequency of outbreaks Reduced transmission of HSV-2
Therapeutic vaccine (GI-5005) for chronic hepatitis C infection	Patients with chronic HCV infection whose disease has failed to respond to standard treatment	Effective treatment for chronic HCV infection is needed. Therapeutic vaccine GI-5005 is composed of a recombinant fusion protein composed of sequences from HCV nonstructural protein 3 (NS3) and core antigens expressed on the surface of the yeast *Saccharomyces cerevisiae*; these proteins are highly conserved regions from HCV; immunization with the recombinant yeast is intended to induce cellular immunity against HCV to resolve chronic infection. GlobeImmune, Inc., Louisville, CO Phase IIb trial ongoing	INFa-2a Protease inhibitors (in phase III development) Ribavirin	Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Therapeutic vaccine (V5) for tuberculosis	Patients in whom TB has been diagnosed	Therapeutic vaccine (V5) intended for use as adjunctive TB immunotherapy in combination with standard drugs. Oral pill. Immunitor USA, Inc., College Park, MD Phase II trial completed	Isoniazid, rifampicin, pyrazinamide, and ethambutol	Improved treatment compliance Resolution of active TB Reduced treatment failures Reduced antibacterial resistance Reduced spread of TB infection Improved quality of life
TMC435 for treatment of chronic hepatitis C infection	Patients in whom chronic HCV infection has been diagnosed	Current standard of care is ineffective in as many as half of patients with chronic HCV infection, so new, more effective treatment is needed. TMC435 in an oral, once daily NS3/NS4A HCV protease inhibitor which may be used to limit viral replication in combination with pegylated INF and ribavirin. Administered orally, 150 mg, once daily. Tibotec BVBA, Beerse, Belgium Phase III trials ongoing; FDA fast track designation	Boceprevir Pegylated INF Ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Slowed or halted disease progression (fibrosis and cirrhosis) Sustained virologic response (defined as undetectable virus at 24 weeks) Decreased need for liver transplant Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
VAX125 vaccine to prevent seasonal influenza	Persons at risk for infection/complications from influenza	Influenza is one of the most communicable diseases, resulting in significant morbidity and mortality each year; changes in seasonal flu strains can leave even immunized patients poorly protected; vaccines that can be rapidly produced to relevant strains are needed. VAX125 is a recombinant fusion protein that consists of *Salmonella typhimurium* flagellin type 2, a Toll-like receptor 5 ligand designed to enhance immunogenicity, fused to the globular head domain of the hemagglutinin influenza A HA1 protein; VAX125 is purported to be the first recombinant bacterial expressed vaccine for influenza, which will increase the speed and decrease the cost of seasonal influenza vaccine development. Administered as a single intramuscular injection. VaxInnate, Inc., Cranbury, NJ Phase II trial completed	Trivalent influenza vaccine Quadrivalent influenza vaccine (in development) Virus-like particle vaccine (in development)	Decreased transmission rates of viral influenza Improved immunogenicity in older patients Lower morbidity and mortality from influenza
Virus-like particle seasonal flu vaccine for prevention of viral influenza	People who are eligible for influenza vaccination	Seasonal flu vaccine composed of virus-like particles containing hemagglutinin, neuraminidase, and M1 matrix proteins from seasonal influenza viruses produced in recombinant insect cells; commercial quantities of the virus-like particle vaccine can be produced in 10 to 14 weeks; standard vaccines produced in chicken eggs require production times of 4 to 6 months. Novavax, Inc., Rockville, MD Phase II trials ongoing	Seasonal flu vaccine formulations	Faster production and distribution of vaccine Reduced incidence of viral influenza Vaccination option for people allergic to eggs who want flu vaccination

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
VP 20621 for treatment of recurrent *Clostridium difficile* infection	Patients in whom recurrent CDI has been diagnosed	Recurrent CDI is responsible for significant morbidity mortality, and costs; recurrent CDI can be extremely resistant to treatment; up to 60% of patients previously treated for recurrent CDI with antibiotics develop further recurrence after therapy is stopped, which suggests that other therapeutic options are needed. VP 20621 consists of nontoxin producing spores of *C. difficile* which are orally administered following initial treatment of acute CDI with an antibiotic such as vancomycin; following initial treatment of CDI with antibiotic therapy, VP 20621 is used to recolonize the gastrointestinal (GI) tract and prevent the wild-type toxin producing strains from recolonizing colon until normal GI flora returns and the patient is no longer susceptible to disease. ViroPharma, Inc., Exton, PA Phase II trial ongoing	Fecal transplant Fidaxomicin Metronidazole Vancomycin Vaccination (Sanofi-Aventis)	Reduced hospitalization time Reduced presence of toxin-producing *C. difficile* in stool Reduced use of additional antibacterial drugs
XF-73 for prevention of postsurgical infections due to *Staphylococcus aureus*	Patients undergoing surgery who may be at risk for infection	Antibacterial drugs with a low propensity for inducing bacterial resistance are needed to prevent and treat multidrug-resistant bacteria in health care settings. XF-73 is a novel dicationic porphyrin, purported to have rapid bactericidal activity against gram-positive bacteria including *Staphylococcus aureus*, the number one global cause of hospital-acquired bacterial infections. XF-73 has also shown activity against drug-resistant strains of methicillin-resistant *S. aureus* (MRSA); XF-73, is purported to be less likely to develop antibacterial resistance than currently available antibiotics commonly used to treat MRSA infections; its mechanism of action remains to be elucidated, however XF-73 may interact with bacterial membranes in a way distinct from any other antibiotic; because of the low propensity of developing resistance, XF-73 may be used to prophylactically in patients undergoing surgery who may be at risk for developing serious postsurgical infections. Destiny Pharma, Ltd., Brighton, UK in collaboration with National Institute of Allergy and Infectious Disease, Bethesda, MD Phase I trials completed	Daptomycin Fluoroquinolones Fusidic acid Minocycline Vancomycin	Reduction in bacterial infections

Table 10. AHRQ Priority Condition: 10 Obesity: 16 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Controlled-release phentermine-topiramate (Qnexa) for treatment of obesity	Obese patients or overweight patients with T2DM or other comorbidities	Only one long-term weight loss drug is currently on the market in the U.S., and this drug results in 5% weight loss in only 50% of patients. Qnexa® is a combination of the appetite suppressant phentermine (approved for short-term use in weight loss) and topiramate (an approved anti-epileptic agent with known weight loss side effects); Qnexa is a controlled-release pill that is intended to be taken once daily. Vivus, Inc., Mountain View, CA After a Jul 2010 FDA advisory panel meeting recommending against approval, in Oct 2010, FDA issued a response letter to the company's new drug application (NDA) stating the agency could not approve the NDA in its current form because of the drug's link to an increase in birth defects and major cardiovascular events. In Oct 2011, the manufacturer announced the resubmission of its NDA to FDA after a Sept 2011 meeting with FDA about next steps. The resubmission presents a new contraindication for "women of childbearing potential." In Nov 2011, FDA accepted the revised NDA with a decision date set for Apr 17, 2012.	Orlistat Other anti-obesity drugs in development	Excess weight loss Decreased rate of obesity-related comorbidities (e.g., prediabetes, high blood pressure) Improved quality of life
Endoluminal sleeve (EndoBarrier) for preoperative weight loss or treatment for obesity	Patients with body mass index (BMI) > 35 who need to lose weight before bariatric surgery	Gastrointestinal (GI) liner (EndoBarrier®) is a 60 cm impermeable sleeve intended to allow partially digested food to move through GI tract without allowing nutrients to be absorbed in order to achieve weight loss. GI Dynamics, Inc., Lexington, MA Medtronic, Inc., Minneapolis, MN One U.S. pilot trial completed; several trials completed in Europe, South America; marketed in Europe	Diet Anti-obesity drugs Exercise Intragastric balloon	Preoperative weight loss Improved patient safety Reduced side effects Reduced morbidity

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
FGFR4 antagonist (ISIS-FGFR4Rx) for treatment of obesity	Patients with BMI ≥ 30	Currently, one weight loss drug is available for treatment of obesity in the U.S. and FDA approval of other drugs in development has been delayed due to concerns over long-term safety. The available drug results in about 5% weight loss in only approximately 50% of patients. ISIS-FGFR4Rx is a new candidate intended to block production of fibroblast growth factor receptor 4 (FGFR4) in the liver and fat tissue. FGFR4 seems to underlie fatty liver disease with a chronic high fat intake diet and obesity. ISIS-FGFR4 is purported to not reduce FGFR4 expression in the central nervous system or heart, therefore avoiding side effects associated with many pharmacologic products developed for obesity. ISIS Pharmaceuticals, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ Phase I trial being planned	Diet Anti-obesity drugs Exercise	Total weight loss Excess total weight loss
Food-based polymer (Attiva) for treatment of obesity	Overweight patients with body mass index (BMI) of 30 or higher	Currently, only one FDA-approved drug is available for treatment of obesity. Attiva™ is a polymer that may promote weight loss without any unwarranted central nervous system effects. Attiva is a highly absorbent hydrogel containing polymer particles solely comprised of food materials that expand when in contact with liquid in the stomach; the polymer expands into numerous hydrogel beads in the stomach, giving a "full" feeling to suppress hunger; the hydrogel keeps food in the stomach longer, giving stomach acid more time to break down both the food and the hydrogel, which begins to release its water; everything then moves to the small intestine where the gel can re-expand to some extent, slowing the absorption of fatty materials and sugars. Attiva capsules may be taken orally after meals. Gelesis, Inc., Boston, MA Pilot study completed; company intends to pursue FDA 510(k) clearance	Lifestyle changes Weight loss drugs on the market and under development Bariatric surgery	Total weight loss Excess weight loss Decline in obesity-associated comorbidities (e.g., prediabetes, high blood pressure)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gastric pacemaker (Abiliti) for treatment of obesity	Patients with a body mass index (BMI) higher than 40 or a BMI of 35 or higher with comorbidity	Current surgical options for treating obesity are often effective, but some of them alter the size, shape, and/or architecture of the GI tract, potentially leading to side effects such as nausea, digestive issues, and nutritional deficits. The Abiliti® gastric pacemaker is proposed as an alternative that does not alter the structure of the GI tract, but senses the ingestion of food and stimulates the stomach with electrical pulses to try to induce satiety, which might lead to weight loss. IntraPace, Inc., Mountain View, CA No currently registered U.S. trials; CE marked in Mar 2011; IntraPace is discussing with FDA requirements for a U.S. investigational device exemption (IDE) pivotal trial by early 2012	Gastric bypass surgery Sleeve gastrectomy surgery Gastric banding surgery Intragastric balloon	Percent excess weight loss Percent total weight loss Decreased obesity-associated comorbidities (e.g., prediabetes, high blood pressure) Improved quality of life
Lorcaserin (APD-356) for treatment of obesity	Obese individuals with a body mass index of 30 to 45	Lorcaserin (APD-356) is in a new class of selective serotonin 2C receptor agonists that are taken daily. Arena Pharmaceuticals, Inc., San Diego, CA Three phase III trials completed; NDA submitted Dec 2009; FDA rejected NDA Oct 2010; Company plans to resubmit NDA by the end of 2011	Dietary modification Exercise Other diet drugs	Weight loss Decreased comorbidities Adverse events Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Melanocortin receptor partial agonist (AZD2820) for treatment of obesity	Adults with a body mass index (BMI) 18 or more and 30 or less who weigh at least 50 kg (110 lb.) and no more than 100 kg (220 lb.)	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Currently, only one FDA-approved drug is available for treatment of obesity and FDA approval of other drugs in development has been rejected because of concerns over long-term safety. AZD2820 is a peptide melanocortin receptor partial agonist that purportedly acts by stimulating the melanocortin-3 and melanocortin-4 receptors that have been implicated in regulating food intake, body weight, and energy homeostasis. AZD2820 will be administered as a subcutaneous injection in abdomen or thigh AstraZeneca, London, UK, in partnership with Palatin Technologies, Inc., Cranbury, NJ Phase I trial completed	Dietary and lifestyle modifications Variable obesity drugs on the market and under development	Improved weight loss Improved insulin sensitivity Decreased obesity-associated comorbidities (e.g., prediabetes, high blood pressure) Improved quality of life
Methionine aminopeptidase 2 inhibitor (ZGN-433) for treatment of obesity	Patients in whom severe obesity (body mass index between 32 and 45 with or without comorbidities) has been diagnosed	Pharmacologic options to treat severe obesity are very limited and severely obese patients who are not candidates for bariatric procedures and cannot lose and maintain weight loss with lifestyle changes want other options. ZGN-433 inhibits methionine aminopeptidase 2, which reduces blood flow to fatty tissues, starving them; researchers purport that this can potentially induce weight loss. Given as a subcutaneous injection in ongoing trials (previous trials gave intravenously prior to reformulation as a subcutaneous injection). Zafgen, Inc., Cambridge, MA Phase Ib trial completed; second phase Ib trial ongoing; phase IIa trials planned for first half of 2012	Bariatric surgery Diet Exercise Orlistat (Alli, Xenical)	Weight loss Decreased comorbidities Fewer adverse events Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Naltrexone and bupropion extended-release (Contrave SR) for treatment of obesity	Individuals with body mass index 30 to 45 or 27 to 45 with comorbidities	Naltrexone and bupropion extended release (Contrave SR®) is taken orally once a day. Orexigen Therapeutics, Inc., La Jolla, CA Completed COR-I trial; FDA rejected NDA Feb 2011; requested additional trial on cardiovascular effects; manufacturer met with FDA's Office of New Drugs in Sept 2011 to discuss pathway to regulatory approval; cardiovascular outcomes trial required by FDA is not scheduled to begin until the first half of 2012; the manufacturer anticipates submitting results and having the drug become eligible for approval in 2014	Dietary modification Exercise Other weight-loss drugs	Weight loss Adverse events Improved quality of life
Neuropeptide Y antagonist (velneperit) for treatment of obesity	Patients with a body mass index (BMI) of 30 or more	Only one weight loss drug is currently on the market in the U.S. and this drug results in about 5% weight loss in only approximately 50% of patients. Velneperit is an oral neuropeptide Y (NPY) Y5 receptor antagonist, which appears to be the main mediator of the orexigenic effect of NPY; the NPY system is a crucial component of the central hypothalamic mechanisms implicated in the control of food intake and energy metabolism; in preclinical studies, it has reduced hyperphagia and visceral adipose tissue. Velneperit is administered orally, 1,600 mg (4 x 400 mg) per day, once daily. Shionogi & Co., Ltd., Osaka, Japan Phase IIb trial completed Jan 2009; trial investigating use with orlistat halted after endpoints not reached; company intends to resume investigation in U.S. as single therapy	Diet and exercise Weight-loss drugs on the market and under development	Total weight loss Excess weight loss Decline in obesity-associated comorbidities (e.g., prediabetes, high blood pressure)

Neuropeptide Y antagonist (velneperit) for treatment of obesity	Patients with a Body Mass Index (BMI) greater than or equal to 30	Currently, one weight loss drug is available for treatment of obesity in the U.S. and FDA approval of other drugs in development has been rejected due to concerns over long-term safety. The available drug results in about 5% weight loss in only approximately 50% of patients. Velneperit is an oral neuropeptide Y (NPY) Y5 receptor antagonist, which appears to be the main mediator of the orexigenic effect of NPY. The NPY system is a crucial component of the central hypothalamic mechanisms implicated in the control of food intake and energy metabolism. In preclinical studies, has reduced hyperphagia and visceral adipose tissue. Velneperit is administered orally, 1600 mg (4x400 mg) per day, once daily. Shionogi USA, Inc., Florham Park, NJ Phase IIb study completed Jan 2009; study investigating use with orlistat halted after endpoints not reached; intend to resume investigation in U.S. as single therapy (current phase II study in Japan)	Orlistat Exercise Dietary modifications Antiobesity drugs in development	Total weight loss Excess weight loss Reduced risk of diabetes Reduced risk of cardiovascular disease Improved quality of life
PRX00933 (5-HT2C serotonin receptor agonist) for treatment of obesity	Patients in whom obesity has been diagnosed	Only one long-term weight management drug is currently on the market, and it is not effective for many patients. PRX00933 is one in a new class of antiobesity drugs in development; it is an agonist of the 5-HT2C serotonin receptor, which is involved in appetite control; preclinical studies have demonstrated that stimulation of the 5-HT2C receptor results in appetite suppression. Another 5-HT2C receptor agonist (lorcaserin) has completed phase III trials and its NDA was not approved by FDA in late 2010; FDA requested additional data and the company plans to resubmit in late 2011. Proximagen Group, plc, London, UK Phase II trial completed	Orlistat Lorcaserin (in late phase development) Contrave (combination naltrexone/bupropion in late phase development)	Percent excess weight loss Reduced rate of obesity-associated comorbidities (e.g., prediabetes, high blood pressure) Improved quality of life
Restorative obesity surgery (endoluminal ROSE) for postgastric-bypass weight regain	Patients who have undergone gastric bypass, but regained weight and stretched the stomach pouch or stoma	Restorative obesity surgery (endoluminal ROSE) is intended to restore the stomach or stoma to the original post-surgical size; procedure is minimally invasive and incisionless because it is performed through the mouth. Van Den Bossche and Elemental Healthcare, Ltd., UK Pilot study ongoing	Bariatric revision surgeries	Reduction in stoma Weight loss Quicker recovery than open revision surgery No scarring

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Serotonin-noradrenaline-dopamine reuptake inhibitor (tesofensine) for treatment of obesity	Patients in whom obesity has been diagnosed	Tesofensine is a serotonin-noradrenaline-dopamine reuptake inhibitor; intended to result in twice the amount of weight loss as achievable with currently approved drugs. NeuroSearch a/s, Ballerup, Denmark Phase II trial completed (in Denmark)	Other anti-obesity drugs	Total body weight loss Adverse advents
Stent-like device (Full Sense) for treatment of obesity	Obese patients who want a nonsurgical, nondrug approach for weight loss	Full Sense™ device is a stent-like weight-loss device made of silicone and nitinol and implanted endoscopically through the mouth with patient under general anesthesia; procedure is reversible; device applies pressure to top of stomach and bottom of esophagus, theoretically making brain think stomach is full; intended to provide a safer option than bariatric surgery for weight loss; not intended to achieve as great a weight loss as bariatric surgery. Sentinel Group, LLC, Grand Rapids, MI Sentinel Group seeking a medical device company to take on development and trials and shepherd device through FDA marketing approval	Traditional open gastric bypass surgery Endoluminal sleeve	Weight loss Reduced adverse effects because of noninvasive procedure
Vagus nerve blocking (Maestro system) for treatment of obesity	Obese patients with body mass index of 40 to 45 or 35 or more with comorbidities	High frequency, low-energy electrical impulses are emitted to block the vagus nerve in an effort to inhibit gastric motility and increase feelings of fullness; electrical impulses are delivered by an implanted neuroregulator which is powered either by an external controller (Maestro™ RF System) or an integrated rechargeable battery (Maestro RC System); implanted laparoscopically. EnteroMedics, Inc., St. Paul, MN Pivotal ReCharge trial ongoing; phase III EMPOWER trial ongoing, expected completion in 2013	Minimally invasive bariatric procedures Anti-obesity drugs Similar marketed devices (in European Union)	Amount of weight loss Duration of weight loss Resolution of comorbidity (cardiovascular, diabetes)

Table 11. AHRQ Priority Condition: 11 Peptic Ulcer Disease and Dyspepsia: 15 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
A3309 oral agent to treat chronic idiopathic constipation	Patients with chronic idiopathic constipation (CIC)	A3309 is an oral drug that is intended to inhibit ileal bile acid transporter (IBAT or ASBT) to increase fluid secretion and colonic motility without disrupting the lower intestinal track. Albireo, Gothenburg, Sweden Phase II trial completed	Laxatives Enemas	Relief of constipation Fewer side effects
Acetylcholinester-ase inhibitor (acotiamide) for treatment of functional dyspepsia	Patients in whom functional dyspepsia (FD) has been diagnosed	FD is a highly prevalent condition, but currently, no efficacious treatments are available. Acotiamide represents a novel drug class for this indication; it is a muscarinic receptor antagonist and acetylcholinesterase inhibitor under development for the treatment of FD; intended to inhibit peripheral acetylcholinesterase (an important neurotransmitter for gastrointestinal [GI] motility) activities; intended to increase acetylcholine release in the enteric nervous system, thereby enhancing gastric contractility and accelerating gastric emptying (etiology of FD is still unclear, but delayed gastric emptying is closely associated with FD); also known as Z-338 or YM443. Administered orally, 100 mg, three times daily. Zeria Pharmaceutical Co., Ltd., Tokyo, Japan, in collaboration with Astellas Pharma, Inc., Tokyo, Japan Phase III trial completed in Japan; phase II trial completed in U.S.; submitted application for marketing authorization in Japan Sept 2010	Antacids Gas remedies H2 receptor blockers Proton pump inhibitors Prokinetic agents Antispasmodic agents Low-dose antidepressants Antibiotics Behavior therapy	Postprandial fullness Early satiety Decreased upper abdominal bloating Improved rate of gastric emptying Improved gastric accommodation Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Allogeneic stem cells (MultiStem) for treatment of ulcerative colitis	Patients in whom moderate to severe ulcerative colitis (UC) has been diagnosed	Current therapies for UC have not achieved desired results, especially for moderate to severe cases, and have undesirable side effects; no stem cell products for UC are currently available. MultiStem® is a proprietary allogeneic stem cell product made from nonembryonic stem cells obtained from bone marrow donors; the cells are intended to exert their effects through the production of therapeutic proteins and other molecules produced in response to inflammation and tissue damage; the company states that MultiStem is designed for "off-the-shelf" use because it can be used without the need for tissue matching or need for immunosuppressive drugs. Administered by injection. Athersys, Inc., Cleveland, OH Pfizer, Inc., New York, NY Phase II trial ongoing	5-Aminosalicylates Antimicrobial therapy Corticosteroids Immunosuppressive agents Monoclonal antibodies Sulfasalazine	Reduced relapse rates Healing of colon Reduced UC-related complications Improved quality of life
Fecal transplantation for treatment of ulcerative colitis	Patients in whom UC has been diagnosed	Patients with UC have an abnormally and chronically activated immune system in the absence of any known invader, leading to periodic bouts of abdominal pain, diarrhea, and rectal bleeding; UC is typically treated with antiinflammatory drugs with varied success, and there is no long-term cure or strategy to prevent periodic disease flares besides surgery. Fecal microbiota transplantation is a procedure designed to restore balance to the microbiota of the bowel after it has been disturbed by antibiotics or other environmental changes in the colon leading to the dominance of toxin producing strains that can cause disease; fecal matter from a healthy donor is collected and mixed with a solution and transplanted into the recipient via colonoscopy. Acceptance of procedure in UC patients studied by University of Chicago Medical Center, Chicago, IL Procedure may be adopted by gastroenterologists who are using the procedure for treatment of recurrent *Clostridium difficile* infection	Antiinflammatory drugs Immunosuppressive drugs Biological therapy Colectomy Over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs) and herbal medications	Reduction in the frequency of relapses Reduction in the use of medications reduction of symptoms Reduced or postponed need for surgery Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Teduglutide (Gattex) for treatment of short bowel syndrome	Patients in whom short bowel syndrome (SBS) has been diagnosed	SBS typically arises after extensive resection of the bowel because of Crohn's disease and is a highly disabling condition that can lead to serious, life-threatening complications as well as malnutrition, severe diarrhea, dehydration, fatigue, osteopenia, and weight loss due to the reduced intestinal absorption. Current treatments supplement and stabilize nutritional needs; however, parenteral support does not improve absorption and is associated with infections, blood clots, liver damage, poor quality of life, and high costs. Teduglutide (Gattex™) is a recombinant analog of human glucagon-like peptide 2 that is purported to increase nutrient absorption and intestinal cell growth in patients with SBS. NPS Pharmaceuticals, Bedminster, NJ Phase III trials completed; new drug application submitted to FDA Aug 2011	Intravenous fluids Parenteral nutrition	Improved hydration Improved nutritional status Weight gain Reduced diarrhea Improved quality of life
GSK1605786 (Traficet-EN) for treatment of Crohn's disease	Patients who have been given a diagnosis of moderate to severe Crohn's disease	GSK1605786 (Traficet-EN™) is an oral CCR9 antagonist. CCR9 is a chemokine receptor that plays a central role in the inappropriate inflammatory response thought to underlie Crohn's disease. By blocking CCR9, GSK'786 selectively impairs the movement of activated T cells that are involved in causing inflammation of the digestive tract. GlaxoSmithKline, Middlesex, UK Phase III trials ongoing	Immunomodulators (azathioprine, etc.) Monoclonal antibodies (natalizumab, infliximab, etc.) Corticosteroids (prednisone, etc.) Antibiotics (for acute flares) Aminosalicylates (mesalazine) Low-dose naltrexone Helminthic therapy	Delayed or avoided surgery Improved quality of life Reduced flare-ups Reduced side effects Remission Symptom improvement

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Helminthic therapy (pig whipworm) for treatment-resistant ulcerative colitis	Patients in whom treatment-resistant UC has been diagnosed	Patients ingest 2,500 pig whipworm eggs every 2 weeks for 3 months; rationale is that inflammatory bowel diseases are uncommon in developing countries where helminths are common, and people with helminth infection have an altered immunological response to antigens; parasites obtained from U.S. Department of Agriculture; in animal models, helminths prevent or improve colitis by the induction of regulatory T cells and modulatory cytokines. University of California, San Francisco, San Francisco, CA One trial ongoing at NYU School of Medicine; two trials completed; one for ulcerative colitis and one for Crohn's disease	Anti-inflammatory drugs Immunosuppressive drugs Biologic therapy targeting specific components of the immune response Colectomy Over-the-counter drugs and herbal medications	Increased safety Reduced flare symptoms Maintained remission Reduced or postponed need for surgery Improved quality of life
IntelliCap (formerly iPill) to deliver localized drug therapy in digestive tract	Patients with digestive tract diseases (e.g., colon cancer) or irritable bowel disease (Crohn's disease, UC)	The iPill, recently renamed IntelliCap, is the size of an average pill; capsule includes a microprocessor, battery, pH sensor, temperature sensor, radiofrequency wireless transceiver, fluid pump, and drug reservoir; communicates navigational feedback by measuring the local acidity (pH) of its environment via its wireless transceiver to a control unit outside the body; the internal pump, under control of the microprocessor, releases drugs to the programmed target; drugs can be given with a bolus, progressive release, or multi-location dosing; it is also designed to pass through the digestive tract naturally. Royal Philips Electronics, Eindhoven, the Netherlands Prototype developed in 2008, redesigned and renamed in 2009; platform would be used by other companies to develop specific medications delivered by IntelliCap	No direct comparators	Reduced medication side effects Improved efficacy due to local delivery of drugs

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Linaclotide for treatment of irritable bowel syndrome with constipation	Patients in whom irritable bowel syndrome (IBS) with constipation has been diagnosed	Linaclotide is a peptide agonist of guanylate cyclase 2C; taken orally. Ironwood Pharmaceuticals, Cambridge, MA Phase III trials completed; company filed new drug application with FDA Aug 2011 and plans to file a marketing authorization application with the European Medicines Agency second half 2011	Serotonin agonists Laxatives Antispasmodic drugs Tricyclic antidepressants	Reduced abdominal pain and constipation symptoms Long-term relief
Magnetically guided capsule endoscopy (MGCE) for diagnosis of gastrointestinal disorders	Patients appropriate for GI endoscopic examinations	Current GI endoscopic procedures are invasive, require sedation, and have low rates of patient acceptance and satisfaction; existing capsule endoscopy technology does not enable clinicians to guide the capsule as it travels through the GI tract to ensure images of desired areas are captured. MGCE is intended to allow the clinician more control of where the capsule travels and captures images; the patient swallows a capsule, which wirelessly transmits images to processing system, as the clinician navigates the capsule via a joystick and a magnetic field; the procedure is noninvasive and requires no sedation. Siemens Healthcare, Munich, Germany Olympus Medical Systems, Center Valley, PA Feasibility trial completed Oct 2010	Endoscope procedure Pill Cam	Increased sensitivity Increased specificity Positive and negative predictive values Improved diagnostic accuracy Impact on clinical decision making for managing symptoms
MuDelta (JNJ-27018966) for treatment of diarrhea-predominant irritable bowel syndrome	Patients who have been given a diagnosis of diarrhea-predominant irritable bowel syndrome (IBS-d)	MuDelta is a mu-opioid receptor agonist and delta-opioid receptor antagonist that may provide relief for both pain and diarrheal symptoms of IBS-d without the constipating effects typically seen with mu receptor agonists. Pharmacology data suggest that MuDelta acts locally in the digestive tract, thus having a low potential for systemic side effects. Furiex Pharmaceuticals, Morrisville, NC Phase II trial completed; received fast track designation from FDA Jan 2011	Antispasmodic drugs Opioids Serotonin agonists Tricyclic antidepressants	Reduced abdominal pain and bloating symptoms Long-term relief

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PerOral endoscopic myotomy for treatment of esophageal achalasia	Patients in whom esophageal achalasia has been diagnosed	Current surgical treatment for esophageal achalasia generally requires at least five abdominal incisions to access the blocked esophageal pathway. PerOral endoscopic myotomy is a procedure proposed for treatment of esophageal achalasia by inserting an endoscope through the mouth and esophagus, allowing surgeons to directly cut abnormal muscle fibers of the lower esophageal sphincter at the base of the esophagus. It is intended to allow food to enter the stomach, and the procedure is purported to be less invasive, thereby potentially reducing complications, recovery time, and pain. Northwestern Memorial Hospital, Chicago, IL Case reports published	Heller myotomy	Improved Esophageal Function Tests (upper endoscopy, barium swallow, esophageal manometry, pH test) scores Improved quality of life
Rifaximin (Xifaxan) for treatment of nonconstipating irritable bowel syndrome	Patients in whom nonconstipating IBS has been diagnosed	Rifaximin (Xifaxan®) is a nonabsorbable oral antibiotic currently approved for treatment of traveler's diarrhea. Salix Pharmaceuticals, Inc., Morrisville, NC Company received complete response letter from FDA Mar 2011, received advice from FDA advisory committee	Antispasmodic drugs Opioids Serotonin agonists Tricyclic antidepressants	Reduced abdominal pain and bloating symptoms Long term relief
Tumor necrosis factor-alpha kinoid for treatment of Crohn’s disease	Patients in whom moderate to severe Crohn’s disease has been diagnosed (Crohn’s Disease Activity Index of between 220 and 400)	Tumor necrosis factor alpha-kinoid is a novel immunotherapy platform technology that uses inactivated cytokines, conjugated to a carrier protein and delivered with an adjuvant, or immune stimulant, to elicit a natural polyclonal antibody response. Delivered by three-part injections. Neovacs S.A., Paris, France Phase II trial ongoing	Immunomodulators (azathioprine, etc.) Monoclonal antibodies (natalizumab, infliximab, etc.) Corticosteroids (prednisone, etc.) Antibiotics (for acute flares) Aminosalicylates (mesalazine) Low-dose naltrexone Helminthic therapy	Delayed or avoided surgery Improved quality of life Reduced flareups Reduced side effects Remission Symptom improvement

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vedolizumab for treatment of moderate to severe ulcerative colitis	Patients in whom moderate to severe UC has been diagnosed	Vedolizumab is an infused monoclonal antibody; current treatments for ulcerative colitis have limited effectiveness; the only cure is surgery. This may provide an alternative treatment. Millennium Pharmaceuticals, a unit of Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trial ongoing	Anti-inflammatory drugs Immunosuppression drugs Biological therapy targeting specific components of the immune response Colectomy Over-the-counter drugs and herbal medications	Reduced flare symptoms Maintained remission Reduced or postponed need for surgery Improved quality of life

Table 12. AHRQ Priority Condition: 12 Pregnancy, including Preterm Birth: 14 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bentamapimod (PGL5) to treat endometriosis	Women in whom endometriosis has been diagnosed	Bentamapimod (PGL5) is the first oral drug developed to prevent recurrence of endometriosis; preclinical data have demonstrated PGL5 has antiinflammatory and antifibrotic properties. Preglem SA, Geneva, Switzerland Phase I, II trials to start in 2011	Other pharmacologic treatments for endometriosis	Improved treatment of endometriosis, potential avoidance of surgical treatment.
Bentamapimod to prevent abdominal surgery adhesions from gynecologic pelvic surgery	Women undergoing gynecologic surgery in the pelvic or abdominal area	Oral drug to prevent postsurgical abdominal adhesions in patients undergoing tubal ligation, surgery for endometriosis. PregLem, Geneva, Switzerland Phase I, II trials planned for 2011	Physical adhesion barriers Sprayed adhesion barriers	Fewer postsurgical adhesions compared with conventional treatments Less pain from adhesions
Blood test for predicting spontaneous preterm birth	All pregnant women	Approximately 1 in 10 pregnant women have a spontaneous preterm birth in the U.S. each year; however, no diagnostic test is currently available to identify women at risk for preterm birth early in pregnancy to plan preterm birth prevention strategies. Sera Prognostics has developed a panel of proteomic markers that purportedly indicate the likelihood of spontaneous preterm birth. The proteomic assay is performed on a blood sample taken at 28 weeks of pregnancy. Sera Prognostics, Salt Lake City, UT Clinical trial ongoing; company states it is developing a commercial assay	Home uterine activity monitoring (HUAM) Salivary estriol testing Fetal fibronectin Detection of bacterial vaginosis Assessment of cervical length	Earlier intervention for women at risk of preterm birth Reduced incidence of preterm birth Reduced neonatal complications Reduced use of neonatal intensive care services

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cell phone bi-directional communication educational program for pregnant women and new mothers	Pregnant women, new mothers, and perinatal case managers and providers	A public-private partnership to support free mobile (cell phone texting) educational service to deliver timely health education and information about prenatal care during pregnancy and neonatal/infant care through baby's first year. Text-4-baby. National Healthy Babies, Healthy Mothers Coalition, Alexandria, VA	No intervention Traditional case management (face -to-face) Telephone contact Health education services Home visits	Increased awareness of appropriate prenatal care and infant care Compliance with recommended prenatal care and infant care Reduction in missed appointments Reduced preterm births Reduced infant morbidity and mortality (e.g., low birth weight due to smoking)
Copolymer styrene maleic anhydride/dimethyl sulfoxide (Vasalgel) for male contraception	Male patients pursuing contraception	Vasalgel ™ is a male contraceptive intended to inhibit sperm under guidance (RISUG). It is a copolymer styrene maleic anhydride/dimethyl sulfoxide that becomes hydrated in seminal fluid and degrades sperm cell membrane as sperm attempts to pass through vas deferens. It is purported to provide a safer, less costly alternative to contraception and is intended to be reversible. One dose injected into vas deferens per 10 years. Indian Institute of Technology, Powai, Mumbai, India Phase III clinical trials ongoing (in India); has secured a U.S. patent with intent to bring to U.S. market.	Condoms Vasectomy Undecanoate (under phase development in China)	Long-acting male contraception

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Donor human milk program for very low birthweight infants	Very low birthweight infants (less than 1,501 g weight at birth)	Women who give birth to very low weight infants who must remain in the intensive care unit often are unable to supply sufficient breast milk. Donated breast milk for very low birthweight infants whose mothers cannot supply sufficient breast milk is purported to lead to better health and neurodevelopmental outcomes than observed in preterm infants fed formula. The milk is collected from lactating volunteers and screened for safety before administration to infants. University of Iowa, Iowa City, IA Phase III trial ongoing	Formula	Reduced health care costs Normal Bayley Scales of Infant Development, III (at 18 to 22 months of age)
Electronic early physiologic response test (PhysiScore) to predict risk of illness in preterm infants	Preterm infants	PhysiScore is an electronic version of the Apgar score; collects physiologic data (heart rate, respiratory rate and oxygen saturation) during first 3 hours of life in a neonatal intensive care unit; software would enable PhysiScore to be displayed on existing bedside monitors. Stanford University School of Medicine, Palo Alto, CA Pilot phase trial ongoing	Apgar score	Improved sensitivity Improved predictive value for risk of life-threatening events Avoided invasive testing Improved health outcomes Decreased long-term disabilities
Endoglin urine screening test for screening for preeclampsia in pregnancy	Pregnant women at risk of pre-eclampsia	Urine test intended to detect endoglin, a cell surface glycoprotein that has been shown to be elevated in pregnant women who develop preeclampsia. Miraculins, Inc., Winnipeg, Manitoba, Canada Inverness Medical Professional Diagnostics, Princeton, NJ Assay development and optimization ongoing	Screening pregnant women for elevated blood pressure and high levels of protein in the urine	More specific and earlier detection of preeclampsia Earlier management of secondary preeclampsia symptoms

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Fetal programming for prevention of metabolic disorders	Pregnant women	Many metabolic abnormalities may stem from the fetal environment and how the fetus' metabolism becomes established during pregnancy; measures taken to ensure healthy fetal development include adherence to prenatal vitamin intake and routine prenatal care. Fetal programming (FP) is a comprehensive concept that aims to enhance a child's metabolism into adulthood by using drug therapy, nutritional supplements, and enhanced nutrition during pregnancy. FP aims to decrease risk of many adult diseases, including coronary artery disease, breast cancer, and diabetes, by improving the uterine environment through programming of hormone-production levels with intention of maintaining healthy organ function throughout life. An example of FP is treating obese pregnant women with metformin even if they do not have a diagnosis of diabetes because blood glucose levels tend to be higher during pregnancy and glucose may pass through the placenta to the fetus. University of Edinburgh, Scotland, UK Clinical trial ongoing	Nutritional programs alone for pregnant women Prenatal vitamins alone Routine prenatal care (examination/monitoring of fetal development)	Improved health in newborns Decreased risk for development of metabolic disorders
Gonadotropin-releasing hormone (GnRH) antagonist (Elagolix) for treatment of endometriosis	Patients in whom endometriosis has been diagnosed	Elagolix is the first oral nonpeptide gonadotropin-releasing hormone (GnRH) antagonist that, unlike currently used injectable GnRH agonists (which take up to several weeks to work), has a rapid onset in suppressing hormones (stops ovulation and endometriosis symptoms) without a hormonal flare or injection site reactions; titration might made it possible to maintain appropriate levels of estrogen, thus preventing menopausal-like hormonal levels and the need for management of bone loss while treating endometriosis. Neurocrine Biosciences, Inc., San Diego, CA Phase II trial completed	Leuprolide (Lupron) and goserelin (Zoladex) - peptides, depot injection Nafarelin acetate (Synarel) - nasal spray 2 times daily Hormonal contraceptives Danazol Pain medications Medroxyprogesterone (Depo-Provera) Removal endometrial growths, scar tissue and adhesions Hysterectomy	Improved composite pelvic signs and symptoms score (measures dysmenorrhea, non-menstrual pelvic pain, dyspareunia, pelvic tenderness and induration) Maintained bone mineral density Improved patient global impression of change Less pain (Visual Analog Scale)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
In utero surgery to repair myelomeningocele (spina bifida)	Pregnant women with a fetus at 19 to 25 weeks gestation in whom myelomeningocele lesion has been diagnosed that starts no higher than T1 and no lower than S1 with lowest parts of the cerebellum (hindbrain) herniation present	Surgery in a newborn with spina bifida to repair the defect does not restore function to nerve damage that occurred during gestation; thus, neurologic outcomes are not optimal. Researchers hypothesized that earlier repair of the defect in utero might lead to better neurologic outcomes in affected neonates; the surgery involves intrauterine repair of fetal myelomeningocele at 19 to 25 weeks of gestation (before 26 weeks) with delivery by C-section scheduled for 37 weeks gestation. Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), part of the National Institutes of Health, Bethesda, MD Late-phase trial completed 2010; earlier than 2013 estimated completion date because of improved success of in utero surgery	Postnatal closure of the spina bifida defect (does not restore function to the already damaged nerves)	Increased neonatal survival Improved Bayley Scales of Infant Development (Mental Development Index) Improved functional-anatomical level of lesion at 30 months of age Reduced need for ventricular shunt by 1 year of life
N-acetylcysteine for treatment of intra-amniotic infection and inflammation during pregnancy	Pregnant women in whom intra-amniotic infection and/or inflammation has been diagnosed	Intra-amniotic inflammation in utero early in gestation is thought to possibly trigger a cascade of events that lead to preterm birth (i.e., premature rupture of membranes, cervical ripening, uterine contractions). N-acetylcysteine, an antioxidant, is a derivative of amino acid, L-cysteine and mucolytic agent; proposed for treatment of pregnant women with intra-amniotic infection to prevent adverse neonatal outcomes by potentially reducing intracellular concentration of free radicals and cell damage. Administered intravenously. Yale University, New Haven, CT Phase II trial ongoing	Standard care without N-acetylcysteine Standard care plus N-acetylcysteine	Reduced early onset neonatal sepsis Prevention of neonatal death

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Nurse home visits for reducing second pregnancies in high-risk first-time mothers	Low-income, high-risk, first-time mothers	Nurse home-visitation programs in which information on women's health, preconception health, and family planning are provided to low-income women who have already delivered one child and are at high risk of a second unplanned pregnancy. Children's Hospital of Philadelphia Pennsylvania Department of Public Welfare Pilot trial completed	Lay women home visitation programs (e.g., Resource Mothers, Promotoras) Family planning clinics Healthy Start (Health Resources & Services Administration)	Improved health outcomes for mother and child Improved planning of subsequent pregnancies
Screening test (XSense) for fragile X syndrome	Women who are pregnant or wish to become pregnant and have a personal or family history of fragile X syndrome (FXS) and or intellectual disabilities	XSense® - laboratory test for screening for FXS Quest Diagnostics, Madison, NJ Phase IV trial ongoing	FMR-1 DNA genetic test	Increased sensitivity and specificity Improved positive and negative predictive value Informed decision making about reproduction choices
Trisomy 21 DNA test (MaterniT21 test) for first trimester detection of Down syndrome	Pregnant mothers at risk for trisomy 21 mutation	Trisomy 21 test (MaterniT21™) examines fetal DNA from the expectant mother's blood in first trimester; massively parallel sequencing is performed to detect excess chromosome 21 DNA of fetal origin, which is indicative of trisomy 21 (Down syndrome). Could possibly replace invasive tests that pose a risk of miscarriage and allow earlier definitive screening to enable pregnant women to make decision earlier about continuing the pregnancy. Sequenom, Inc., San Diego, CA Late phase clinical trials completed; as of Oct 2011, lab-developed test has been made available to physicians in the United States; Sequenom plans to submit PMA to FDA in late 2012 with hope for approval in 2013	Amniocentesis Chorionic villus sampling Blood serum markers for trisomy 21 Ultrasound detection of fetal abnormalities	Increased sensitivity and specificity Improved predictive values Avoidance of invasive procedures Earlier diagnosis for earlier decision making

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ulipristal acetate (CDB-2914) for treatment of uterine fibroids and excessive uterine bleeding	Premenopausal women in whom symptomatic uterine fibroids have been diagnosed	Ulipristal acetate (CDB-2914; EllaOne) is a selective P receptor modulator with antiprogestin effects. Given orally, 10 or 20 mg, once daily. Laboratoire HRA Pharma, SA, Paris, France Phase IIb and phase III trials ongoing	Cryomyolysis noninvasive surgery ExAblate Gonadotropin-releasing hormone agonists Hysterectomy Uterine artery embolization	Avoided or delayed hysterectomy Reduced total fibroid volume Prevention of anemia due to heavy menstrual bleeding Reduced symptoms (e.g., pain) Improved quality of life
Vaginal progesterone gel to prevent preterm birth in women with a short cervix	Pregnant women in whom a sonographic short cervix (10 to 20 mm) has been diagnosed	A sonographic short cervix has been demonstrated to be a good predictor of preterm birth (a major cause of perinatal morbidity and mortality). Current interventions for short cervix include hospital care, bed rest, surgery, and removable devices. According to investigators, progesterone appears to relax the myometrium by repressing the expression of genes that promote labor; micronized vaginal progesterone gel is being investigated to reduce the risk of preterm birth and associated neonatal complications in women with a sonographic short cervix; women self-administer the drug once daily in the morning using a vaginal progesterone capsules kit to prevent dispensing errors; Prochieve 8%, also known as Crinone 8%, is an off-white gel, in a single use, one-piece, disposable polyethylene vaginal applicator. Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICDH), part of the National Institutes of Health, Bethesda, MD, and Columbia Laboratories, Inc., Livingston, NJ Phase III trial completed	Hospital admission for bed rest At-home bed rest Tocolytic therapy Steroid administration Cervical cerclage: invasive (tracheloplasty) or placement of stitches in the cervix to hold it closed Vaginal pessary: noninvasive (removable device placed into the vagina designed to support areas of pelvic organ prolapse)	Sustained pregnancy to full-term Reduced preterm (delivery at <3 weeks) birth rate Fewer admissions to neonatal intensive care unit Reduced neonatal morbidity (e.g., respiratory distress syndrome) Reduced perinatal mortality (fetal death or neonatal death) Reduced infant mortality rates Shorter length of neonatal stay

Table 13. AHRQ Priority Condition: 13 Pulmonary Disease, Asthma: 13 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
APD811 (oral prostacyclin) for treatment of pulmonary arterial hypertension	Patients in whom pulmonary arterial hypertension (PAH) has been diagnosed	PAH has no cure and can result in heart failure (HF) and death; prostacyclin is an approved therapy for treating PAH, but no orally dosed prostacyclin therapy is available in the U.S.; available prostacyclin therapies are intravenous, subcutaneous injection, or inhaled. APD811 would be the first oral, once-daily selective agonist of the prostacyclin receptor that regulates vascular smooth muscle tone; believed to have the potential to reduce mortality in patients with advanced PAH. Arena Pharmaceuticals, Inc., San Diego, CA Phase I trial completed; phase Ib trial planned	Currently available: Phosphodiesterase-5 inhibitors (PDE-5), prostanoids, endothelin receptor antagonists, and calcium channel blockers, atrial septostomy, lung transplant, heart-lung transplant Investigational: Selexipag (ACT-293987) non-prostanoid prostacyclin receptor agonist Macitentan (endothelin receptor antagonist)	Reduced mortality Improved quality of life
ASM8 for treatment-resistant asthma	Patients in whom severe asthma that has not responded to current standard of care has been diagnosed	ASM8 is a proprietary oligonucleotide technology intended to reduce the recruitment and persistence of chronic inflammatory cells and their associated release of cytokines. It inhibits multiple targets associated with inflammation in asthma. Pharmaxis, Sydney, Australia Phase II trials ongoing	Inhaled corticosteroids Leukotriene modifiers Long-acting beta agonists Theophylline Short-acting beta agonist Ipratropium (Atrovent) Treatment for allergy-induced asthma: Allergy shots Omalizumab (Xolair) Antihistamines and decongestants	Reduced symptoms Fewer days lost from work or school Prevent permanent narrowing of the bronchial tubes Reduced number of emergency room visits and hospitalizations Prevent/delay side effects from long-term use of some asthma medications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ataluren for treatment of nonsense mutation cystic fibrosis	Patients in whom cystic fibrosis (CF) due to a nonsense mutation (nmCF) has been diagnosed	No treatments are available that address the cause of CF rather than only the symptoms. Ataluren is a protein-restoration therapy designed to enable the formation of full-length, functional cystic fibrosis transmembrane regulator (CFTR) protein in patients with nmCF; nonsense mutations are the cause of CF in an estimated 10% of U.S. and European Union cases and more than 50% of CF cases in Israel; Ataluren is intended to improve lung function, which could lead to improved survival. PTC Therapeutics, Inc., South Plainfield, NJ Phase III trials ongoing	Bronchodilators (albuterol or salmeterol) DNase (such as Pulmozyme®) Mucolytics (acetylcysteine) Hypertonic saline	Improved lung function as measured by forced expiratory volume in 1 second (FEV1) Reduced daily therapy needed in adults
BIBF-1120 (intedanib) to preserve lung function in idiopathic pulmonary fibrosis	Patients in whom idiopathic pulmonary fibrosis (IPF) has been diagnosed	BIBF-1120 (intedanib) is an inhibitor of tumor angiogenesis; under study for treatment of IPF and slowing of disease progression and symptoms. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing	Bosentan Corticosteroids Pirfenidone	Improved lung function measured by forced vital capacity Improved quality of life Improved ability to perform activities of daily living Slowed disease progression
BIO-11006 for treatment of chronic obstructive pulmonary disease	Patients in whom chronic obstructive pulmonary disease (COPD) has been diagnosed	COPD is the third leading cause of death in the U.S. and is characterized by airway obstruction, inflammation, and excess mucus production; currently no COPD medications directly inhibit excess mucus production. BIO-11006 is an inhaled soluble small peptide consisting of 10 amino acids purported to inhibit the myristoylated alanine-rich C kinase substrate, which has been shown to be involved in the secretion of mucus and inflammatory mediators. Administered 75 mg, twice daily. BioMarck Pharmaceuticals, Ltd., Durham, NC Phase II trial completed	Corticosteroids Ipratropium bromide	Decreased cough frequency Decreased inflammation Decreased sputum production Improved pulmonary function

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bronchial thermoplasty system (Alair) for treatment of poorly controlled asthma	Adults in whom asthma has been diagnosed that is not well controlled with inhaled corticosteroids and long-acting beta agonists	Bronchial thermoplasty system (Alair®) uses thermoplasty to thin airway smooth muscle tissue mass; intended to decrease narrowing of airways without causing tissue damage or scarring. Asthmatx, Inc., Sunnyvale, CA FDA approved mid-2010; diffusion has accelerated; number of sites offering doubled between Jan and Jul 2011; as of Jul 2011, 46 clinical sites in 22 U.S states offer the procedure	Albuterol Ipratropium bromide Epinephrine Corticosteroids Long acting beta-adrenoceptor agonists Leukotriene antagonists Mast cell stabilizers	Reduced emergency department visits Reduced missed work and school days Reduced need for rescue medication Improved quality of life
Corticosteroid/beta 2 agonist (Relovair) for treatment of COPD	Patients in whom COPD has been diagnosed	Relovair™ (100/25 mg) is an inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) combination treatment made up of fluticasone furoate and vilanterol that may relieve chronic inflammation and resultant fibrosis, leading to obstruction of small airways caused in COPD; might replace current treatment that uses corticosteroids, short-acting or long-acting beta agonists, or a combination of both that may be administered twice daily or more frequently. Relovair is administered once daily, which could address the unmet need of better compliance, greater convenience for patients. GlaxoSmithKline, Middlesex, UK Theravance Inc., San Francisco, CA Pivotal phase III trial ongoing	Symbicort Advair Perforomist Short-acting beta agonists Flovent	Improved compliance with therapy Reduced symptoms (if prolonged bronchodilation is achieved) May be first-line corticosteroid/LABA for COPD Reduced health disparities
Endobronchial valve system (Zephyr) for treatment of heterogeneous emphysema	Patients in whom heterogeneous emphysema has been diagnosed	Endobronchial valve system (Zephyr®) is intended to allow air to escape from a pulmonary lobe but not enter it to try to reduce lobar volume improve lung function. Pulmonx Inc. (formerly Emphasys), Redwood City, CA Phase III trials completed under investigational device exemption (IDE) status, FDA rejected premarket approval (PMA) application in 2009; CE marked in 2010; U.S. development unclear	Lung volume-reduction surgery Physical therapy	Improved lung function Improved activities of daily living Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ex vivo lung perfusion assessment with Steen solution to increase viable donor lungs	Patients awaiting lung transplant	Donor lungs that might otherwise not be usable were subjected to ex vivo lung perfusion (mechanical ventilation with controlled perfusion flows and pressures in the pulmonary vasculature) plus Steen Solution™ restorative solution for 4 hours in an effort to recondition donor lungs and make them suitable for transplantation. Vitrolife AB, Göteborg, Sweden Phase II trial initiated	Blood-based lung perfusion systems (do not enable lung repair/reconditioning)	Increased number of donor lungs Increased number of successful lung transplantations
GPS and Wi-Fi-enabled inhaler (Spiroscout) for treatment of asthma	Patients in whom asthma has been diagnosed	The few alternatives available for asthma patient data recording may introduce patient error, leading to less accurate and more subjective judgments about when inhaler doses are needed. The GPS and Wi-Fi-enabled inhaler (Spiroscout®) is a device that attaches to the top of a metered-dose inhaler, using GPS and Wi-Fi to accurately record time, geographic location, and frequency of inhaler use; this information is sent to a central server/database for analysis, and physicians and epidemiologists can use the information to make determinations about events and environments correlating to patients' inhaler use; if implemented, Spiroscout might provide an affordable and more accurate way for both physicians and patients to decrease triggers to asthma and consequent dependence on asthma inhalers. Spiroscout takes one reading per inhaler use. Asthmapolis, Madison, WI Trial completed (no phase); anticipated date to market, fall 2011	Self-recorded logs (hand-written, mobile, Web)	Reduced need for recording logs for patients with asthma Enhanced detection of triggers for asthma Reduced health disparities Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Heparin (VR-496) dry inhaled powder for treatment of cystic fibrosis	Patients in whom CF has been diagnosed	Current CF inhaled therapies target only one disease element, such as infection or viscid mucus; furthermore, not all patients respond well to currently available mucolytics. VR-496, a proprietary formulation of dry powder heparin sodium; intended to be the first agent to treat CF that can potentially provide antiinflammatory, mucolytic, antibronchoconstrictor and antiinfective activity; active component is heparin, which acts on multiple sites in the coagulation pathway. VR-496 is to be administered (inhaled) twice daily; in trials it was given for 4 weeks. Vectura Group, Wiltshire, UK Phase II trial completed; FDA granted orphan drug status	Hypertonic saline (to clear mucus) Mucolytics: Pulmozyme TOBI: tobramycin solution for inhalation antibiotic treatment Physical therapy for mucolysis Investigational: Ataluren, Denufosol, VX-770, VX-809	Reduced chest infections Reduced antiinflammatory activity Improved mucolysis
Human monoclonal antibody (FG-3019) for treatment of idiopathic pulmonary fibrosis	Patients in whom IPF has been diagnosed	FG-3019 is a human monoclonal antibody against connective tissue growth factor; could potentially reduce collagen deposition and slow/reverse progressive scarring of lung tissue that occurs in IPF; currently available anti-inflammatory agents and immune modulators have shown minimal effectiveness in modifying the natural course of IPF and are associated with many side effects. FibroGen, Inc., San Francisco, CA Phase II trials ongoing	Corticosteroid (prednisone) Immunosuppressant (azathioprine, cyclophosphamide) Oxygen therapy Pulmonary rehabilitation Lifestyle changes (smoking, diet, exercise) Lung transplantation	Improved lung function Improved survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Inhaled amikacin (Arikace) for treatment of nontuberculous *Mycobacteria* infection	Patients in whom pulmonary nontuberculous mycobacterial lung infection has been diagnosed	Most nontuberculous mycobacterial (NTM) infections are resistant to many common antibiotics; NTM infection requires treatment with lengthy multidrug regimens and there are limited effective treatments. Amikacin, an approved antibiotic against a variety of NTM, is a semisynthetic aminoglycoside derived from kanamycin; Arikace® is being developed as a sustained-release formulation of amikacin encapsulated inside small fat particles designed for administration via inhalation once daily using an optimized, investigational eFlow Nebulizer; Arikace is intended to deliver higher levels of drug to the lungs than previously possible through current formulations of amikacin while also minimizing systemic exposure to the drug. Insmed, Inc., Richmond, VA Phase III trials halted Aug 2011; FDA requesting animal safety data; FDA granted orphan drug status	Amikacin (injectable) Other antibiotics such as: Amoxicillin/clavulanate Capreomycin Clarithromycin Clofazimine Ethambutol Ethionamide Fluoroquinolones Imipenem/cilastatin Isoniazid Kanamycin Linezolid p-Aminosalicylic acid Protionamide Pyrazinamide Streptomycin Terizidone Thioacetazone	Resolved abnormalities as seen on computed tomographic scan Higher rate of culture conversion to negative Improved 6-minute walk distance and improved oxygen saturation Time to “rescue” antimycobacterial drugs
Inhaled mannitol (Bronchitol) for treatment of mucus in noncystic-fibrosis bronchiectasis and cystic fibrosis	Patients in whom CF or non-CF bronchiectasis has been diagnosed	No curative treatments exist for CF or non-CF bronchiectasis mucus accumulation; treatment is aimed at controlling infections, secretions, airway obstructions and complications; no product is available to effectively clear excess mucus secretions. Bronchitol is a new approach to treatment as a proprietary formulation of mannitol administered as a dry powder through a hand-held inhaler; it is being developed to reduce the amount of mucus build-up in the lungs; restoration of airway surface liquid by hydration of the lungs could help restore normal lung clearance and clear excess mucus. Pharmaxis, Ltd., Frenchs Forest, Australia Phase III trial completed	Antibiotics Chest mucus clearance therapy	Improved lung function Reduced pulmonary exacerbations Reduced antibiotic use Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
KL4 synthetic lung surfactant (Aerosurf and Surfaxin) for prevention of neonatal respiratory distress syndrome	Very-low- and low-birthweight premature infants at risk for respiratory distress syndrome	KL4 surfactant is a synthetic peptide-containing surfactant intended to closely mimic the essential attributes of human lung surfactant; two forms in development. One (Aerosurf®), a combination drug/device is administered in conjunction with noninvasive nasal continuous positive airway pressure (nCPAP); other (Surfaxin®) is delivered through other ventilation modalities; purported to be the first potential opportunity to deliver a clinically relevant dose of synthesized surfactant with key polypeptides missing in existing synthetic surfactant. Discovery Laboratories, Inc., Warrington, PA Phase III for Surfaxin completed; Sept 2, 2011, company submitted Complete Response to FDA's 2009 Complete Response Letter; company expects FDA to designate response as a resubmission of the new drug application, which would result in review and potential approval of Surfaxin in first quarter of 2012. Phase IIa trial for aerosolized Aerosurf formulation completed.	Animal-derived surfactants delivered by endotracheal intubation with or without mechanical ventilation	Improved survival Reduced pulmonary complications Reduced intubation and mechanical ventilation Prevention of risks associated with intubation and mechanical ventilation
Lebrikizumab for treatment of moderate to severe uncontrolled asthma	Patients in whom moderate to severe uncontrolled asthma has been diagnosed	Despite currently available therapies some patients with asthma remain unable to control their symptoms. Lebrikizumab is a humanized monoclonal antibody designed to block the activity of interleukin-13 (IL-13), a contributor to asthma which is produced by T-helper type 2 cells; lebrikizumab may be more effective in patients with elevated serum periostin levels (a surrogate marker for elevated IL-13). Administered subcutaneously. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trials being planned as of Sept 2011	Glucocorticoids Long-acting beta agonists	Improved change in quality of life and symptom scores Improved forced expiratory volume in 1 second (FEV_1) Improved peak flow Reduced rate of asthma exacerbations Reduced rescue medication use

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Lung volume reduction coil (RePneu) for treatment of emphysema	Patients in whom upper and/or lower lobe heterogeneous emphysema and/or multiple emphysematous lobes with focal tissue defects has been diagnosed	Treatment for advanced emphysema involves lung volume reduction (LVR) surgery and a less invasive approach to LVR is desirable. RePneu™ is a minimally invasive procedure intended to reduce lung volume by implanting devices that compress the volume of diseased hyperinflated lung tissue to make room the healthier lung tissue to function; RePneu is a wire-like device described as a lung volume nitinol preformed coil; intended to compress the volume of lung tissue where deployed and is delivered to the lung uncoiled (in a straight line) using a bronchoscope and fluoroscopic visualization (conscious sedation or general anesthesia); about 10 coils are delivered during a procedure; once deployed in the desired locations of the diseased alveolar tissue, the catheter is retracted and the coils regain their original curved shape, pulling and compressing diseased hyperinflated tissue to reduce the lung volume and enable healthy lung tissue to expand and contract to improve breathing. PneumRx, Inc., Mountain View, CA Pivotal phase III trial ongoing; CE marked in Oct 2010	Antibiotics Bronchodilators Corticosteroids Oxygen Pulmonary rehabilitation program Surgery: LVR surgery, bullectomy, lung transplantation	Improved lung function, physical endurance and activities of daily living Improved scores in St. George's Respiratory Questionnaire (measures impaired health and perceived well-being in airways disease)
Milrinone lactate for treatment of persistent pulmonary hypertension of the newborn	Newborns (up to 10 days) in whom persistent pulmonary hypertension of the newborn (PPHN) has been diagnosed	The current standard of care is treatment with inhaled nitric oxide (iNO) for PHHN; however, for many babies this treatment does not provide sufficient improvement in oxygenation and the condition is associated with high morbidity and mortality. In PPHN pulmonary vasculature fails to relax after birth resulting in severe hypoxemia (decreased partial pressure of oxygen in blood); milrinone lactate will be given as an IV infusion for 24 hours in addition to nitric oxide (NO) to try to improve oxygenation. Milrinone is indicated for the short-term intravenous treatment of patients with acute decompensated HF. Children's Hospital of Philadelphia, Philadelphia, PA, and Bedford Laboratories, Bedford, OH (maker of generic milrinone) are collaborating Pilot study of 18 newborns to be completed by late 2011; to be followed by a randomized controlled trial; milrinone is indicated for the short-term intravenous treatment of patients with acute decompensated HF	Assisted ventilation Extracorporeal membrane oxygenation High frequency oscillatory ventilation NO Oxygen	Improved oxygenation index Decreased signs of pulmonary hypertension Improved safety profile

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral sustained-release prostacyclin (treprostinil UT-15C) for treatment of pulmonary arterial hypertension	Patients in whom pulmonary arterial hypertension (PAH) has been diagnosed	PAH has no cure and can result in HF and death; no approved oral prostacyclin therapies are available in the U.S.; only intravenous, injected, or inhaled formulations are available. Sustained release oral treprostinil, if approved, could be the first oral prostacyclin for PAH, and is intended for use early in the PAH disease continuum; treprostinil diethanolamine vasodilates pulmonary and systemic arterial vascular beds, and inhibits platelet aggregation; intended as an add-on therapy to current oral therapies. United Therapeutics Corp., Silver Spring, MD Phase III trials ongoing; one phase III combination trial, FREEDOM-C, missed its primary endpoint due to aggressive dosing that patients did not tolerate well. Lower strength tablets were developed for a "start low and escalate slow" approach for two ongoing phase III trials–the monotherapy FREEDOM-M and combination FREEDOM-C2; the company announced positive preliminary results from the former Jun 2011; the latter trial completed enrollment Mar 2011	Phosphodiesterase-5 inhibitors (PDE-5), prostanoids, endothelin receptor antagonists, and calcium channel blockers, atrial septostomy, lung transplant, heart-lung transplant. antagonist)	Reduced mortality Improved quality of life
Oral vaccine (HI-164OV) for treatment of chronic obstructive pulmonary disease	Patients in whom COPD has been diagnosed	Immunotherapy (HI-164OV) using *Haemophilus influenza*; intended to treat moderate to severe exacerbations (those that would require corticosteroid therapy) of COPD. Taken orally. Hunter Immunology Ltd., Brighton, Victoria, Australia Phase IIb trial ongoing	Corticosteroid therapy	Reduced duration of episodes Fewer hospitalizations for exacerbations Reduced number and severity of exacerbations

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pirfenidone for treatment of idiopathic pulmonary fibrosis	Patients in whom IPF has been diagnosed	IPF is a progressive, debilitating disease characterized by inflammation and scarring (fibrosis) in the lungs, with a median survival time from diagnosis of 2 to 5 years; 5-year survival rate is approximately 20%; no approved treatments currently exist. Pirfenidone is a small molecule that inhibits the synthesis of transforming growth factor-beta, which is purported to be involved in fibrosis, and tumor necrosis factor alpha (TNF alpha), which is involved in mediating inflammation. Administered orally. InterMune, Inc., Brisbane, CA Phase III trial initiated Jun 2011; FDA granted fast track and orphan drug status	Corticosteroids Intedanib Pirfenidone	Improved ability to perform activities of daily living Improved lung function measured by forced vital capacity Slowed disease progression Improved quality of life
PL-3994 for treatment of acute exacerbations of asthma	Patients with asthma who experience acute exacerbations	Some patients are unresponsive to beta-2 adrenergic receptor agonists and improvement after an acute exacerbation of asthma in these patients usually takes several hours. PL-3994 is being developed as a self-administered subcutaneous injection for rapid treatment and resolution of acute exacerbations of asthma; a synthetic molecule and natriuretic peptide receptor A (NPR-A) agonist that activates NPR-A, a receptor involved in cardiovascular homeostasis; PL-3994 induces a pharmacologic response consistent with the effects of endogenous natriuretic peptides (smooth muscle relaxation, blood pressure decrease, sodium excretion); PL-3994 works through a different pathway from beta-2 adrenergic receptor agonists and other approved bronchodilators, which are used to treat acute exacerbations of asthma. Palatin Technologies, Inc., Cranbury, NJ Phase II trial ongoing	Short-acting beta-agonists, anticholinergics (severe exacerbations), and systemic corticosteroids Albuterol inhalation (Accuneb, ProAir HFA, Proventil, Proventil HFA, Ventolin HFA) Formoterol (Foradil Aerolizer, Perforomist inhalant solution) Levalbuterol (Xopenex, Xopenex-HFA) Salmeterol (Serevent)	Increased forced expiratory volume in one second (FEV_1) Improved forced vital capacity (FVC)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Portable inhaled nitric oxide device (Nitrosyl) for treatment of pulmonary diseases	Patients in whom pulmonary hypertension secondary to IPF and pulmonary arterial hypertension has been diagnosed	No medications are currently approved for treatment of pulmonary hypertension associated with IPF. Portable NO device (Nitrosyl) delivers NO therapy for pulmonary indications and is the first portable device to enable ambulatory delivery of NO. Intended to enhance pulmonary vasodilation. GeNO, LLC, Cocoa, FL Phase II trials ongoing	Lung transplantation Prescription therapies Pulmonary rehabilitation Supplemental oxygen	Reduced morbidity and mortality
Rituximab off-label for treatment of systemic sclerosis-associated pulmonary arterial hypertension	Patients in whom systemic sclerosis-associated pulmonary arterial hypertension (SSc-PAH) has been diagnosed	One-year survival for patients with SSc-PAH ranges from 50% to 81% and treatment is limited to vasodilator therapy. Rituximab, a genetically engineered anti-CD20 antibody for the treatment of B-cell lymphoma, is being investigated for immune mechanisms associated with B-cell dysregulation and pathogenic autoantibody response in SSc-PAH. It is being administered in two infusions, 1,000 mg each, 14 days apart. National Institute of Allergy and Infectious Diseases, Bethesda, MD, is trial sponsor Phase II trial ongoing	Vasodilator therapy Prostacyclin (e.g., epoprostenol) - vasodilator Sildenafil Combined therapy: epoprostenol and sildenafil	Improved pulmonary vascular resistance Improved exercise capacity Increased oxygen saturation Improved quality of life
Roflumilast (Daliresp) for treatment of chronic obstructive pulmonary disease	Patients in whom severe COPD associated with chronic bronchitis and a history of exacerbations have been diagnosed	Approximately 20% of patients with COPD have chronic bronchitis and pulmonary exacerbations; overall only about 10% of COPD patients respond to inhaled corticosteroids, so more effective treatments are needed. Roflumilast (Daliresp™) is the first and only orally formulated selective phosphodiesterase-4 (PDE4) inhibitor; as a PDE4, the drug is intended to inhibit COPD-related inflammation. Administered as a once-daily, 500 mcg tablet (in contrast to multiple inhalations per day), to reduce the risk of COPD exacerbations. Forest Laboratories, Inc., New York, NY FDA approved Jan 2011; now available	Inhaled bronchodilators Inhaled corticosteroids	Increased forced expiratory volume in 1 second (FEV_1) Reduced exacerbation rate

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Selective prostacyclin (PGI2) receptor agonist (selexipag) for treatment of pulmonary arterial hypertension	Patients in whom pulmonary arterial hypertension PAH has been diagnosed	PAH has no cure and can result in HF and death. Selexipag (ACT-293987) is a first-in-class, selective prostacyclin (PGI2) receptor agonist; prostacyclin counteracts the vasoconstrictor and prothrombotic activity of endothelin; selexipag is an orally available and long-acting nonprostanoid prostacyclin receptor (IP) receptor agonist that mimics the actions of endogenous prostacyclin and exerts vasodilating effects. Selexipag is an oral tablet taken twice daily. Actelion Pharmaceuticals, Ltd., Allschwil, Switzerland Phase III trial ongoing	Phosphodiesterase-5 inhibitors (PDE-5), prostanoids, endothelin receptor antagonists, and calcium channel blockers, atrial septostomy, lung transplant, heart-lung transplant Epoprostenol (Flolan) Treprostinil (Remodulin) Iloprost (Ventavis) Treprostinil inhaled (Tyvaso) Bosentan (Tracleer) Ambrisentan (Letairis) Sildenafil (Revatio) Tadalafil (Adcirca) Calcium channel blockers (not for all patients) Investigational: APD811 (selective agonist of the prostacyclin receptor) Macitentan (endothelin receptor antagonist)	Reduced pulmonary vascular resistance Improved 6-minute walk distance Reduced PAH-related morbidity Improved survival
Surface-enhanced Raman spectroscopy for rapid diagnosis of *Mycoplasma pneumoniae* infection	Adults, older children, and young adults suspected of having *M. pneumoniae* infection	A throat swab is taken and evaluated using enhanced Raman spectroscopy signals to detect bacteria in the specimen; detects spectral signatures of a near-infrared laser as it scatters off a biological specimen. University of Georgia, Athens, GA Pilot trial planned	Existing tests for possible *M. pneumoniae* infection Serology and nucleic acid amplification tests	Early diagnosis Avoided unnecessary antibiotic treatment Reduced transmission

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
TC-6987 oral neuronal nicotinic receptor alpha-7 modulator for treatment of asthma	Patients in whom persistent mild to moderate asthma has been diagnosed	While several effective inhaled antiinflammatory treatments are available for chronic asthma, compliance with therapy is an issue. TC-6987 is an oral therapy that is a modulator of alpha-7 neuronal nicotinic receptor, which has been shown to play a role in controlling inflammation pathways; chronic inflammation of the bronchial tubes is thought to be the underlying cause of asthma; modulation of NNR alpha-7 has been shown to lead to a reduction in the production and release of proinflammatory cytokines. Administered orally, as a 50 mg hard-gel capsule. Targacept, Inc., Winston Salem, NC Phase II trial ongoing	Mast cell stabilizers (e.g., cromolyn) Inhaled corticosteroids Omalizumab	Improved forced vital capacity Increased forced expiratory volume Improved quality of life
Tissue-engineered donor trachea for trachea replacement	Patients who need replacement of irreversibly damaged respiratory tract	Tissue-engineered trachea made from a donor trachea in which a tissue scaffold of fibrous protein collagen is prepared and then repopulated with the recipient's cells (cells lining the windpipe, and adult stem cells) in laboratory; once cultivated with recipient's cells, the donor trachea is transplanted to recipient. Paolo Macchiarini and colleagues, Barcelona, Spain Ministerio de Sanidad y Consumo, Madrid, Spain First transplant reported in late 2010	None	Restored trachea Restored respiratory function/capacity Increased or restored lung capacity Improved quality of life
VX-770 for treatment of cystic fibrosis in patients with G551D-CFTR mutation	Patients in whom CF has been diagnosed who have the G551D-CFTR gene mutation (10% to 15% of cystic fibrosis patients)	VX-770 agent is intended to improve lung function by improving function of mutant CFTR protein; regulator protein is an epithelial ion channel involved in salt and fluid transport. Given orally. Vertex Pharmaceuticals, Inc., Cambridge, MA Phase III trial ongoing; NDA submitted to FDA Oct 2011.	Currently, no treatment exists to treat the cause of the gene mutation	Reduced lung damage Improved lung function Slowed disease progression

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
VX-809 for treatment of cystic fibrosis	Patients in whom cystic fibrosis has been diagnosed who have the delta F508-cystic fibrosis transmembrane conductance regulator (*CFTR*) gene mutation	VX-809 is considered a corrector of the *CFTR* gene mutation; intended to increase regulator's function by increasing its movement to the cell surface. Given as oral monotherapy and in combination with VX-770 (Vertex's other CF drug). Vertex Pharmaceuticals, Inc., Cambridge, MA Phase II trials ongoing	Antibiotics Gene therapies (viral vector or liposome delivery of normal *CFTR*) Transplantation (lungs) Chest physiotherapy Bilevel positive airway pressure ventilators	Improved lung function Increased survival Improved quality of life

Table 14. AHRQ Priority Condition: 14 Substance Abuse: 17 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Buprenorphine implants (Probuphine) for treatment of opioid dependence	Patients in whom opioid dependence has been diagnosed	Sublingual buprenorphine-naloxone tablet induction followed by buprenorphine implants; partial agonist of opioid receptors and binds more strongly to receptors in the brain than other opioids and may reduce reaction of opioids when in system. Titan Pharmaceuticals, Inc., South San Francisco, CA Phase III confirmatory trial completed; held pre-NDA meeting with FDA in Oct 2011	Methadone maintenance treatment (efficacious, but restricted to licensed specialty clinics, requires frequent clinic sits, has risk of mortality associated with overdose) Sublingually (under the tongue) administered buprenorphine	Resolution problems with adherence, diversion Reduced illicit use of opioids
Interactive text message program (Text2Quit) for smoking cessation	Patients attempting smoking cessation	About 20% of the adult population in the U.S. smoke, and more than a third of adult smokers (17 million of 46 million) smokers try to quit each year, but only 1.3 million succeed with currently available interventions. Text2Quit is an interactive text-messaging program based on the same platform as Text4Baby, and intended to aid smokers in stopping smoking; the messaging system is intended to deliver customized educational content based on the user's own quit date; the program enables users to complete surveys to receive advice, play games to fight off cravings, select the best possible prescription or over-the-counter therapies as cessation aids, and collect data to help user monitor their achievement towards their own goals; it is designed to be especially useful for reaching underserved communities. The company intends to make the program available publicly and also through employers, health plans, and public health departments. Voxiva, Inc., and the George Washington University School of Public Health, Washington, DC Initial trials completed; program launched Jun 2011	One-way text messaging smoking cessation plans (not diffused) Hardcopy patient education Internet-based patient education Patient support groups	Increased number of successful smoking cessation attempts Reduced number of relapses Improved long-term health outcomes Reduced health disparities and improved access to cessation program

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mecamylamine (Inversine) for treatment of alcohol dependence	Patients in whom alcohol dependence has been diagnosed	Mecamylamine (Inversine®) is a nonselective, noncompetitive, high affinity nicotinic acetylcholine receptor antagonist intended for alcohol dependence; also used as antismoking therapy (alcohol boosts pleasure of smoking, suggesting some relationship between the two); will block euphoric effects of alcohol by antagonizing ethanol-induced dopamine release and reduce craving for alcohol; new target/mechanism of action. Manufactured by Targacept, Inc., Winston-Salem, NC, but investigated for this indication by Yale University, New Haven, CT, Phase II trial ongoing	Drugs for alcoholism (acamprosate [Campral], disulfiram [Antabuse], naltrexone)	Reduced alcohol consumption Abstinence from alcohol Improved long-term health outcomes associated with alcohol abstinence
Mecamylamine (Inversine) for treatment of dual diagnosis of depression and alcohol dependence	Patients in whom depression and alcohol dependence have been diagnosed who are on stable background depression medication	Mecamylamine (Inversine®) is a nonselective, noncompetitive, high affinity nicotinic acetylcholine receptor antagonist; clinical relationship between depression and alcohol dependence suggests common mechanism underlying both disorders; agent is being investigated as adjunct treatment for patients with dual-diagnoses; alcohol is a depressant and is incompatible with many antidepressants. Manufactured by Targacept, Inc., Winston-Salem, NC Yale University, New Haven, CT, and National Alliance for Research on Schizophrenia and Depression, Great Neck, NY, conducting trial Phase III trial ongoing	Drugs for alcoholism (acamprosate [Campral], disulfiram [Antabuse], naltrexone) Drugs for depression (alcohol incompatible with many of these) Psychotherapy	Reduced depression symptoms Reduced alcohol use Improved health outcomes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Naltrexone extended-release (Vivitrol) for treatment of opioid dependence	Patients in whom opioid dependence has been diagnosed	Treatment compliance is an issue with opioid dependence. Extended-release naltrexone (Vivitrol®) is a monthly injectable opioid receptor antagonist intended to reduce pleasure from taking opioids; an oral formulation is approved for alcoholism and opioid dependence and an injectable form is approved for alcoholism only; this formulation would offer a once-monthly injectable option instead of daily dosing and it would be the first injectable therapy for this indication. Alkermes, Waltham, MA FDA approved in Oct 2010 for prevention of relapse to opioid dependence, following opioid detoxification	Current oral or sublingual pharmacotherapies (buprenorphine, clonidine, levomethadyl acetate, methadone, naltrexone)	Decreased pleasure derived from opioid use Lower relapse rates Improved long-term health outcomes Improved quality of life
Neurokinin 1 receptor antagonist (LY686017) for treatment of alcohol dependence	Patients in whom alcohol dependency has been diagnosed	LY686017 is a neurokinin 1 receptor antagonist (novel class of drugs); relationship with substance P, which affects stress levels and thus, alcohol cravings (substance P is released in amygdala in response to stress, acts at neurokinin 1 receptors to mediate behavioral stress responses); intended to decrease alcohol cravings. Eli Lilly & Co., Indianapolis, IN Phase II trials completed	Disulfiram (Antabuse) Acamprosate (Campral) Naltrexone	Suppressed spontaneous alcohol cravings Abstinence from alcohol Prevented relapse Improved long term health outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label aprepitant (Emend) for treatment of alcohol dependence in patients with posttraumatic stress disorder	Patients in whom alcoholism secondary to posttraumatic stress disorder (PTSD) has been diagnosed	Aprepitant (Emend®, approved for use in chemotherapy-induced nausea and vomiting) is a substance P antagonist that blocks neurokinin 1 receptor; substance P (release in amygdala in response to stress) acts at neurokinin 1 receptors to mediate behavioral stress responses; blocking the receptors represents novel approach (new target) for antistress actions; in alcoholism, it is intended to decrease alcohol cravings, attenuate cortisol response to stress, and decrease insula activation in response to negative sensory input. Aprepitant manufactured by Merck & Co., Inc., Whitehouse Station, NJ; investigated for this indication by National Institute on Alcohol Abuse and Alcoholism Phase II trial ongoing	Antabuse Campral Naltrexone No therapies indicated specifically for alcoholism secondary to PTSD disorder	Abstinence from alcohol use Prevented relapse Improved long-term health outcomes associated with prevention of relapse
Off-label carvedilol for treatment of cocaine dependence	Patients in whom cocaine dependency has been diagnosed and who are recently abstinent from cocaine	Carvedilol is a nonselective beta blocker/alpha-1 blocker indicated for treatment of mild to moderate heart failure, but has been observed to lessen cocaine cravings. It is under study for reducing cocaine self-administration in cocaine-dependent participants. Manufactured by GlaxoSmithKline, Middlesex, UK; investigated for this indication by Yale University, New Haven, CT, National Institute on Drug Abuse, Bethesda, MD, University of Arkansas, Little Rock, AK Phase II trials ongoing	Antabuse (off-label use) Gamma-vinyl gamma aminobutyric acid (antiepileptic, not approved in U.S. due to visual field defects) Other beta blockers (off-label use) TA-CD Vaccine (off-label use) Tiagabine (off-label use) Topiramate (off-label use)	Reduced self-administration of cocaine Prevented relapse Long-term abstinence from cocaine Improved health outcomes associated with abstinence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label cycloserine for treatment of cocaine dependence	Patients in whom cocaine dependency has been diagnosed	Cycloserine is a broad spectrum antibiotic used for treatment of tuberculosis; psychotropic responses to it are related to the action of the D-enantiomer of the compound, which is a partial agonist of neuronal N-methyl D-aspartic acid receptor for glutamate; calcium flux through the receptors is thought to play a role in synaptic plasticity, the cellular mechanism for learning and memory; cycloserine is intended to facilitate extinction of response to drug-related cues. Administered orally. Manufactured by Elan Corp., plc, Dublin, Ireland, but investigated for this indication by Medical University of South Carolina, Charleston, SC; University of Arkansas, Fayetteville, AR; National Institute on Drug Abuse (NIDA), Bethesda, MD Phase II trials ongoing	Antabuse (off-label use) Beta blockers (off-label use) Gamma-vinyl gamma aminobutyric acid (antiepileptic, not approved in U.S. because of visual field defects) TA-CD Vaccine (off-label use) Tiagabine (off-label use) Topiramate (off-label use)	Reduced association with cocaine cues Reduced self-administration of cocaine Prevented relapse Long-term abstinence Improved health outcomes associated with abstinence
Off-label dronabinol for treatment of cannabis dependence	Patients in whom marijuana dependence has been diagnosed	No medications are FDA approved (or used off-label) for the treatment of marijuana dependence. Dronabinol is approved (generic and brand name Marinol) for the treatment of chemotherapy-induced nausea and vomiting; it is synthetic form of delta-9-tetrahydrocannabinol (THC), a pharmacologically active component of marijuana and is intended to target withdrawal syndrome, similar to nicotine patches for smokers; intended to reduce anxiety, feelings of misery, difficulty sleeping, and chills. National Institute on Drug Abuse (NIDA), Bethesda, MD, and New York State Psychiatric Institute, New York, NY Phase II trial completed	Behavioral interventions (e.g. cognitive behavioral therapy)	Decreased cravings Decreased Feelings of misery Improved sleeping ability Decreased chills Decreased cannabis use Improved quality of life Improved long-term health

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label gabapentin for initiating abstinence in alcohol dependence	Patients in whom alcoholism has been diagnosed who are experiencing alcohol withdrawal symptoms	Gabapentin is an analog of gamma aminobutyric acid (GABA; chief inhibitory neurotransmitter in the vertebrate central nervous system); indicated for anti-seizure purposes, and being explored for anti-alcohol dependence indications. Manufactured by Pfizer, Inc., (Parke-Davis), New York, NY, and Teva Pharmaceutical Industries Ltd., Petach Tikva, Israel, but being investigated for this indication by New York State Psychiatric Institute Phase II/III trial ongoing	Benzodiazepine (for withdrawal) Anti-seizure medications (for seizures associated with withdrawal) Drugs for alcohol dependence (disulfiram [Antabuse], acamprosate [Campral], Trexan) Drugs for depression associated with alcohol abuse (Prozac)	Reduced relapse rates Delayed relapse
Off-label ondansetron for treatment of alcohol dependence	Patients in whom alcohol dependence has been diagnosed	Only 36% of patients with alcohol dependence fully recover when using currently available pharmacotherapy; serotonin 5-HT3 receptors are a novel therapeutic target for this population. Ondansetron is a serotonin 5-HT3 receptor antagonist, approved for the treatment of chemotherapy-induced nausea and vomiting and first marketed by GlaxoSmithKline (Middlesex, UK) as Zofran; intended to exert its effects on alcohol dependency through cortico-mesolimbic dopamine system modulation; the 5HT system has been found to be a major regulator of the severity of alcohol consumption, which underpins the hypothesis that medications that affect the function of the 5-HT transporter may be viable treatments for this population. Under study at Johns Hopkins University, Baltimore, MD, National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD, University of Virginia, Charlottesville, VA, and Medical University of South Carolina, Charleston, SC. (No ondansetron manufacturers are sponsoring these studies.) Phase II and phase III trials ongoing	Acamprosate Disulfiram Naltrexone	Decreased severity of alcohol consumption (e.g., drinks per drinking day) Reduced preference for alcohol Reduced craving for alcohol Sustained abstinence Improved long-term health Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Opioid receptor antagonist (nalmefene) for treatment of alcohol dependence	Patients in whom alcohol dependence has been diagnosed	No medications that can be taken on an as-needed basis are approved for alcohol dependence. Nalmefene is a small molecule tablet opioid receptor antagonist that inhibits the reward pathway in the brain responsible for desire/craving for alcohol; intended to lessen a person's desire to drink, thereby potentially controlling and limiting their intake of alcohol; designed to be taken on an as-needed (PRN) basis; not intended for abstinence, only to reduce intake to less harmful levels; indicated for but then discontinued for reversal of opioid drug effects. Biotie Therapies Corp., Turku, Finland Phase III trial completed; company plans to file a marketing application authorization in Europe by end of 2011	Acamprosate Disulfiram Naltrexone	Reduced harmful levels of alcohol consumption Improved willingness to initiate abstinence treatment Improved sense of control over disease Improved long-term health outcomes
Pentoxifylline for treatment of alcoholic hepatitis	Patients in whom severe alcoholic hepatitis has been diagnosed	Pentoxifylline (normally used to improve circulation) has anti-tumor necrosis factor (TNF); a competitive nonselective phosphodiesterase inhibitor; inhibits tumor necrosis factor-alpha (TNF-alpha) (TNF promotes inflammation; probably why it has an effect on these patients) and has antifibrogenic properties; being studied as adjunctive therapy to corticosteroids. University Hospital of Lille in France Phase III trial completed	Stand-alone corticosteroid therapy	Increased survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vaccine (NicVax) for treatment of nicotine addiction in smokers	Patients who smoke and are addicted to nicotine	Vaccine (NicVax®) stimulates the immune system to produce antibodies that bind to nicotine, creating an antigen/antibody complex that is too large to cross the blood-brain barrier; blocks nicotine from reaching receptors in the brain; fewer stimulants (e.g., dopamine) are released, and the pleasurable, highly-addictive effects of nicotine are diminished, thereby making it easier to quit smoking. Nabi Biopharmaceuticals, Rockville, MD Phase III trials ongoing	"Cold-turkey" quitting Drug therapy (Zyban, Chantix) Nicotine replacement aids Acupuncture Hypnosis	Smoking cessation Prevented relapse Long-term abstinence
Vaccine (Nic002) for treatment of nicotine addiction	Patients in whom nicotine addiction has been diagnosed	Though 75% of smokers want to quit smoking, fewer than 5% who make a quitting attempt are successful; vaccines represent a new treatment modality for this condition. Nic002, formerly named CTY002-NicQB, is a therapeutic vaccine in development for the treatment of nicotine addiction. Nicotine is conjugated to a virus-like particle formed by recombinant expression of the protein coat of bacteriophage Qb; intended to induce nicotine-specific antibodies that bind to nicotine in the bloodstream; once nicotine is attached to an antibody, the molecule becomes too large to cross the blood-brain barrier, so nicotine uptake into the brain (and, therefore, the subsequent neuronal response) is reduced. Cytos Biotechnology, AG, Schlieren, Switzerland, in collaboration with Novartis AG, Basel, Switzerland Phase II trial ongoing in collaboration with Duke University, Durham, NC and Wake Forest University, Winston-Salem, NC	"Cold-turkey" quitting Oral pharmacotherapy (Zyban, Chantix) Nicotine replacement aids Acupuncture Hypnosis NicVax (in development)	Smoking cessation Decreased relapse rates Long-term abstinence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vaccine (TA-CD) for treatment of cocaine dependence	Patients in whom cocaine dependency has been diagnosed	Cocaine conjugate vaccine (TA-CD), consists of succinyl norcocaine covalently linked to recombinant cholera toxin B (rCTB) subunit protein and adsorbed onto aluminum hydroxide gel adjuvant; it is a large protein molecule that attaches to cocaine, stimulating antibody response, which then destroys the molecule; also intended to prevent cocaine from crossing the blood-brain barrier; intended to prevent high rewarding effect of cocaine caused by dopamine release; not believed to affect desire for cocaine, only physical effects. Celtic Pharma Management L.P., Hamilton, Bermuda Phase II trial ongoing	Antabuse (off-label use) Beta blockers (off-label use) Gamma-vinyl gamma aminobutyric acid (antiepileptic, not approved in U.S. because of visual field defects) Tiagabine (off-label use) Topiramate (off-label use)	Reduced self-administration of cocaine Prevented relapse Long-term abstinence from cocaine Improved health outcomes associated with abstinence from cocaine

Table 15. AHRQ Priority Area: 15 Cross-cutting: 12 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Automated pharmacy kiosk (MedCentre) for dispensing medications	Patients in need of commonly prescribed pharmacotherapies	Retail pharmacies may not be available in remote locations; high patient volume for routine medication pick-up makes it difficult for pharmacists to spend time with individual patients; patient medication compliance rates are sub-optimal. PharmaTrust MedCentre™ is a free-standing, automated medication dispensing and management system with four main components: remote access point for complete, personal, private pharmacist counseling, a point-of-care dispensary of patient medications, home delivery service, and a pharmaceutical distribution system designed to ensure the correct drugs are dispensed to patients; 340 common (many generic) medications are stored inside the machine, which is linked to a "tele-pharmacist"; tele-pharmacist verifies the patient's prescription, and the machine fills the prescription. Intended to be deployed in hospitals, medical clinics, and pharmacies, as well as retail, employer, and other public locations. PCA Services, Inc., Oakville, Ontario, Canada Released in Canada and UK; if pursued in U.S., likely to be regulated as class II device	Retail pharmacy Mail-order pharmacy	Improved access to prescription medication Increased patient compliance/adherence with medications Increased patient volume in retail pharmacies

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Barbershop-based medical screening and education programs	Patrons of community barbershops	Health disparities exist in minority communities, especially in cardiovascular, diabetic, cancer, and mental health disease areas. For example, African-American men have the highest death rate from hypertension of any race or ethnic group, or compared with women in the U.S. Furthermore, the U.S. Centers for Disease Control and Prevention has issued a new priority to develop novel hypertension-based outreach programs with community partners and deliver intervention messages that resonate with African-American men, because of a paucity of programs to address this need. Barbershops are being utilized as an access point to conduct screenings for hypertension, diabetes, prostate cancer, and mental health. One program, the Black Barbershop Health Outreach Program (BBHOP), uses medical and nonmedical volunteers (including barbers) to screen for hypertension and diabetes, because African-American-owned barbershops are considered a cultural institution with a large African-American male customer base, and they provide an environment of trust and a means for disseminating health education. A second program, the Barbershop Health Network (expected to become operational in Aug 2011), includes screening for mental health, which will be conducted by physicians; this program also will also open special evening-hour clinics at UMass Memorial Medical Center, Worcester, MA, for patient followup. BBHOP: Diabetic Amputation Prevention Foundation, Inglewood, CA Barbershop Health Network (Worcester, MA) Trial completed.	Clinic-based health screenings	Improved health outcomes Improved access to care Reduced health disparities
Intelligent pills for chronic conditions requiring long-term drug therapy	Patients in whom long-term drug therapy is needed for various chronic conditions	Edible microchip affixed to oral drugs (tablets) to monitor patient compliance; wearable data recorder captures actual drug consumption and vital statistics, reminds patients of missed doses, and transmits patient data to clinicians. Proteus Biomedical, Inc., Redwood City, CA Trials ongoing for one component; external data recorder component FDA 510(k) cleared; CE marked	Conventional oral drug therapy Patient medication reminders via telephone, text message, and/or e-mail	Improved disease management by maintaining consistent oral drug dosing and reducing missed doses

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Medical homes network (South Side Healthcare Collaborative) to link emergency department patients to community care	Patients who do not currently have a primary care medical home (PCMH)	Patients without PCMHs often adopt less preventative care, experience exacerbations of ambulatory-care-sensitive conditions (ACSCs), contract illnesses and health conditions earlier, and seek care in the emergency department (ED), placing an avoidable burden on the health care system (e.g., ED overcrowding) and negatively affecting their personal health; EDs are not intended to treat or manage chronic illness, or to offer preventive care. South Side Healthcare Collaborative is a program intended to link ED patients with (18 hospital-affiliated) community providers via an ED-based patient navigator (i.e., patient advocate); patient advocates approach eligible patients who are flagged by an ED electronic tracking system, and offer patients services provided by primary-care referral and appropriate dental, mental health, and substance abuse facilities. Appointments are scheduled for the patient, and pertinent ED medical data is faxed to the outlying sites. University of Chicago Medical Center, Chicago, IL Pilot trial completed	Current use of ED system for nonurgent conditions ED-MC Connect (Primary Care Coalition [PCC] of Montgomery County, MD - PCMH model) ED Diversion Project (District of Columbia Primary Care Association [DCPCA] PCMH model)	Appropriate primary care utilization Increased mental health, dental, substance abuse care utilization Improved health prevention and promotion Improved patient health outcomes Reduced ED utilization for nonemergency conditions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Motivational interviewing in the pharmacy setting to improve patient medication adherence	Patients who are at risk of noncompliance or nonadherence with prescribed medication regimen(s)	According to the New England Healthcare Institute, medication nonadherence is responsible for approximately $290 billion annually in avoidable medical spending. Motivational Interviewing (MI) is a patient-centered style of counseling that has shown efficacy in many health issues, such as substance abuse, physical exercise, health screenings, and medication adherence; MI is intended to be positive, empathetic, and nonconfrontational, and is designed to help patients resolve their ambivalence about (health behavior) change. Training pharmacists (either in pharmacy school or in the professional setting) to engage in brief (e.g., 2- to 5-minute long) motivational interviews with patients may cultivate patient self-efficacy and improve medication adherence and compliance. Pharmacists are taught overall interviewing techniques and strategies for dealing with patient resistance to medication adherence. University of Missouri, Columbia, MO; University of Pittsburgh School of Medicine, Pittsburgh, PA; Highmark Blue Cross Blue Shield, Pittsburgh, PA; Rite-Aid Pharmacies, Harrisburg, PA Trials completed.	Current pharmacist-patient communication curriculum Medication review by pharmacist Nonpharmacy based adherence programs (e.g., reminder services)	Increased patient motivation to comply Improved medication adherence and compliance Reduced costs of medical care from treating noncompliant patients
Natural orifice transluminal endoscopic surgery (NOTES)	Surgical patients undergoing thoracic, abdominal, gastrointestinal, gynecologic, or urologic procedures	Minimally invasive endoscopic surgery that avoids skin incisions by inserting instrumentation though the abdomen or thorax using natural orifices as entry points. Minos Medical, Inc., Irvine, CA USGI Medical, Inc., San Clemente, CA Ethicon Endo-Surgery, Inc., Cincinnati, OH Trials ongoing.	Traditional open surgery Laparoscopic surgery Robot-assisted surgery	Less pain and reduced medication need Less external scarring Quicker recovery Less blood loss/need for transfusion Shorter hospital stay

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Partnering urban academic medical centers and rural primary care clinicians for treatment of complex chronic diseases	Patients with chronic or complex diseases living in rural or otherwise medically underserved areas (e.g., prisons)	For patients with chronic or complex diseases living in rural or medically underserved areas (e.g., prisons), receiving high-quality specialty care can be challenging, because of access barriers, specialist shortages, geographical isolation, and other factors. Project ECHO (Extension for Community Healthcare Outcomes) is a health care delivery model that is intended to help develop rural communities' capacity to treat chronic, common, and complex disease in rural and underserved areas; the program utilizes telehealth technology and clinical management tools to train and support rural primary care providers in developing knowledge on diseases that would normally fall within the realm of specialist care; clinicians are organized into learning networks with specialists at academic medical centers, which are intended to aid the clinicians in developing knowledge of and capability to treat certain complex conditions. University of New Mexico Health Sciences Center, Albuquerque, NM Trials ongoing.	Current model of specialist care for rural or underserved patient populations Other telemedicine delivery systems (e.g., Indian Health Service and the Veterans Health Administration)	Expanded primary care physician knowledge of complex conditions Improved patient health outcomes Reduced health disparities
Patient group appointments with physicians for management of chronic conditions	Patients in whom chronic conditions have been diagnosed	Many physicians find it difficult to incorporate patient education and other followup care into their daily appointments with single patients; also, followup appointments for chronic conditions are characterized by limitations, such as long wait times and patients who are less then optimally engaged. Scheduling group appointments is an approach in which several patients with the same chronic condition (e.g., diabetes, Parkinson's disease) share an extended appointment (1.5 hours) for followup visits; patients receive a few minutes each for private discussion with the doctor, then a clinician shares information relevant to all patients and takes questions; this is not intended to replace annual in-depth physicals. Physicians can bill for individual patient appointments as long as certain criteria are met, such as the visit includes one-on-one time and education. University of Rochester, Rochester, NY; Veterans Affairs Medical Centers (NC and VA) Trial completed.	Individual appointments	Increased number of patients seen Reduced waiting times for appointments Improved patient engagement Increase patient education Improved compliance with therapy/disease management

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Portable ultrasound to assess pedicle and intrathoracic omental flap	Patients requiring surgical reconstruction of chest wall using intrathoracic omental flap (part of the peritoneum) transposition technique (often associated with deep sternal wound infections after coronary artery bypass grafting)	Use of portable ultrasound scanner to assess the viability and perfusion of buried intrathoracic omental flap following surgical reconstruction of the chest wall; intended to address deep sternal wound infections. University of Amsterdam, the Netherlands Case studies completed	Postoperative computed tomography scans	Rapid bedside assessment of viability and perfusion of the omental flap Avoided unnecessary revision surgery Reduced cost of care
Reservation or appointment-making system for emergency care visits	Patients with non-life-threatening conditions who intend to seek care in the emergency department (ED)	The national average for ED wait times is more than 4 hours (and can be as long as 8 hours in places such as Utah). Long wait times are costly, inconvenient for patients, and can result in poorer patient outcomes. InQuickER® is an online service that forms partnerships with hospitals, so patients with non-life-threatening injuries or illnesses can "reserve" an "appointment" time at their local ED, then wait at home until that time comes. The service is a "check-in process" that holds a patient's place in line and projects his or her anticipated treatment time, using data from EDs. Once patients arrive at the hospital at the projected time, the service guarantees that they will be seen in 15 minutes or their convenience fee ($9.99) is refunded. Checkpoints are put in place to ensure that patients with emergent injuries or illnesses do not wait at home. InQuickER, LLC, Nashville, TN Launched in Sept 2011	Traditional approach to ED visits	Reduced wait times for patients Improved patient convenience and quality of life Improved outcomes for patients (especially those with life-threatening injuries or illnesses)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Self-service kiosks to automate triage and treatment in the emergency department	Noncritical patients visiting the emergency department (ED)	Nearly half of ED patients experience long wait times because they are classified as low-risk; wait times and overcrowding contribute to poorer health outcomes and patient dissatisfaction. Kiosk-based patient self-service triage and treatment enables a patient to, without direct staff interaction, complete registration and assessment, measure vital signs, and dispense medication based on telemedicine control by a physician and pharmacist. The approach is intended to be implemented as follows: (1) patients register at the first kiosk by swiping/scanning their insurance card; kiosk touch screen guides them through self-assessment where they register, describe symptoms, and outline the reasons for their visit; (2) patients' vital signs are taken at the second kiosk; and (3) patients speak with a doctor via video conferencing for diagnosis and, if medication is prescribed, it is dispensed. NCR Corp., Duluth, GA; PharmaTrust, Oakville, Ontario, Canada; StayHealthy, Monrovia, CA Launched in Canada in Sept 2010	Standard, non-automated ED triage and treatment	Reduced ED wait times Reduced ED overcrowding Improved health outcomes Improved patient satisfaction Reduced costs of ED visits for minor conditions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Senior-specific emergency departments for treatment of elderly patients	Senior or elderly patients who visit the emergency department (ED)	Twenty percent of all seniors use an ED at least once a year, and half of all ED patients are seniors. General EDs are not senior-specific, and can be uncomfortable or unsafe for elderly patients. Additionally, risk for hospital readmission and drug interactions are high in this population. Finally, EDs do not always have access to geriatrician staff members. EDs for seniors are designed specifically for the elderly population. Structural, safety, and comfort changes include wider hallways (for wheelchairs), hand rails, different lighting systems, easier-to-read visuals, pressure-reducing beds, and alarms for wandering patients. Care teams and care delivery are redesigned to include clinicians and nurses with special training in geriatric medicine, including education on issues related to ageism and sensory appreciation in the elderly (so that these skills can be used to communicate more effectively with older adults and their caregivers). The different approach to care involves being more thorough with each patient and conducting on a routine basis assessments that typically are only made as needed (e.g., cognitive exams to detect issues that normally would go unchecked in other EDs). Health systems piloting this change include Trinity Health System, Novi, MI, and Mount Sinai Medical Center, New York, NY. Trinity Health System opened a senior ED at its Holy Cross Hospital in Silver Spring, MD, in 2008 and planned to build in 19 other hospitals by 2013. Launched in 2008	General EDs	Improved health outcomes for seniors Improved quality of life

Section 2. Interventions Added Since Last Update: 138 Interventions

Table 16. AHRQ Priority Condition: 01 Arthritis and Nontraumatic Joint Disease: 4 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Interleukin-1-beta antagonist canakinumab (Ilaris) for treatment of systemic juvenile idiopathic arthritis	Patients in whom systemic juvenile idiopathic arthritis (SJIA) has been diagnosed	Currently available treatments for SJIA only partially mitigate symptoms and do not prevent long-term damage associated with the condition. Additionally, prolonged use of steroids can cause slowed growth and delayed puberty. Canakinumab (Ilaris™) is a long-acting fully human monoclonal antibody against interleukin-1-beta (IL-1b). IL-1b is a major mediator of inflammatory responses, which are purported to play a role in SJIA pathology. Canakinumab is intended to block the inflammatory activity of IL-1b. Canakinumab has been administered to patients with SJIA as a single subcutaneous dose, 4 mg/kg of body weight, to patients aged 2 to 19 years, in a clinical trial. Novartis AG, Basel, Switzerland Phase III trials ongoing; approved for cryopyrin-associated periodic syndromes	Anakinra Corticosteroids Hydroxychloroquine Methotrexate Nonsteroidal antiinflammatory drugs (NSAIDs)	Improved adapted American College of Rheumatology (ACR) pediatric 30/50/70/90/100 disability criteria Improved Child Health Assessment Questionnaire (CHAQ) clinical response Decreased Child Health Questionnaire (CHQ) pain intensity as assessed on a 100-mm visual analog scale Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Interleukin-6 receptor antagonist tocilizumab (Actemra) for treatment of systemic juvenile idiopathic arthritis	Patients in whom SJIA has been diagnosed	Currently available treatments for SJIA only partially mitigate symptoms and do not prevent long-term damage associated with the condition. In addition, prolonged use of steroids can cause slowed growth and delayed puberty. Tocilizumab (Actemra®) is a humanized monoclonal antibody interleukin-6 (IL-6) receptor antagonist. IL-6 is a proinflammatory cytokine produced by a variety of cell types including lymphocytes, monocytes, and fibroblasts, as well as synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes. IL-6 is purported to upregulate lymphocyte activity, initiate acute phase protein synthesis, and stimulate hematopoietic precursor cell proliferation and differentiation. IL-6 can also stimulate osteoclast activity leading to inflammation and erosion of joint structures. Inhibiting IL-6 activity may relieve symptoms associated with SJIA. Tocilizumab can be used as monotherapy or in combination with methotrexate and is administered as an intravenous infusion, 12 mg/kg or 8 mg/kg, in patients weighing less than or more than 30 kg, respectively, every 2 weeks. F. Hoffmann-La Roche, Ltd., Basel, Switzerland FDA approved for treatment of SJIA Apr 2011	Anakinra Canakinumab Corticosteroids Hydroxychloroquine Methotrexate NSAIDs	Improved adapted ACR pediatric 30/50/70/90/100 disability criteria Improved CHAQ clinical response Decreased CHQ pain intensity as assessed on a 100-mm visual analog scale Improved quality of life
KIT tyrosine kinase inhibitor masitinib for treatment of rheumatoid arthritis	Patients in whom rheumatoid arthritis (RA) has been diagnosed	Biologic therapies have become standard of care for patients with RA that no longer responds to disease-modifying antirheumatic drugs (DMARDs). However, biologics must be administered by injection and are associated with increased incidence of serious infections, including tuberculosis. DMARDs with improved efficacy and tolerability as well as convenient dosing are needed. Masitinib is an orally administered tyrosine kinase inhibitor that is purported to target the activity of mast cells, which are involved in mediating inflammation in the synovium. Masitinib purportedly targets mast cells through selectively inhibiting KIT, platelet-derived growth factor receptor, Lyn, and to a lesser extent, fibroblast growth factor receptor 3. Masitinib is administered orally, 3 or 6 mg/kg, daily, in clinical trials. AB Science S.A., Paris, France Phase III trial ongoing	Analgesics Antiinflammatory agents: glucocorticoids, NSAIDs DMARDs: methotrexate, hydroxychloroquine, sulfasalazine; biologic monoclonal antibodies and inhibitors	Improved symptom scores (as measured by ACR 20/50/70) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Purine nucleoside phosphorylase inhibitor BCX4208 to prevent acute gout flares	Patients in whom chronic gout has been diagnosed	Despite new treatment options, some patients do not respond adequately to current gout therapies; thus, treatments with new mechanisms of action are needed. BCX4208 is purported to be a purine nucleoside phosphorylase inhibitor, which blocks the generation of uric acid precursors and works upstream of xanthine oxidase inhibitors in the metabolic pathway, thus representing a new mechanism of action to lower serum uric acid levels and potentially prevent acute gout flares. BCX4208 is intended to be used in combination with allopurinol to lower serum uric acid levels. In trials, it is administered orally, 5 to 40 mg, once daily. BioCryst Pharmaceuticals, Inc., Research Triangle, NC Phase II trials ongoing	Allopurinol Febuxostat Probenecid Rilonacept	Reduced frequency of gout flares Reduced serum uric acid levels Improved quality of life

Table 17. AHRQ Priority Condition: 02 Cancer: 64 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Albumin-coupled doxorubicin (INNO-206) for treatment of soft tissue sarcoma	Patients in whom unresectable soft tissue sarcoma has been diagnosed	Patients with soft tissue sarcoma have few treatment options and poor prognosis. INNO-206 is a novel formulation of doxorubicin, a chemotherapy compound approved for use in treating soft tissue sarcoma, intended to provide targeted delivery of the compound to tumors. In this formulation, doxorubicin is coupled to albumin via an acid-sensitive linker. Circulating albumin preferentially accumulates in tumor tissues, which also generate acidic microenvironments. In these acidic conditions, the linker is cleaved, potentially releasing active doxorubicin locally at the site of the tumor. CytRx Corp., Los Angeles, CA Phase IIb trial planned for end of 2011; FDA granted orphan drug status	Doxorubicin	Increased overall survival Increased progression-free survival Improved quality of life
Antibody-drug conjugate (inotuzumab ozogamicin) for treatment-resistant or recurrent non-Hodgkin's lymphoma	Patients with treatment-resistant or recurrent CD20- and CD22-positive non-Hodgkin's lymphoma (NHL) who are not candidates for high-dose chemotherapy	With current treatment options, patients with recurrent or treatment-resistant NHL have poor prognoses. Only 5% to 10% of patients are alive 2 years after diagnosis. Cases of NHL typically express B-cell cell surface markers such as CD20 and CD22. While an anti-CD20 antibody (rituximab) has been used in the treatment of NHL for several years, an effective treatment targeting CD22 is not currently available. Inotuzumab ozogamicin is a novel antibody-drug conjugate that couples a CD22-specific antibody to a highly toxic chemotherapeutic agent. In clinical trials, inotuzumab ozogamicin (1.8 mg/m^2 by intravenous infusion once every 4 weeks) is being administered as an adjunct to treatment with rituximab. Pfizer, Inc., New York, NY Phase III trial ongoing	Combination chemotherapies such as: Cyclophosphamide/ etoposide/ prednisone/ procarbazine plus or minus rituximab Cyclophosphamide/ etoposide/vincristine/ prednisone plus or minus rituximab Etoposide/prednisone/ vincristine/ cyclophosphamide/ doxorubicin plus or minus rituximab Gemcitabine/ dexamethasone/cisplatin plus or minus rituximab Lenalidomide plus or minus rituximab	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anti-CD200 monoclonal antibody (samalizumab) for treatment of chronic lymphocytic leukemia	Patients with recurrent or treatment-refractory chronic lymphocytic leukemia (CLL)	While currently available chemotherapy treatments are often able to slow the progression of CLL, these treatments are not curative and recurrent disease often develops. Samalizumab is a novel, intravenously administered monoclonal antibody being studied for the treatment for CLL. Samalizumab is specific for CD200, and antibody binding to CD200 is purported to block CD200's binding to its cognate receptors. CD200 activation of CD200 receptors on cells of the immune system appears to downregulate the activity of these immune cells. Multiple cancers including CLL have been shown to upregulate CD200, which may lead to immune tolerance of the cancer. Alexion Pharmaceuticals, Inc., Cheshire, CT Phase I/II trial completed	Multiple combination chemotherapy regimens, such as: Alemtuzumab plus or minus rituximab Bendamustine/rituximab Cyclophosphamide/ doxorubicin/vincristine/ prednisone/rituximab Fludarabine/alemtuzumab Fludarabine/ cyclophosphamide/ rituximab, ofatumumab Pentostatin/ cyclophosphamide/ rituximab	Increased overall survival Increased progression-free survival Improved quality of life
Anti-CS1 monoclonal antibody (elotuzumab) for treatment of multiple myeloma	Patients in whom newly diagnosed multiple myeloma or relapsed/refractory multiple myeloma has been diagnosed	While treatments for multiple myeloma have improved, the median life expectancy for patients in whom multiple myeloma is diagnosed is only 5 to 7 years. Currently, no immunotherapeutic option exists for multiple myeloma. CS1 was recently identified as a glycoprotein expressed preferentially on multiple myeloma cells. Elotuzumab is a humanized monoclonal antibody specific for CS1 that is purported to have an anticancer effect through antibody-dependent cellular cytotoxicity. In clinical trials, elotuzumab is being administered as an adjunct to conventional therapy with a combination of lenalidomide and dexamethasone. Bristol-Myers Squibb, New York, NY Phase III trials ongoing	For stem- cell-transplant-eligible patients, first-line therapy such as: Bortezomib/dexamethasone Cyclophosphamide/ dexamethasone Doxorubicin/dexamethasone Lenalidomide/ dexamethasone Thalidomide/dexamethasone For patients ineligible for stem cell transplant, first-line therapy such as: Bortezomib/ dexamethasone Lenalidomide/low-dose dexamethasone Melphalan/prednisone/ plus bortezomib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anti-DLL4 monoclonal antibody (OMP-21M18) for treatment of cancer	Patients with treatment-resistant advanced solid tumors	While many chemotherapeutic approaches are available for advanced solid tumors, treatment is rarely curative and the cancer typically develops resistance to therapy and progresses. OMP-21M18 is a monoclonal antibody specific for delta-like ligand 4 (DLL4), a protein that has been implicated in the maintenance of cancer stem cells and promotion of angiogenesis. By inhibiting DLL4, OMP-21M18 is intended to both target the difficult-to-treat population of tumor-initiating cancer stem cells in solid tumors and reduce the blood supply to solid tumors. OncoMed Pharmaceuticals, Inc., Redwood City, CA Phase I trials ongoing	Large variety of anti-cancer chemotherapies	Increased overall survival Increased progression-free survival Improved quality of life
Anti-ErbB3 monoclonal antibody (MM-121) for treatment of ER- or PR-positive HER2-negative breast cancer	Patients in whom estrogen receptor (ER)- and/or progesterone receptor (PR)-positive, HER2-negative breast cancer has been diagnosed	For patients whose breast cancer progresses after treatment with first-line antiestrogen therapy, followup anti-aromatase therapy can delay progression in some but not all patients. MM-121 is a monoclonal antibody specific for the ErbB3 receptor tyrosine kinase. Like its orthologous receptor tyrosine kinases epidermal growth factor receptor (EGFR) and HER2, ErbB3 is capable of activating signaling pathways that control cell growth and proliferation and, therefore, its inhibition has the potential to limit cancer growth and survival. In the second-line setting, MM-121 is being administered in combination with the steroidal aromatase inactivator exemestane. In the neoadjuvant setting, MM-121 is being administered in combination with the taxane paclitaxel. Merrimack Pharmaceuticals, Inc., Cambridge, MA Phase II trials ongoing	Second-line setting: Exemestane Non-steroidal aromatase inhibitors (anastrozole, letrozole) Fulvestrant Tamoxifen Toremifene Neo-adjuvant setting: paclitaxel	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anti-ErbB3 monoclonal antibody (MM-121) for treatment of lung cancer	Patients in whom EGFR-positive nonsmall cell lung cancer (NSCLC) has been diagnosed	While anti- epidermal growth factor receptor (EGFR) therapy has improved outcomes in EGFR-positive NSCLC, the cancer becomes treatment resistant in many patients. One demonstrated mechanism of resistance to anti-EGFR therapy is activation of a related receptor tyrosine kinase ErbB3; therefore, concomitant targeting of EGFR and ErbB3 may improve outcomes. MM-121 is a monoclonal antibody inhibitor of ErbB3 that is being tested in combination with the EGFR inhibitor erlotinib. Merrimack Pharmaceuticals, Inc., Cambridge, MA, in collaboration with Sanofi-Aventis, Paris, France Phase I/II trial ongoing	Erlotinib monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Antifolate receptor monoclonal antibody (farletuzumab) for treatment of ovarian cancer	Patients with recurrent ovarian cancer that is platinum-sensitive, platinum-resistant, or platinum-refractory	Patients with recurrent ovarian cancer have median overall survival times of less than 2 years and few treatment options. Farletuzumab is a monoclonal antibody specific for the folate receptor, which is expressed on the majority of ovarian cancer cells, but not on cells of normal tissues. Farletuzumab is purported to lead to antibody-dependent cell-mediated cytotoxicity of folate-receptor-expressing cells. In late-phase clinical trials, farletuzumab is being administered intravenously, once weekly, at a dose of 1.25 or 2.5 mg/kg of body weight. In platinum-sensitive disease, farletuzumab is being tested in combination with carboplatin/taxane doublet therapy. In platinum-resistant/refractory disease, farletuzumab is being tested in combination with taxane monotherapy. Morphotek, Exton, PA, a subsidiary of Eisai Co., Ltd., Tokyo, Japan Phase III trials ongoing	Platinum-sensitive ovarian cancer: Carboplatin plus paclitaxel Carboplatin plus docetaxel or pegylated liposomal doxorubicin or gemcitabine or topotecan Cisplatin plus gemcitabine Platinum-refractory ovarian cancer: Docetaxel Etoposide Gemcitabine Paclitaxel Pegylated liposomal doxorubicin Topotecan	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Antigen-specific cancer immunotherapeutic (GSK2132231A) for advanced melanoma	Patients with stage IIIB or IIIC cutaneous melanoma that expresses MAGE-A3 antigen who have macroscopic lymph node involvement suitable for surgery	Patients in whom stage III melanoma has been diagnosed frequently experience disease recurrence after surgical resection of the primary tumor. Current immunotherapies used in the adjuvant setting have shown little effect on the duration of overall survival in this patient population. GSK2132231A is a peptide-based therapeutic vaccine directed at the cancer-specific antigen MAGE-A3, which is expressed by a significant proportion of melanomas. It is currently being tested in the adjuvant setting for treatment of melanoma. In a late-phase clinical trial, GSK2132231A is being administered as a course of 13 injections. GlaxoSmithKline, London, UK Phase III trial ongoing	Granulocyte-macrophage colony stimulating factor Interferon-alpha (INFa) Radiation therapy	Increased overall survival Increased progression-free survival Improved quality of life
Antiplacental growth factor monoclonal antibody (TB-403) for treatment of glioblastoma	Patients with recurrent glioblastoma multiforme	Current antiangiogenic antibodies (e.g., bevacizumab) are directed against vascular endothelial growth factor (VEGF); however, other angiogenic signaling growth factors may be upregulated in cancers and may play a role in resistance to anti-VEGF treatment. One such angiogenic factor is placental growth factor (PGF). TB-403 is a humanized monoclonal antibody specific for PGF. In a clinical trial, it is being administered intravenously in combination with the approved anti-VEGF antibody bevacizumab. F. Hoffmann-La Roche, Ltd., Basel, Switzerland, licensed from BioInvent International AB, Lund, Sweden Phase Ib/II trial initiated	Bevacizumab monotherapy Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Antitelomerase therapeutic cancer vaccine (TeloB-Vax) for treatment of prostate cancer	Patients in whom advanced prostate cancer has been diagnosed	Patients with advanced prostate cancer have poor prognosis and few treatment options. TeloB-Vax is a cancer vaccine that is purported to work by inducing a T-cell response against telomerase reverse transcriptase (hTRT), an enzyme expressed at high levels by many cancers and responsible for allowing cancer cells to continually divide without undergoing senescence. An hTRT-encoding plasmid is transduced into patient-derived B cells, which express the antigen for up to 5 days, potentially eliciting an immune response. Adamis Pharmaceuticals Corp., San Diego, CA Phase I trial completed	Abiraterone Docetaxel Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Autologous dendritic cell vaccine (BPX-101) for treatment of metastatic, castration-resistant prostate cancer	Patients in whom metastatic, castration-resistant prostate cancer (CRPC) has been diagnosed	Currently, median overall survival for patients with CRPC is only about 18 months. BPX-101 is a novel autologous dendritic-cell therapeutic cancer vaccine that consists of two parts: (1) an antigen consisting of prostate membrane specific antigen (PMSA) and (2) transmembrane proteins encoding a chemical induction of dimerization (CID) construct that allows activation of the CD40 pathway by addition of a chemical stimulator (AP1903). Dendritic cells (DC) are isolated from the patient and transduced with both PMSA antigen and CID construct. On day 1 the DCs are injected into the patient and purportedly migrate to lymph nodes. On day 2 the AP1903 activator is added to activate the CD40 pathway in lymph-node resident DCs. CD40 activity potentiates the generation of cytotoxic T cells and memory B cells, potentially leading to a more robust immune response. Bellicum Pharmaceuticals, Inc., Houston, TX Phase I/II trial completed	Abiraterone Cabazitaxel Docetaxel Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Brussels sprout extract (sulforaphane) for treatment of prostate cancer	Patients with recurrent prostate cancer after radical prostatectomy or definitive radiation therapy	While hormone therapy for recurrent prostate cancer is known to extend survival in some patients, the treatment is rarely curative and disease typically progresses to CRPC over time. Sulforaphane, a chemical found in various vegetables, has been purported to have anticancer activity. One potential mechanism of action ascribed to sulforaphane is histone deacetylase activity, which can disrupt chromatin structure and may cause DNA repair inhibition or modification of cell cycle proteins that could impact quickly dividing cells. Sulforaphane is administered as an oral tablet. Oregon Health Sciences University, Portland, OR Phase II trial ongoing	Androgen deprivation therapy Salvage radiation therapy Salvage surgery Watchful waiting	Increased overall survival Increased progression-free survival Improved quality of life
Bruton's tyrosine kinase inhibitor (AVL-292) for treatment of B-cell malignancies	Patients with treatment-resistant B-cell malignancy (e.g., NHL, B-cell CLL, Waldenstrom's macroglobulinemia)	Patients in whom a treatment-resistant B-cell malignancy has been diagnosed have poor prognoses and few treatment options. Many B-cell malignancies are dependent on B-cell receptor (BCR) signaling for survival. AVL-292 is a novel kinase inhibitor that is specific for the Bruton's tyrosine kinase, which is a signaling kinase essential for transduction of the BCR signaling pathway. Avila Therapeutics, Bedford, MA Phase I trial ongoing	Various cytotoxic chemotherapy regimens combined with various immunotherapeutic drugs	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Carbon ion beam radiation therapy for cancer	Patients with cancer amenable to treatment with radiation	The properties of heavy ion beams (e.g., carbon ion) may allow improved administration of radiation therapy compared with photon or proton beam radiation. Like proton beams, particles in carbon ion beams lose the majority of their energy immediately before depositing the energy at a tumor target. This phenomenon is known as the Bragg peak, which potentially allows planning for targeting the radiation dose to a specific tissue depth and sparing adjacent tissue. Compared with protons, the path of heavier carbon ions is less influenced by passage through overlying tissue and, therefore, the peak of ionizing radiation is tighter, potentially allowing more precise targeting and delivery. Additionally, heavier particles such as carbon ions have a more severe impact on atoms within target cells, which produces more intense cellular damage and can potentially increase the biologic effectiveness of carbon ion beams relative to proton or photon beams. In particular, the relative biologic effectiveness of carbon ions purportedly increases with tissue depth, coinciding with the Bragg peak. Lastly, collisions between carbon ions and atomic nuclei produce positrons through nuclear fragmentation. The generated positrons can be imaged using positron emission tomography (PET), potentially allowing visualization of the delivered dose distribution. Developers include Ion Beam Applications S.A., Louvain-la-Neuve, Belgium, in joint venture with SAPHYN (SAnté et PHYsique Nucléaire, or Nuclear Health and Physics, a semi-public company, Caen, France) and financial partners; Siemens AG, Munich, Germany Two carbon ion beam facilities are currently operating—one in Japan for 10 years, and one that went online at University Hospital Heidelberg, Germany, in 2009. Another, planned to open in Germany in 2012, is NRoCK, the North European Radiooncological Center Kiel, Schleswig-Holstein, Germany. Ten trials are ongoing or planned in Germany. In the U.S., Colorado State University announced in 2010 a partnership with the Japanese center to perform carbon ion therapy research; collaborations among several hospitals in Michigan and Ohio to explore developing carbon ion centers were announced in 2008, but further development is unclear at this time.	Photon radiation therapy Proton radiation therapy	Increased overall survival Increased progression-free survival Decreased adverse/side effects from radiation therapy Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
DCC-2036 for treatment of Philadelphia chromosome-positive chronic myelogenous leukemia and acute lymphoblastic leukemia	Patients in whom Philadelphia chromosome-positive chronic myelogenous leukemia (CML) or acute lymphoblastic leukemia (ALL) has been diagnosed	Inhibitors of the BCR-ABL1 fusion protein kinase have demonstrated efficacy in treating Philadelphia chromosome-positive CML and ALL; however, many patients develop resistance to the available kinase inhibitors because of mutation of the BCR-ABL kinase. Therefore, novel kinase inhibitors that are able to inhibit resistant isoforms of BCR-ABL are needed. DCC-2036 is an orally administered ABL kinase inhibitor that functions via a fundamentally different mechanism from currently available ABL kinase inhibitors. Rather than blocking ATP binding to the kinase, DCC-2036 inhibits the transition of the kinase from an inactive to active conformation. Because it acts at a different site on the kinase, DCC-2036 might inhibit kinase isoforms that are resistant to current inhibitors. Deciphera Pharmaceuticals, LLC, Lawrence, KS Phase I/II trial ongoing	Placebo There are no standard pharmacologic treatments for patients with CML/ALL who have developed resistance to imatinib, nilotinib, and dasatinib. Some patients may be eligible for hematopoietic stem cell transfer.	Increased overall survival Increased progression-free survival Improved quality of life
Depot anti-androgen formulation (Liproca) for treatment of localized prostate cancer	Patients in whom localized prostate cancer has been diagnosed	Prostate cancer often responds to treatment with anti-androgens; however, these treatments have significant side effects due to systemic exposure to the antiandrogen. Liproca® is a depot formulation of 2-hydroxyflutamide, which is prepared in a calcium sulfate paste that cures upon local injection to the prostate. Local administration of flutamide could provide higher local doses of antiandrogen as well as avoid systemic exposure to the drug. LIDDS AB, Helsingborg, Sweden Phase I/II trial ongoing	Bicalutamide Flutamide	Equivalent progression-free survival to systemic antiandrogens Equivalent overall survival to systemic antiandrogens Reduced systemic side effects relative to systemic antiandrogens Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Diphtheria toxin expression vector (BC-819) for treatment of pancreatic cancer	Patients with locally advanced, unresectable pancreatic adenocarcinoma that is amenable to intratumoral injection under ultrasound guidance and expresses high levels of H19	Patients in whom pancreatic cancer has been diagnosed have a 5-year survival rate of only 5%, and effective treatment options are not available. H19 is a noncoding RNA that is expressed in a wide variety of cancers, including many pancreatic cancers, but is not actively transcribed in the majority of adult tissues. BC-819 is a DNA plasmid that encodes the highly cytotoxic diphtheria toxin under the control of the H19 promoter and is intended to induce the expression of diphtheria toxin exclusively in H19-expressing cancer cells. In current clinical trials, BC-819 is administered by intratumoral injection as an addition to the standard systemic chemotherapy drug gemcitabine. BioCancell Therapeutics, Inc., Jerusalem, Israel Phase IIb trial ongoing	5-fluorouracil/leucovorin monotherapy Gemcitabine monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Dual ALK and EGFR kinase inhibitor (AP26113) for treatment of nonsmall cell lung cancer	Patients with ALK translocation-positive non-small cell lung cancer (NSCLC)	While the development of an ALK kinase inhibitor has improved outcomes for the small subset of patients in whom ALK translocation-positive NSCLC has been confirmed, many patients who initially respond to currently available ALK inhibitors develop resistance to the therapy. Studies have identified multiple resistance mechanisms, including mutations to the ALK kinase domain and activation of the EGFR signaling pathway. AP26113 is a novel kinase inhibitor that has the potential to address both of these resistance mechanisms. AP26113 has activity against both resistant forms of the ALK kinase and activated forms of the EGFR kinase. ARIAD Pharmaceuticals, Inc., Cambridge, MA Phase I/II trial ongoing	Bevacizumab Cisplatin Crizotinib Pemetrexed	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Electro-immunotherapy (OncoSec Medical System) for treatment of metastatic melanoma	Patients in whom metastatic melanoma has been diagnosed	Patients with metastatic melanoma have a median survival time of about 18 months when treated with current therapies. The OncoSec Medical System™ is an electroporation device that is intended to enhance the ability of cells to take up DNA. In clinical trials, it is being used to enhance delivery of a plasmid encoding the cytokine interleukin-12 (IL-12). Expression of IL-12 by cancer cells could potentially stimulate a systemic immune response against tumor antigens. In the treatment, IL-12 plasmid is injected at the tumor site followed by electrical stimulation using the OncoSec Medical System. OncoSec Medical, Inc., San Diego, CA Phase I trial completed; phase II trial expected to begin enrollment by end of 2011	Dacarbazine Ipilimumab Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life
Ghrelin receptor agonist (anamorelin) for treatment of cancer-related cachexia/anorexia	Patients in whom cancer-related cachexia/anorexia (CRCA) has been diagnosed	While a number of treatments have been applied to CRCA, many patients do not respond to current treatment options. CRCA may limit the ability of patients to tolerate further treatment and/or directly affect survival. CRCA is caused by metabolic and neurochemical alterations in the body that lead to the loss of the desire to eat (anorexia) and the wasting of skeletal muscle mass (cachexia). Ghrelin, through its activity on the growth hormone secretagogue receptor, may increase appetite and inhibit leptin and proinflammatory cytokine expression. Anamorelin is an orally administered ghrelin receptor agonist that has the potential to address both the appetite and metabolic (e.g., proinflammatory) aspects of CRCA. In clinical trials it is being administered as a daily dose of 100 mg. Helsinn Healthcare S.A., Lugano/Pazzallo, Switzerland Phase III trials ongoing	Appetite stimulants: Cannabinoids Corticosteroids Cyproheptadine Progesterone derivatives Dietary counseling Melanocortin antagonists Metabolic disturbance modulators: Anti-cytokine antibodies, Pentoxifylline Thalidomide	Improved lean body mass Improved muscle strength Increased body weight Increased overall survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
HER2 therapeutic cancer vaccine (NeuVax) for breast cancer	Patients with HER2 HLA-A2 and/or HLA-A3 positive early stage breast cancer	While many patients in whom early-stage breast cancer has been diagnosed achieve remission after first-line chemotherapy, a significant proportion eventually have disease recurrence. While some patients undergo maintenance therapy with trastuzumab, only patients whose tumors express high levels of HER2 are eligible for trastuzumab. NeuVax™ is a therapeutic cancer vaccine that combines an HER2-derived peptide (E75) with the immune stimulant granulocyte-macrophage colony-stimulating factor (GM-CSF). The vaccine is designed to induce a cytotoxic T-cell response against cells expressing HER2. NeuVax is currently under study as maintenance therapy for patients whose tumors express low levels of the HER2 protein. RXi Pharmaceuticals Corp., Worcester, MA Phase III trial to begin under an FDA special protocol assessment in early 2012	Aromatase inhibitors Tamoxifen	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Histone deacetylase 6 inhibitor (ACY-1215) for treatment of multiple myeloma	Patients with treatment-resistant or recurrent multiple myeloma	While treatments for multiple myeloma have improved, the median life expectancy is only 5 to 7 years. ACY-1215 is a novel histone deacetylase (HDAC) inhibitor that is specific for HDAC6. While multiple HDAC inhibitors have come to market, none are approved for the treatment of multiple myeloma. In addition, currently available HDAC inhibitors are pan-HDAC inhibitors, which have inhibitory activity against a wide range of HDACs. By targeting HDAC6 specifically, ACY-1215 might avoid some of the toxicity associated with pan-HDAC inhibition. HDAC6 is purported to be an appropriate anticancer target because of its function in a protein degradation pathway known as the aggresome. Due to their high rate of protein production, cancer cells produce a large number of aggresome substrates (e.g., misfolded proteins) and HDAC6 may lead to the preferential accumulation of toxic levels of waste proteins in cancer cells. Acetylon Pharmaceuticals, Inc., Boston, MA Phase I/II trial ongoing	Bendamustine Bortezomib Bortezomib/ dexamethasone Bortezomib/lenalidomide/ dexamethasone Bortezomib/liposomal doxorubicin Cyclophosphamide/ bortezomib/ dexamethasone Cyclophosphamide/ lenalidomide/ dexamethasone Dexamethasone/ cyclophosphamide/ etoposide/cisplatin Dexamethasone/ thalidomide/cisplatin/ doxorubicin/ cyclophosphamide/ etoposide with or without bortezomib High-dose cyclophosphamide Lenalidomide/ dexamethasone Thalidomide/ dexamethasone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Histone deacetylase inhibitor (panobinostat) for prevention of recurrent Hodgkin's lymphoma	Patients with Hodgkin's lymphoma who have achieved complete remission after autologous peripheral blood/bone marrow stem cell transfusion	After treatment with high-dose chemotherapy and autologous peripheral blood/bone marrow stem cell transfusion, a significant proportion of this patient population will have disease progression. Therapies intended to maintain the complete response are needed. HDAC inhibitors are a class of anticancer drugs whose exact mechanism of action is unclear, but might be related to DNA damage repair inhibition or modification of cell cycle proteins. While two HDAC inhibitors (vorinostat and romidepsin) have been approved for treatment of cutaneous T-cell lymphoma, no HDAC inhibitor is currently approved for treatment of Hodgkin's lymphoma. Novartis AG, Basel, Switzerland Phase III trial ongoing	Placebo Watchful waiting	Increased overall survival Increased progression free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Histone deacetylase inhibitor (panobinostat) for treatment of relapsed multiple myeloma	Patients with multiple myeloma whose disease requires retreatment following at least one round of chemotherapy treatment	While treatments for multiple myeloma have improved, the median life expectancy for patients in whom multiple myeloma is diagnosed is only 5 to 7 years. Additionally, as several newer treatments for multiple myeloma have been moved into the frontline setting as combination therapies, additional salvage treatments are needed. HDAC inhibitors are a class of anticancer drugs whose exact mechanism of action is unclear, but might be related to DNA damage repair inhibition or modification of cell cycle proteins. While two HDAC inhibitors (vorinostat and romidepsin) have been approved for treatment of cutaneous T-cell lymphoma, no HDAC inhibitor is currently approved for treatment of multiple myeloma. In a currently ongoing registration-phase clinical trial, panobinostat is being tested in combination with the proteasome inhibitor bortezomib and the glucocorticosteroid dexamethasone. Novartis AG, Basel, Switzerland Phase III trial ongoing	Bendamustine Bortezomib Bortezomib/ dexamethasone Bortezomib/lenalidomide/ dexamethasone Bortezomib/liposomal doxorubicin Cyclophosphamide/ bortezomib/ dexamethasone Cyclophosphamide/ lenalidomide/ dexamethasone Dexamethasone/ cyclophosphamide/ etoposide/cisplatin Dexamethasone/ thalidomide/cisplatin/ doxorubicin/ cyclophosphamide/ etoposide with or without bortezomib High-dose cyclophosphamide Lenalidomide/ dexamethasone Thalidomide/ dexamethasone	Increased overall survival Increased progression-free survival Improved patient quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Histone deacetylase inhibitor (vorinostat) for treatment of multiple myeloma	Patients with multiple myeloma who have undergone at least one prior round of chemotherapy	While treatments for multiple myeloma have improved, the median life expectancy for patients in whom multiple myeloma is diagnosed is only 5 to 7 years. Additionally, as several newer treatments for multiple myeloma have been moved into the frontline setting as combination therapies, additional salvage treatments are needed. HDAC inhibitors are a class of anticancer drugs whose exact mechanism of action is unclear, but might be related to DNA damage repair inhibition or modification of cell cycle proteins. While two HDAC inhibitors (vorinostat and romidepsin) have been approved for treatment of cutaneous T-cell lymphoma, no HDAC inhibitor is currently approved for treatment of multiple myeloma. In a currently ongoing pivotal clinical trial, vorinostat (oral tablets at 400 mg/day) is being tested in combination with the proteasome inhibitor bortezomib. Merck & Co. Inc., Whitehouse Station, NJ Phase III trial ongoing	Bendamustine Bortezomib Bortezomib/ dexamethasone Bortezomib/lenalidomide/ dexamethasone Bortezomib/liposomal doxorubicin Cyclophosphamide/ bortezomib/dexamethasone Cyclophosphamide/ lenalidomide/ dexamethasone Dexamethasone/ cyclophosphamide/ etoposide/cisplatin Dexamethasone/ thalidomide/cisplatin/ doxorubicin/ cyclophosphamide/ etoposide with or without bortezomib High-dose cyclophosphamide Lenalidomide/ dexamethasone Thalidomide/ dexamethasone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Hsp90 inhibitor (ganetespib) for treatment of advanced nonsmall cell lung cancer (NSCLC)	Patients with treatment-resistant, advanced or metastatic NSCLC	Patients with advanced NSCLC that has progressed after prior chemotherapy have a poor prognosis and few treatment options. Ganetespib is a novel anticancer agent that acts as an inhibitor of hsp90 activity. Hsp90 is a molecular chaperone that is responsible for the proper folding and stability of a wide range of proteins in the cell. In particular, hsp90 has been implicated in maintaining the stability of multiple mutated proteins with proneoplastic properties including mutated p53, BCR-ABL, Raf-1, Akt, ErbB2, and hypoxia-inducible factor 1 alpha. In addition, hsp90 has been shown to increase the activity of proteins known to have a cytoprotective effect in cells exposed to cytotoxic chemotherapy; therefore, hsp90 inhibition might act synergistically with cytotoxic agents. In the treatment of NSCLC, ganetespib is being tested as an adjunct to the cytotoxic agent docetaxel. Synta Pharmaceuticals Corp., Lexington, MA Phase II/III trial ongoing	Docetaxel monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Huachansu for treatment of pancreatic cancer	Patients in whom pancreatic cancer has been diagnosed	Patients in whom pancreatic cancer has been diagnosed have few treatment options and poor prognosis. Huachansu is a traditional Chinese medicine derived from Bufo toad venom. The agent is delivered intravenously. It has been approved in China for use against lung cancer, liver cancer, and pancreatic cancer. In current clinical trials for pancreatic cancer, huachansu is administered by intravenous infusion in combination with the standard chemotherapy drug gemcitabine and is intended for use as part of first-line treatment. MD Anderson Cancer Center, Houston, TX Phase II trial ongoing	5-Fluorouracil/leucovorin Gemcitabine alone	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Hypoxia-activated DNA alkylating agent (TH-302) for treatment of advanced and metastatic soft tissue sarcoma	Patients in whom locally advanced unresectable or metastatic soft tissue sarcoma has been diagnosed	The disordered growth of tumors often leads to areas of tissues with inadequate blood supply, leading to hypoxic conditions. These hypoxic areas of tumors are often refractory to conventional chemotherapy because of the tissues' inaccessibility to standard drugs and/or slow rate of cell division. TH-302 is a novel cytotoxic agent that is purported to be preferentially activated in hypoxic conditions. In its activated form, TH-302 is a potent DNA alkylating agent (dibromo isophoramide mustard). Selective activation of TH-302 in hypoxic conditions might target alkylating activity to tumors. In clinical trials for soft tissue sarcoma, TH-302 is being used as first-line therapy in combination with doxorubicin to try to target both the hypoxic and normoxic regions of the tumor. Threshold Pharmaceuticals, South San Francisco, CA Phase III trial ongoing	Doxorubicin monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Interleukin-3 receptor-targeting biologic conjugate (SL-401) for treatment-refractory acute myeloid leukemia	Patients with treatment-refractory acute myeloid leukemia (AML)	Patients with treatment-refractory AML have few treatment options and typically survive for less than a year when disease recurs. SL-401 is a novel biologic conjugate between interleukin-3 (IL-3) and diphtheria toxin that targets cells expressing the IL-3 receptor (CD123). The IL-3 receptor has been shown to be expressed by leukemic cells known as cancer stem cells, which may be highly resistant to conventional chemotherapy and have high potential to cause recurrence. SL-401 is intended to target the cancer stem cell component of AML. Stemline Therapeutics, Inc., New York, NY Phase I/II trial complete; FDA granted orphan drug status	Cladribine/cytarabine/ GM-CSF plus or minus mitoxantrone or idarubicin High dose cytarabine/ anthracycline Fludarabine/cytarabine/ GM-CSF plus or minus idarubicin Mitoxantrone/etoposide/ cytarabine	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Irreversible electroporation (NanoKnife) for treatment of hepatocellular carcinoma	Patients in whom early-stage hepatocellular carcinoma that is not surgically resectable has been diagnosed	Surgical resection and/or ablation of locally advanced tumors is the only potentially curative treatment option for patients in whom hepatocellular cancer has been diagnosed. However, many patients are not eligible for surgical resection because the location of their tumors is in close proximity to essential structures (e.g., major blood vessels). The NanoKnife® system uses a novel treatment modality known as irreversible electroporation in which pulses of high-voltage direct current are applied to the target tissue using needle-like electrodes, a process that induces the irreversible formation of nanopores in cellular membranes. The formation of these nanopores is highly toxic to cells, leading to cell death via an apoptosis-like process. Unlike other local ablation technologies (e.g., radiofrequency ablation, cryotherapy), irreversible electroporation does not suffer "heat sink" effects and can leave the extracellular structure of large blood vessels intact, potentially allowing local ablation of tumors in close proximity to vessels while retaining vessel patency. In treatment of hepatocellular carcinoma, irreversible electroporation is performed in a minimally invasive laparoscopic procedure. AngioDynamics, Latham, NY Phase II trial ongoing; cleared by FDA through the 510(k) process for the surgical ablation of soft tissue; under investigational device exemption status for a premarket approval (PMA) application for this indication	Cryotherapy Radiofrequency ablation	Increased overall survival Increased clinical downstaging to surgically resectable tumor Improved adverse event profile Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Irreversible electroporation (NanoKnife) for treatment of pancreatic cancer	Patients in whom locally advanced pancreatic cancer that is not resectable by surgery has been diagnosed	Surgical resection and/or ablation of locally advanced tumors is the only potentially curative treatment option for patients in whom pancreatic cancer has been diagnosed. However, many patients are not eligible for surgical resection because the location of their tumors is in close proximity to essential structures (e.g., major blood vessels). The NanoKnife system uses a novel treatment modality known as irreversible electroporation in which pulses of high voltage direct current are applied to the target tissue using needle-like electrodes, a process that induces the irreversible formation of nanopores in cellular membranes. The formation of these nanopores is highly toxic to cells, leading to cell death via an apoptosis-like process. Unlike other local ablation technologies (e.g., radiofrequency ablation, cryotherapy), irreversible electroporation does not suffer "heat sink" effects and can leave the extracellular structure of large blood vessels intact, potentially allowing local ablation of tumors in close proximity to vessels while retaining vessel patency. In treatment of pancreatic cancer, irreversible electroporation is performed in a minimally invasive laparoscopic procedure. AngioDynamics, Latham, NY Phase II trial ongoing; cleared by FDA through the 510(k) process for the surgical ablation of soft tissue; in trials for various cancer applications under PMA process	Cryotherapy Radiofrequency ablation	Increased overall survival Increased rate of clinical downstaging to surgically tumor Improved adverse event profile Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
KRN5500 for treatment of chronic cancer pain	Patients with chronic cancer pain, especially chemotherapy-induced neuropathic pain	Current pain management medications are not always effective in controlling chronic cancer pain and their long-term use carries significant side effects (e.g., constipation, nausea, possible opioid addiction, kidney damage, gastrointestinal [GI] bleeding associated with nonsteroidal antiinflammatory drugs [NSAIDs]). KRN5500 is a novel spicamycin derivative that was originally identified as a potential cancer treatment, a compound that could induce differentiation of myeloid leukemia cells. While KRN5500 did not exhibit efficacy against leukemia, one patient with chronic neuropathic pain from previous cancer treatments experienced significant relief from that pain. Additional studies of KRN500 for pain have been undertaken. DARA BioSciences, Inc., Raleigh, NC Phase II trial completed; FDA granted fast-track status	NSAIDs Opioid analgesics	Reduced pain Improved quality of life
Liposome encapsulated irinotecan (MM-398) for treatment of pancreatic cancer	Patients with treatment-refractory, metastatic pancreatic cancer	Only approximately 25% of patients with metastatic pancreatic cancer have disease that responds to first-line therapy with gemcitabine; patients have poor prognosis with current second-line treatment options. MM-398 (PEP-02) is a novel formulation of the topoisomerase 1 inhibitor irinotecan that encapsulates the drug in liposomal particles and is intended to be used as a second-line treatment. Liposomal encapsulation of irinotecan has three potential benefits: (1) liposomal particles may preferentially accumulate in tumor tissues because of increased porosity of tumor vasculature; (2) liposomes may provide slow release of the active drug, potentially increasing duration of exposure to therapeutic dose; and (3) irinotecan is hydrolyzed to a relatively inert form in aqueous solutions and liposomal encapsulation might protect the drug from this hydrolysis. In clinical trials, MM-398 is being administered by intravenous infusion as a monotherapy. Merrimack Pharmaceuticals, Inc., Cambridge, MA Phase III trial to begin late 2011/early 2012; FDA granted orphan drug status for second-line treatment of pancreatic cancer	5-Fluorouracil/ leucovorin/oxaliplatin Capecitabine Capecitabine/oxaliplatin Gemcitabine	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Marine depsipeptide (plitidepsin) for treatment of relapsed/refractory multiple myeloma	Patients with multiple myeloma who have undergone at least three treatments, including bortezomib- and lenalidomide-based regimens	While treatments for multiple myeloma have improved, the median life expectancy for patients in whom multiple myeloma is diagnosed is only 5 to 7 years. Additionally, as several newer treatments for multiple myeloma have been moved into the frontline setting as combination therapies, additional salvage treatments are needed. Plitidepsin is a cyclodepsipeptide that demonstrated anticancer activity in preclinical studies and was isolated from the tunicate *Aplidium albicans*. The purported mechanism of action of plitidepsin is the induction of cell cycle arrest and apoptosis through the induction of oxidative stress, activation of Rac1, and the sustained activation of Jun N-terminal kinase and p38 MAP kinase. In a late-stage clinical trial for treatment of multiple myeloma, plitidepsin is being administered by infusion at a dose of 5 mg/m^2 in combination with orally administered dexamethasone. PharmaMar subsidiary of Grupo Zeltia, Madrid, Spain Phase III trial ongoing	Various chemotherapy regimens such as: Bendamustine/bortezomib Bortezomib/ dexamethasone Bortezomib/lenalidomide/ dexamethasone Cyclophosphamide/ lenalidomide/ dexamethasone Dexamethasone/ cyclophosphamide/ etoposide/cisplatin High-dose cyclophosphamide Lenalidomide/ dexamethasone Thalidomide/ dexamethasone	Increased overall survival Increased progression-free survival Improved quality of life
MEK inhibitor (AZD6244) for treatment of advanced solid tumors	Patients in whom advanced solid cancers have been diagnosed	The mitogen-activated protein kinase (MAPK)/extracellular-signal-regulated kinase (ERK) pathway is a central regulator of cellular responses to growth signals. Aberrant activity of this pathway has been implicated in the development of many cancer types. The MAPK kinase (MEK) is a protein kinase that plays a role in this pathway by controlling activation of ERK; therefore, inhibition of MEK activity could inhibit cancer cell growth and/or survival. However, no MEK inhibitor is currently available. AZD6244 is an orally administered, MEK inhibitor under study for the treatment of various cancers, including ovarian cancer, colorectal cancer (CRC), melanoma, and hepatocellular carcinoma. AstraZeneca, London, UK Phase II trials ongoing	Standard chemotherapeutic regimens	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mitochondrial metabolism inhibitor (elesclomol) for treatment of ovarian cancer	Patients in whom platinum-resistant ovarian cancer has been diagnosed	Patients with platinum-resistant ovarian cancer have a poor prognosis with current treatment options. Elesclomol is a novel agent intended to induce apoptosis and is purported to act by transporting copper into the cell where it is reduced from copper(II) to copper(I) in the mitochondria. This causes a series of redox reactions that perturb mitochondrial energy production and lead to apoptosis. Elesclomol is administered by intravenous infusion, and in current clinical trials it is being administered in combination with the cytotoxic agent paclitaxel. Synta Pharmaceuticals Corp., Lexington, MA Phase II trial ongoing (Gynecologic Oncology Group funded by National Cancer Institute)	Docetaxel Etoposide Gemcitabine Liposomal doxorubicin Paclitaxel Topotecan	Increased overall survival Increased progression-free survival Improved quality of life
Multikinase inhibitor (intedanib, Vargatef) for chemotherapy-resistant ovarian cancer	Patients in whom chemotherapy-naive treatment-resistant ovarian cancer has been diagnosed	A significant fraction of patients with ovarian cancer have disease that is resistant or refractory to current first-line treatments. Intedanib (Vargatef™) is a tyrosine kinase inhibitor that has activity against vascular endothelial growth factor receptor (VEGFR), platelet-derived growth factor receptor (PDGFR), and fibroblast growth factor receptor (FGFR) tyrosine kinases, which regulate tumor growth and angiogenesis. In late-phase clinical trials, intedanib is being tested as an adjunct to the conventional first-line therapy of intravenous carboplatin plus paclitaxel. Intedanib is administered as an oral tablet, twice daily. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trial ongoing	Intraperitoneal carboplatin/paclitaxel Intravenous carboplatin/paclitaxel	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Multikinase inhibitor (intedanib; Vargatef) for treatment-resistant nonsmall cell lung cancer (NSCLC)	Patients with NSCLC whose disease has progressed during or after first-line systemic chemotherapy	The 5-year survival rate for patients in whom NSCLC has been diagnosed is less than 15%, and patients whose disease progresses following first-line chemotherapy have few treatment options. Intedanib is a tyrosine kinase inhibitor that has activity against VEGFR, PDGFR, and FGFR tyrosine kinases, which regulate tumor growth and angiogenesis. In late-phase clinical trials, intedanib is being tested as an adjunct to conventional second-line therapies (pemetrexed monotherapy or docetaxel monotherapy). Intedanib is administered as an oral tablet, twice daily. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing	Various combination therapies that include: Bevacizumab Carboplatin Crizotinib Docetaxel Erlotinib Pemetrexed	Increased overall survival Increased progression-free survival Improved quality of life
Multikinase inhibitor (masitinib) for treatment of activating *c-kit* mutation-positive, metastatic melanoma	Patients with non-resectable or metastatic melanoma that harbors an activating mutation in the *c-kit* gene	A subset of melanomas harbor an activating mutation in the *c-kit* gene, which encodes a receptor tyrosine kinase (mast/stem cell growth factor receptor, KIT, CD117). In particular, between 10% and 20% of acral and mucosal melanomas harbor activating *c-kit* mutations. While KIT kinase inhibitors have been developed for other cancers dependent on KIT activity (e.g., imatinib for treatment of gastrointestinal stromal tumors [GIST]), currently no KIT kinase inhibitor is approved for treatment of *c-kit* mutation-positive melanoma. Masitinib is an orally administered, kinase inhibitor with activity against KIT as well as PDGFRs, the intracellular kinase Lyn, and to a lesser extent FGFR-3. Masitinib is currently under study as a monotherapy for treatment of melanoma. AB Science S.A., Paris, France Phase III trial ongoing	Dacarbazine Interleukin-2 (IL-2) Ipilimumab Nilotinib (in development)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Multikinase inhibitor (nilotinib, Tasigna) for treatment of activating *c-kit* mutation-positive, metastatic melanoma	Patients with non-resectable or metastatic melanoma who harbor an activating *c-kit* mutation	A subset of melanomas harbor an activating mutation in the *c-kit* gene, which encodes a receptor tyrosine kinase (mast/stem cell growth factor receptor, KIT, CD117). In particular, between 10% and 20% of acral and mucosal melanomas harbor activating *c-kit* mutations. While KIT kinase inhibitors have been developed for other cancers dependent on KIT activity (e.g., imatinib for treatment of GIST), currently no KIT kinase inhibitor is approved for treatment of *c-kit* mutation-positive melanoma. Nilotinib (Tasigna®) is an orally administered, tyrosine kinase inhibitor approved for the treatment of Philadelphia chromosome-positive CML. In addition to inhibiting the Philadelphia chromosome-encoded BCR-ABL, nilotinib also has activity against KIT and a number of additional kinases. Nilotinib is currently under study as a monotherapy for treatment of melanoma. Novartis AG, Basel, Switzerland Phase II trial ongoing	Dacarbazine IL-2 Ipilimumab Masitinib (in development)	Increased overall survival Increased progression-free survival Improved quality of life
Multikinase inhibitor (pazopanib, Votrient) to prevent recurrence of ovarian cancer after successful first-line therapy	Patients with stage II to IV ovarian cancer, fallopian tube, or primary peritoneal carcinoma who have undergone surgical debulking and successful treatment with platinum agent/taxane combination therapy	Patients in whom ovarian cancer is diagnosed often respond to first-line treatment with cytoreduction and chemotherapy; however, a large number of these patients will experience disease recurrence and therapies intended to prolong remission are needed. Pazopanib (Votrient™) is a tyrosine kinase inhibitor with activity against multiple kinases including VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-alpha/beta, and c-kit. Inhibition of these kinases may limit tumor angiogenesis and/or tumor growth. In late-phase clinical trials, pazopanib is administered as an oral tablet at a dose of 800 mg/day for up to 2 years. GlaxoSmithKline, London, UK Phase III trial ongoing; FDA approved for renal cell carcinoma	Bevacizumab may be used as maintenance therapy after bevacizumab-containing treatment regimens Paclitaxel Watchful waiting	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
P53 activator (APR-246) for treatment of hematologic malignancies or prostate cancer	Patients with a hematologic malignancy or prostate cancer	*P53* is a tumor-suppressor gene that plays a prominent role in promoting apoptosis. The loss of *p53* function is associated with many cancer types; however, no therapy attempting to restore *p53* function is currently available. APR-246 is a small, peptide molecule that has been shown to promote restoration of the transcriptional activity of mutated *p53*, potentially restoring *p53* function and apoptosis of cancer cells. Aprea AB, Solna, Sweden Phase I/II trial completed	Various cancer therapies	Increased overall survival Increased progression-free survival Improved quality of life
Pan-RAF inhibitor (MLN-2480) for treatment of metastatic melanoma	Patients in whom metastatic melanoma has been diagnosed	The identification of activating *B-RAF* mutations in approximately 50% of melanomas, and the demonstrated antimelanoma activity of B-RAF inhibitors has implicated the centrality of RAF kinase activity in the pathogenesis of melanoma. While targeting *B-RAF* has demonstrated significant anticancer activity, its activity is limited to the subset of melanomas with activating *B-RAF* mutations, and the majority of these cancers develop resistance to *B-RAF* inhibition. Pan-RAF inhibition might allow targeting of a wider range of melanomas and/or overcome some of the resistance mechanisms associated with *B-RAF* inhibition. Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase I trial ongoing	Dacarbazine Ipilimumab Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pegylated human recombinant hyaluronidase (PEG-PH20) for treatment of pancreatic cancer	Patients with metastatic pancreatic cancer and no prior treatment	Only approximately 25% of patients with metastatic pancreatic cancer have disease that responds to first-line therapy with gemcitabine; effective treatments are needed for those whose disease does not respond. PEG-PH20 is a formulation of the enzyme hyaluronidase, which functions to degrade the hyaluronan (HA) component of the extracellular matrix. HA is a gel-like substance that is a component of normal tissues of the body (e.g., skin, cartilage), but it also forms a layer on the surface of tumors, which may limit exposure of the tumor to therapeutic compounds. PEG-PH20 is purported to temporarily degrade HA, potentially increasing the efficacy of chemotherapy. In clinical trials for treatment of pancreatic cancer, PEG-PH20 is being administered in combination with the standard chemotherapy drug gemcitabine. Halozyme Therapeutics, San Diego, CA Phase II trial ongoing	5-Fluorouracil/leucovorin Gemcitabine	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-loaded dendritic cell vaccine (SL-701) for treatment of recurrent glioma	Patients in whom HLA-A2 positive high-grade recurrent glioma has been diagnosed	Median survival of patients with malignant glioma is about 15 months, and current treatments are often ineffective. SL-701 is a therapeutic cancer vaccine that consists of autologous DCs preloaded with a set of HLA-A2-restricted peptides derived from glioma associated antigens (EphA2, interleukin-13 R alpha2, YKL-40, and gp100). The vaccine is administered in combination with an immunostimulant (Poly ICLC). Stemline Therapeutics, Inc., New York, NY Phase I/II trial ongoing	Temozolomide chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PET-based tumor hypoxia imaging to inform personalization of cancer treatment	Patients in whom a solid tumor has been diagnosed	Tumor cells may adapt to hypoxic conditions in such a way that renders them less susceptible to the effects of radiation therapy and/or chemotherapy. Therefore, the identification of hypoxic tumor regions might allow the physician to adapt the radiation therapy or chemotherapeutic dose to more efficiently target tumor cells. Several agents that could potentially allow identification of hypoxic regions of tumors through the use of positron emission tomography (PET) imaging are currently under development. Alberta Health Services, Edmonton, Alberta, Canada (FAZA) Siemens AG. Munich, Germany (HX4) University of Wisconsin, Madison, WI (Cu-ATSM) Washington University, St. Louis, MO (Cu-ATSM) Phase II trials ongoing	No currently available in vivo hypoxia imaging technology	Concurrence with immunohisto-chemical markers of hypoxia (e.g., HIF1-alpha, CA-IX) Improved prognosticating and treatment decision making Increased overall survival Increased progression-free survival Improved quality of life
Phosphatidylinositol -3-kinase inhibitor (GDC-0941) for treatment of breast cancer	Postmenopausal women with ER-positive, metastatic breast cancer that is resistant to aromatase inhibitor therapy	Women with ER-positive, metastatic breast cancer that is resistant to aromatase inhibitor therapy have a poor prognosis (median survival of less than a year) and few treatment options. Phosphatidylinositol-3-kinases (PI3Ks) are a family of kinases that function in a signal transduction pathway controlling multiple cellular activities related to cancer (e.g., apoptosis, angiogenesis, cell growth and proliferation, cell migration and metastasis). Aberrant PI3K activity has been identified in multiple cancer types. GDC-0941 is an inhibitor of PI3K activity that is currently under study as an adjunct to treatment with the ER antagonist fulvestrant. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trial ongoing	Fulvestrant	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Phosphatidylinositol -3-kinase inhibitor (PX-866) for treatment of castration-resistant prostate cancer (CRPC)	Patients in whom symptomatic CRPC has been diagnosed	Patients with CRPC have few treatment options and median overall survival is less than 2 years. PI3Ks are a family of kinases that function in a signal transduction pathway controlling multiple cellular activities related to cancer (e.g., apoptosis, angiogenesis, cell growth and proliferation, cell migration and metastasis). Aberrant PI3K activity has been identified in multiple cancer types. PX-866 is a derivative of the well-characterized PI3K inhibitor wortmannin. Like wortmannin, PX-866 irreversibly inhibits all four class I PI3Ks; however, it has been modified to improve its stability, toxicity profile, and biologic activity. PX-866 is administered orally and is under study as a first-line monotherapy in clinical trials on treatment of symptomatic CRPC. Oncothyreon, Inc., Seattle, WA Phase II trial ongoing	Docetaxel plus prednisone Docetaxel/prednisone/ dasatinib (under development) Docetaxel/prednisone/ lenalidomide (under development)	Increased overall survival Increased progression-free survival Improved quality of life
Photodynamic therapy (Cevira System) with hexaminolevulinate ointment for cervical intraepithelial neoplasia	Patients in whom low-grade cervical intraepithelial neoplasia has been diagnosed	Current treatment options for cervical intraepithelial neoplasia have the potential to cause damage to surrounding healthy tissue and to cause side effects such as posttreatment infections. The Cevira System® consists of a photosensitive drug (hexaminolevulinate ointment), which preferentially accumulates in diseased tissue. The disposable device is fitted inside the vaginal cavity so that it remains in contact with the cervix while it delivers treatment over a period of 10 hours. A cup holds the ointment against the cervix and once the ointment is absorbed, a few hours later, a light source within the cup emits light at a specific wavelength continuously over several hours to deliver the therapy. Photocure ASA, Oslo, Norway, in collaboration with Sagentia, Ltd., Cambridge, UK Phase II U.S.-based trial planned	Cryotherapy Laser therapy Loop electrosurgical excision Surgical conization	Complete lesion eradication

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Photodynamic therapy using Tookad for localized prostate cancer	Patients in whom localized low-risk prostate cancer has been diagnosed	Current treatment of localized prostate cancer can adversely affect surrounding healthy tissue and also lead to debilitating temporary and long-term side effects or complications. Tookad is a photosensitive agent that can be excited by a specific wavelength of light to release energy that can cause local necrosis. In a photodynamic therapy procedure using Tookad, the drug is injected by needle into the prostate. After the drug diffuses into the prostate, laser light is used to excite the drug, potentially leading to destruction of targeted prostate tissue while sparing surrounding healthy tissue. Steba Biotech S.A., Cedex, France Phase III trial ongoing	Radiation therapy Radical prostatectomy Watchful waiting	Increased overall survival Increased progression-free survival Fewer therapy-related side effects Improved quality of life
Rexin-G for treatment of chemotherapy-resistant, metastatic pancreatic cancer	Patients with gemcitabine-resistant, metastatic pancreatic cancer	Patients with gemcitabine-resistant pancreatic cancer have very poor prognoses and few treatment options. Rexin-G is a viral vector that encodes a dominant negative version of cyclin G1. Cyclin G1 is a central mediator of cell cycle progression, and its inhibition leads to cell-cycle arrest and apoptosis. The viral vector is targeted to cancerous sites by the incorporation of a collagen-binding peptide into the viral coat. Collagen is preferentially exposed on cells involved in rearrangement associated with tumor invasion, angiogenesis, and stroma formation. Epeius Biotechnologies, San Marino, CA Phase III trial planned	Fluoropyrimidine-based chemotherapy (e.g., folfirinox)	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Rexin-G for treatment of chemotherapy-resistant sarcoma	Patients with chemotherapy-resistant, recurrent or metastatic soft tissue sarcoma	Patients with chemotherapy-resistant, recurrent or metastatic soft tissue sarcoma have no effective therapeutic options when their disease fails to respond to currently available chemotherapy. Rexin-G is a viral vector that encodes a dominant negative version of cyclin G1. Cyclin G1 is a central mediator of cell-cycle progression, and its inhibition leads to cell cycle arrest and apoptosis. The viral vector is targeted to cancerous sites by the incorporation of a collagen-binding peptide into the viral coat. Collagen is preferentially exposed on cells involved in rearrangement associated with tumor invasion, angiogenesis, and stroma formation. Epeius Biotechnologies, San Marino, CA Phase I/II trial complete; phase III trial planned	Placebo (patients' cancers have progressed after multiple rounds of conventional chemotherapy)	Increased overall survival Increased progression-free survival Improved quality of life
Selective estrogen receptor alpha agonist (Capesaris) for treatment of advanced prostate cancer	Patients in whom advanced prostate cancer has been diagnosed	Current treatment of advanced prostate cancer uses medical or surgical castration to reduce testosterone. However, current mechanisms of antiandrogen therapy result in significant side effects such as bone loss and hot flashes, which may lead to patient morbidity or poor treatment adherence. Capesaris™ (GTx-758)is a novel antiandrogen therapy that acts as a selective ER-alpha agonist to achieve castration levels of testosterone through feedback inhibition of the pituitary and hypothalamus without causing bone loss and hot flashes. GTx, Inc., Memphis, TN Phase II trial completed; additional phase II trials ongoing	Bilateral orchiectomy Luteinizing-hormone-releasing hormone (LHRH) agonists	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Small-molecule drug conjugate (EC145) for treatment of platinum-resistant ovarian cancer	Patients with platinum-resistant ovarian cancer who have undergone one or two rounds of platinum-based chemotherapy	Patients in whom platinum-resistant ovarian cancer has been diagnosed have a poor prognosis and few treatment options. EC145 is a novel, small-molecule drug conjugate that uses a peptide linker to couple a targeting ligand to a cytotoxic agent. In EC145, the targeting ligand is specific for the folate receptor, which is expressed on the majority of ovarian cancer cells, but not on cells of normal tissue. Based on this difference, the cytotoxic drug linked to the folate receptor targeting ligand might be preferentially delivered to malignant cells. EC145 is administered intravenously and is being studied in combination with pegylated liposomal doxorubicin. Endoctye, Inc., West Lafayette, IN Phase III trial ongoing	Pegylated liposomal doxorubicin Docetaxel Etoposide Gemcitabine Paclitaxel Topotecan	Increased overall survival Increased progression-free survival Improved quality of life
Sotatercept (ACE-011) for treatment of chemotherapy-induced anemia	Patients in whom anemia following chemotherapy has been diagnosed	Anemia is one of the most common and debilitating complications of cancer chemotherapy, often significantly reducing the number of red blood cells (RBC) and preventing RBC production. Anemia is commonly treated with therapies targeting the erythropoietin pathway; however, therapies targeting this pathway have exposed patients to increased risk of tumor stimulation and progression, as well as increased risk of thrombosis. ACE-011 is a soluble form of the activin receptor type IIA (ActRIIA), and it inhibits signaling of several members of the transforming growth factor-beta protein super family, responsible for stimulation of RBC production, cell type differentiation, bone formation, and inhibition of tumor growth and metastasis. ACE-011 is administered via subcutaneous injection, every 42 days, up to four doses/cycles at 15, 30, or 45 mg. Celgene Corp., Summit, NJ, in collaboration with Acceleron Pharma, Inc., Cambridge, MA Phase II/III trial ongoing	Erythropoiesis stimulating agents	Decreased risk of thrombosis and tumor stimulation Increased hemoglobin levels Reduced fatigue and inflammation Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Survivin antisense inhibitor (LY2181308) for treatment of castration-resistant prostate cancer (CRPC)	Patients in whom CRPC has been diagnosed	Patients in whom CRPC has been diagnosed who undergo treatment with docetaxel have a median survival of only about 2 years. LY2181308 is an antisense drug that targets the messenger RNA of survivin, a protein that is overexpressed specifically in a number of cancers. Survivin (BIRC5) has been shown to inhibit the activation of pro-apoptotic caspases. Inhibition of survivin may increase caspase activity and lead to cancer cell apoptosis. In the current clinical trial, LY2181308 is being administered intravenously as an adjunct to the standard chemotherapy agent docetaxel. Eli Lilly and Co., Indianapolis, IN (licensed from ISIS Pharmaceuticals, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ) Phase II trial ongoing	Abiraterone Docetaxel	Increased overall survival Increased progression-free survival Improved quality of life
Survivin antisense inhibitor (LY2181308) for treatment of metastatic nonsmall cell lung cancer (NSCLC)	Patients with treatment-resistant, metastatic NSCLC	Patients with advanced NSCLC that has progressed after chemotherapy have a poor prognosis and few treatment options. LY2181308 is an antisense drug that targets the messenger RNA of survivin, a protein that is overexpressed specifically in a number of cancers. Survivin (BIRC5) has been shown to inhibit the activation of pro-apoptotic caspases. Inhibition of survivin may increase caspase activity and lead to cancer cell apoptosis. In the current clinical trial, LY2181308 is being administered intravenously as an adjunct to the standard second-line chemotherapy drug docetaxel. Eli Lilly and Co., Indianapolis, IN (licensed from ISIS Pharmaceuticals, a unit of Johnson & Johnson, Inc., New Brunswick, NJ) Phase II trial ongoing	Combination therapy: Bevacizumab, cisplatin, docetaxel, pemetrexed Monotherapy for appropriately selected patients: Crizotinib Erlotinib	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Targeted cytotoxic luteinizing-hormone-releasing hormone analog (AEZS-108) for treatment of luteinizing-hormone-releasing hormone-receptor-positive cancers	Patients in whom LHRH receptor-expressing cancer has been diagnosed, including ovarian, endometrial, prostate, or bladder cancer	Cytotoxic chemotherapy such as doxorubicin has proven anticancer effects; however, efficacy is inhibited by dose-limiting toxicities on normal tissues. AEZS-108 is a conjugate between an LHRH analog and doxorubicin. The LHRH analog targets cells that express the LHRH receptor, which includes the cells of many cancer types. Compared with naked doxorubicin, AEZS-108 is purported to preferentially target LHRH receptor-expressing cells, potentially sparing normal tissue from the toxic effects of the conjugated chemotherapeutic agent. In trials, the agent is being given as an intravenous infusion in doses of 128, 160, 210 or 267 mg/m^2, every 3 weeks, up to six treatment cycles. AEterna Zentaris, Inc., Quebec, Quebec, Canada Phase II trials ongoing	Doxorubicin	Increased overall survival Increased progression-free survival Improved quality of life
Therapeutic cancer vaccine (GI-4000) for pancreatic cancer harboring activating RAS mutations	Patients with surgically resectable pancreatic cancer that expresses an activated form of RAS	Patients in whom pancreatic cancer has been diagnosed who have undergone surgical resection of the primary tumor have median survival of about 2 years with current adjuvant chemotherapy options. GI-4000 is a novel immune therapy that targets pancreatic cancers harboring an activating mutation in the *RAS* gene, which is present in the majority of pancreatic cancers. GI-4000 is composed of heat-killed yeast cells that have been genetically modified to express a tumor-specific antigen; in the case of GI-4000, activated RAS. The modified yeast cells are purportedly taken up by antigen-presenting cells of the immune system and elicit a cytotoxic T-cell response targeted to antigens derived from activated RAS produced by cancer cells. In clinical trials, GI-4000 is administered subcutaneously in combination with the first-line standard adjuvant chemotherapy drug gemcitabine. GlobeImmune, Inc., Louisville, CO Phase II trial ongoing	5-Fluorouracil/leucovorin Gemcitabine	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Topoisomerase I inhibitor-polymer conjugate (NKTR-102) for treatment-resistant, metastatic breast cancer	Patients with metastatic breast cancer whose disease has progressed after two systemic chemotherapy regimens including anthracycline-, taxane-, and capecitabine-containing regimens	Patients with metastatic breast cancer that has progressed on anthracycline-, taxane-, and capecitabine-containing regimens have few treatment options and poor prognosis. NKTR-102 is a novel formulation of the topoisomerase I inhibitor irinotecan. While approved for treatment of CRC, irinotecan is not currently indicated for treatment of breast cancer. NKTR-102 is a modified version of irinotecan in which the drug is linked to a macromolecule core. The linkage is purported to render the drug inert in the bloodstream and allow the slow release of the drug as the linkages are metabolized in the patient. Slow release extends the time during which the patient's disease is exposed to therapeutic levels of the drug, thus limiting exposure to high levels of the drug at the time of infusion. Additionally, the large drug-polymer conjugate may preferentially accumulate in tumor tissues because of the increased permeability of tumor vasculature. Nektar Therapeutics, San Francisco, CA Phase III trial planned for end of 2011	Eribulin Gemcitabine Ixabepilone Pemetrexed Vinorelbine	Increased overall survival Increased progression-free survival Improved quality of life
Transferrin targeted anticancer agent (NKP-1339) for treatment of metastatic cancer	Patients in whom metastatic cancer has been diagnosed	Many metastatic cancers are unresponsive to current treatments, and new treatments are needed. NKP-1339 is a novel cancer drug that targets the body's natural iron transporter (transferrin), the receptor for which is highly expressed on cancer cells because of these cells' elevated iron requirements. NKP-1339 is injected in an inert form that mimics transferrin and binds to the transferrin receptor. Upon binding, the receptor/drug complex is internalized and the drug becomes activated upon exposure to the redox state of the cytosol. The activated drug leads to the production of free radicals, which potentially lead to apoptosis (programmed cell death). Niiki Pharma, Inc., Hoboken, NJ Phase I trial ongoing	Various anticancer therapies	Increased overall survival Increased progression-free survival Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tryptophan hydroxylase inhibitor (telotristat etiprate, LX1032) for treatment of neuroendocrine tumor-associated carcinoid syndrome	Patients in whom metastatic neuroendocrine tumor-associated carcinoid syndrome has been diagnosed	Patients with carcinoid tumors that are not amenable to surgical resection have few treatment options to control disease symptoms, and not all patients respond to current therapies. A hallmark of many carcinoid tumors is the overproduction of serotonin, which leads to complications such as severe diarrhea, flushing, and cardiac damage. Telotristat etiprate (LX1032) is intended to reduce systemic serotonin levels by inhibiting an enzyme involved in the synthesis of serotonin, tryptophan hydroxylase. Lexicon Pharmaceuticals, Inc., The Woodlands, TX Phase II trials completed; FDA granted fast track status	Chemotherapy (e.g., capecitabine, dacarbazine, 5-fluorouracil, temozolomide) INFa Octreotide	Decreased rate of bowel movements Decreased 5-HIAA levels Decreased rate of flushing episodes Improved quality of life (e.g., less pain, discomfort)
Ultra-low-molecular-weight heparin (semuloparin) for prevention of venous thromboembolism in patients undergoing chemotherapy	Patients who are at high risk for venous thromboembolism (VTE) who are undergoing chemotherapy treatment for cancer	Up to 20% of patients in whom cancer has been diagnosed experience a VTE, and the risk of VTE is further increased in patients undergoing chemotherapy treatment. However, no treatments are currently FDA approved for thromboprophylaxis in this setting (i.e., thromboprophylaxis is recommended only for cancer patients undergoing major surgery and/or hospitalized or critically ill). The potential benefits of thromboprophylaxis in this setting have not been firmly established. Semuloparin is an ultra-low-molecular-weight heparin that has exhibited high anti-Factor Xa and minimal residual anti-Factor IIa (thrombin) activities and is proposed for use in patients receiving chemotherapy at risk of VTE. In a clinical trial, semuloparin was administered daily by subcutaneous injection at a dose of 20 mg. Sanofi-Aventis, Paris, France Phase III trial completed	Low-molecular-weight heparin No treatment	Decreased rate of thromboembolytic events Improved safety profile (e.g., fewer bleeding events)

Table 18. AHRQ Priority Condition: 03 Cardiovascular Disease: 7 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Autologous bone marrow cells (Ixmyelocel-T) for treatment of critical limb ischemia	Patients in whom critical limb ischemia (CLI) has been diagnosed	Outcomes for patients with CLI are poor, and many patients require amputation. This intervention represents a novel treatment modality for this condition. Tissue repair cell (Ixmyelocel-T) technology consists of bone marrow extracted from the patient, expanded over the course of 12 days at the manufacturer's facility using the company's proprietary process, and reinfused into the patient 14 days after extraction. The formulation includes monocytes, macrophages (intended to destroy dead tissue, stimulate regeneration, and reduce inflammation), mesenchymal stem cells (intended to promote angiogenesis), and endothelial progenitor cells (intended to promote blood vessel lining and generate cardiovascular tissue). Aastrom Biosciences, Inc., Ann Arbor, MI Phase III trial planned to begin recruiting in fourth quarter of 2011	Cilostazol and pentoxifylline Cholesterol-lowering agents Percutaneous angioplasty and stenting Surgery	Tissue regeneration Improved circulation Reduced need for amputation Reduced morbidity and mortality
Bioresorbable vascular scaffold (Absorb) for treatment of critical limb ischemia	Patients in whom below-the-knee CLI has been diagnosed	Outcomes for patients with CLI are poor, and many patients require amputation. This intervention represents a novel approach to treatment. Absorb™ bioresorbable vascular scaffold is a drug-eluting stent made of polylactide polymer that elutes everolimus. It is intended to provide support to the vessel, then dissolve over the course of 2 years. The company claims that because the device is not permanent, natural vessel function may be restored. Abbott Laboratories, Abbott Park, IL Trial ongoing (no phase)	Cilostazol and pentoxifylline Cholesterol-lowering agents Percutaneous angioplasty and stenting Surgery	Decreased pain Improved circulation and mobility Reduced need for amputation Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Factor Xa inhibitor (rivaroxaban, Xarelto) for prevention of stroke	Patients in whom atrial fibrillation (AFib) has been diagnosed	Current standard of care (warfarin) for patients with AFib is associated with limitations, including a narrow therapeutic window and the need for frequent measurements of clotting parameters. A recently approved novel medication, dabigatran, operates via a different mechanism of action and requires twice daily dosing. No Factor Xa inhibitors are currently approved for use for this indication in the U.S. Rivaroxaban (Xarelto®) is a member of a new class of anticoagulants in development that are designed to inhibit Factor Xa, which is known to be an important component of the coagulation cascade. It is intended to be administered orally, once daily, and is approved for prevention of venous thromboembolism in patients undergoing knee or hip surgery. Johnson & Johnson, Inc., New Brunswick, NJ FDA approved Nov 2011	Apixaban Betrixaban Dabigatran Edoxaban Warfarin	Reduced stroke incidence Reduced morbidity and mortality
Factor XI inhibitor (ISIS-FXIRX) for anticoagulation	Patients at risk of aberrant blood clot formation	Currently available anticoagulation agents carry a high risk of bleeding, or require ongoing monitoring and dose adjustments. This agent represents a novel mechanism of action for patients at risk of aberrant blood clot formation. ISIS-FXIRX is intended to inhibit Factor XI, a clotting factor that is a component of the coagulation pathway. High levels of Factor XI are a risk factor for clots. Because of its position in the coagulation pathway, this agent may be associated with minimal risk for bleeding. ISIS Pharmaceuticals, Inc., a unit of Johnson & Johnson, Inc., New Brunswick, NJ Phase I trial ongoing	Apixaban Aspirin Betrixaban Coumadin Dabigatran Lovenox Rivaroxaban	Reduced incidence of aberrant clot formation Reduced thrombosis rate Reduced stroke incidence Reduced pulmonary embolism incidence Reduced morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Myosin activator (omecamtiv mecarbil) for treatment of heart failure	Patients in whom heart failure (HF) has been diagnosed	Currently available ionotropic pharmacotherapy for HF increases contractility without prolonging systole, which increases oxygen demand, thereby exacerbating myocardial ischemia and the risk for adverse events. Omecamtiv mecarbil is a myosin activator intended to prolong systole in the heart. The manufacturer claims the agent can increase the duration of systole without changing the rate of left ventricular pressure development, thereby increasing stroke volume and cardiac output. The agent is being developed as both oral and intravenous formulations, for use as both inpatient and outpatient therapy. Cytokinetics, Inc., South San Francisco, CA Phase II trials ongoing	Angiotensin-converting enzyme (ACE) inhibitors Angiotensin receptor blockers (ARBs) Beta blockers Digitalis Diuretics Stem cell therapies	Prolonged systole Improved heart efficiency Reduced adverse events Improved quality of life Reduced morbidity and mortality
Phospholipase A2 inhibitor (darapladib) for treatment of atherosclerosis	Patients with atherosclerosis who are at high risk for myocardial infarction (MI)	Despite available pharmacotherapy, coronary artery disease remains the leading cause of death in the U.S. This intervention represents a novel mechanism of action for the treatment of atherosclerosis. Darapladib is a lipoprotein-associated phospholipase A2 (LP-PLA2) inhibitor that is being investigated as a treatment for atherosclerosis. LP-PLA2 plays a role in atherosclerotic development and progression. Its levels predict cardiovascular risk, and it has been suggested that it is involved in determining plaque stability. By inhibiting LP-PLA2, this agent may help improve atherosclerosis, stabilize unstable plaques, and reduce cardiovascular risk. GlaxoSmithKline, Middlesex, UK Phase III trials ongoing	Ezetimibe Fibrates Niacin Statins	Improved plaque stability Reduced atherosclerosis Reduced morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Warm oxygenated blood perfusion (Organ Care System) for preservation of donor hearts	Patients in whom a need for a heart transplant has been diagnosed	Currently, donor hearts being transported for transplantation are stopped and transported on ice, in a cooler (i.e., cold ischemic storage). This method is associated with limitations, such as a narrow treatment window, the potential for damage, and the inability to test the heart for function. As a result, only about 30% to 40% of suitable donor hearts are used for transplant. The Organ Care System (OCS™) is a heart transplant system that is intended to pump warm, oxygenated, nutrient-rich donor blood through the organ until it is implanted, thereby keeping the heart in a "living" state as it is transported. The manufacturer states that with this method, the heart may withstand longer periods of time outside of the body, be less vulnerable to damage during transportation, and be able to be tested for function and tissue matching. The system has attached consoles to monitor heart function during transport. TransMedics, Inc., Andover, MA Phase II/III trial ongoing	Cold ischemic storage	Improved patient outcomes Increased utilization of available organs Expanded pool of potential donor hearts

Table 19. AHRQ Priority Condition: 04 Dementia (including Alzheimer's): 3 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gamma secretase inhibitor (EVP-0962) for treatment of Alzheimer's disease	Patients in whom Alzheimer's disease (AD) has been diagnosed	No disease-modifying treatments for AD are approved in the U.S. EVP-0962 is a selective gamma secretase modulator with potential disease-modifying capability. Gamma secretase is an enzyme involved in the processing of beta amyloid (a-beta), which contributes to amyloid plaques in the brain, which are believed by some to have a role in the pathophysiology of AD. According to the manufacturer, it does not affect the Notch signaling pathway, and therefore may offer a better safety profile than other gamma secretase modulators. EnVivo Pharmaceuticals, Watertown, MA Phase I trial ongoing	Donepezil Galantamine Memantine Rivastigmine	Slowed disease progression, or regression Improved long-term outcomes Improved quality of life
Monoclonal antibody (RG1450, gantenerumab) for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	No disease-modifying treatments for AD are currently available. Gantenerumab is a fully human monoclonal antibody that is intended to bind specifically to a-beta plaques and reduce a-beta load in the brain. In clinical trials, gantenerumab is given as an intravenous infusion every 4 weeks up to seven times. F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trial ongoing	Donepezil Galantamine Memantine Rivastigmine	Slowed disease progression, or regression Reduced morbidity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label intranasal insulin for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	No disease-modifying interventions for AD are currently available. This intervention represents a new mechanism of action for the treatment of AD. Insulin is known to play a role in normal brain function, modulating glucose utilization in the hippocampus, facilitating memory at optimal levels, modulating levels of a-beta, and providing neuroprotection for synapses against a-beta. Patients with AD have reduced levels of insulin and insulin activity. Insulin cannot be delivered peripherally, because of the risk for hypoglycemia or induction and/or exacerbation of peripheral insulin resistance. Therefore, researchers have begun delivering insulin intranasally (branded insulin, delivered via a nasal drug delivery device), administered at 20 IU or 40 IU total dose, twice daily. It does not appear that the insulin manufacturers are pursuing a labeled indication change. HealthPartners Research Foundation, Minneapolis, MN University of Kansas, Lawrence, KS University of Washington, Seattle, WA Phase II trials completed	Donepezil Galantamine Memantine Rivastigmine	Slowed disease progression, or regression Improved memory Improved long-term outcomes Improved quality of life

Table 20. AHRQ Priority Condition: 05 Depression and Other Mental Health Disorders: 5 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cortisol antagonist (mifepristone, Korlym) for treatment of psychotic depression	Patients in whom psychotic depression has been diagnosed	No treatments are FDA approved for psychotic depression. This intervention represents a novel mechanism of action for the condition. Mifepristone (Korlym™, previously Corlux) is a cortisol antagonist. Patients with psychotic depression have higher levels of cortisol, a hormone that regulates bodily reactions to stress. Elevated levels of circulating cortisol can produce psychiatric disorders. The drug is intended to be administered orally, in tablet form, once daily. Corcept Therapeutics, Menlo Park, CA Phase III trial ongoing; FDA granted fast track status	Antipsychotics in combination with antidepressants Electroconvulsive therapy	Improvement in psychotic symptoms Reduced suicide rate Improved quality of life
Multimodal antidepressant (Lu AA21004) for treatment of major depressive disorder	Patients in whom major depressive disorder (MDD) has been diagnosed	Patients in whom MDD has been diagnosed have high rates of inadequate response to currently available medications, and available pharmacotherapies are associated with undesirable side effects, including sexual dysfunction. Lu AA21004 is a 5-HT3 and 5-HT7 receptor antagonist, 5-HT1A receptor agonist, 5-HT1B receptor partial agonist, and 5-HT transporter inhibitor that has been shown to increase brain levels of serotonin, noradrenaline, dopamine, acetylcholine, and histamine. Clinical trials have suggested that the drug may be associated with low (similar to placebo) rates of sexual dysfunction, compared with currently available products. Planned oral dosages include 10, 15 and 20 mg. Takeda Pharmaceutical Co., Ltd., Osaka, Japan, jointly with Lundbeck Pharma A/S, Copenhagen, Denmark Phase III trials ongoing	Other antidepressants Combination therapy Psychotherapy Electroconvulsive stimulation Transcranial magnetic stimulation Deep brain stimulation Vagus nerve stimulation	Improved scores on validated depression instruments Reduced side effects including sexual dysfunction Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label acamprosate for treatment of binge-eating disorder	Patients in whom binge-eating disorder has been diagnosed	No pharmacotherapies are approved by FDA for binge-eating disorder, and currently used off-label pharmacotherapies are associated with limited efficacy, undesirable side effects, and low compliance. Acamprosate is a glutamate receptor modulator that acts as an antagonist to the N-methyl-D-aspartate receptor, and is approved for the treatment of alcohol dependence. It has been suggested that addiction (e.g., alcohol dependence) and binge-eating disorder are pathophysiologically related, in that they both are moderated by reward circuitry in the brain. Additionally, in patients with alcohol dependence, acamprosate has been shown to reduce food craving and weight gain. In a clinical trial, the drug is being dosed as an oral tablet, administered three times daily. Lindner Center of Hope, Mason, OH Phase II/III trial completed.	Antiepileptics Selective norepinephrine reuptake inhibitors Selective serotonin norepinephrine reuptake inhibitors	Improved symptoms of binge eating Decreased morbidity and mortality
Off-label armodafinil for the treatment of binge-eating disorder	Patients in whom binge-eating disorder has been diagnosed	No pharmacotherapies are approved by FDA for binge-eating disorder, and currently used off-label pharmacotherapies are associated with limited efficacy, undesirable side effects, and low compliance. Armodafinil is a wakefulness-promoting drug with an unknown mechanism of action; it is approved under the brand name Nuvigil® for the treatment of excessive sleepiness associated with narcolepsy, obstructive sleep apnea, and shift work disorder. Some investigators have suggested that binge-eating disorder may mediate the relationship between narcolepsy and obesity, so researchers are investigating the off-label use of armodafinil in patients with binge-eating disorder. In a clinical trial, the drug is being dosed in oral form, at a variable dosage of 150 to 250 mg/day. Cephalon, Inc., Frazer, PA makes the drug, but Lindner Center of Hope, Mason, OH, is studying its use for this indication Phase III trial ongoing	Antiepileptics Selective norepinephrine reuptake inhibitors Selective serotonin/ norepinephrine reuptake inhibitors	Improved symptoms of binge eating Decreased morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label sodium oxybate for the treatment of binge-eating disorder	Patients in whom binge-eating disorder has been diagnosed	No pharmacotherapies are approved by FDA for binge-eating disorder, and currently used off-label pharmacotherapies are associated with limited efficacy, undesirable side effects, and low compliance. This intervention represents a novel mechanism of action for the condition. The active ingredient in sodium oxybate is gamma hydroxybutyrate, a compound endogenously synthesized in the central nervous system, which is known to modulate neurotransmitters (e.g., gamma aminobutyric acid [GABA], dopamine, serotonin, opioids, glutamate) that regulate feeding behavior. This agent is currently marketed under the trade name Xyrem® for treatment of daytime sleepiness and cataplexy in patients with narcolepsy. Some investigators have suggested that binge-eating disorder may mediate the relationship between narcolepsy and obesity. This agent is administered orally, in liquid form, twice every night. Jazz Pharmaceuticals, Inc., Palo Alto, CA (manufacturer listed as a collaborator on clinical trials, but does not list active development for this indication on its Web site) Lindner Center of Hope, Mason, OH (primary investigator) Phase II/III trial completed; regulated as a Class III controlled substance by FDA	Antiepileptics Selective norepinephrine reuptake inhibitors Selective serotonin norepinephrine reuptake inhibitors	Improved symptoms of binge eating Improved morbidity and mortality

Table 21. AHRQ Priority Condition: 06 Developmental Delays, Attention-deficit Hyperactivity Disorder, and Autism: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oxytocin for treatment of autism spectrum disorders	Patients in whom autism spectrum disorder has been diagnosed	According to the U.S. Centers for Disease Control and Prevention, autism spectrum disorders are diagnosed in approximately 9 of 1,000 people in the U.S. Current therapies include behavioral programs, devices, and pharmacotherapies. Oxytocin (OT) is a polypeptide with both peripheral and central actions. OT may regulate repetitive and affiliative behaviors, as an association has been observed between autism and genomic deletion of the oxytocin receptor gene (OXTR) or methylation of OXTR. OT might affect trust and fear via possible inhibition of the amygdala. In trials, OT is being administered intranasally, 48 IU/kg of body weight total, divided into two daily doses; 0.4 IU/kg twice daily; or 24 IU/kg once daily. OT may also be administered intravenously to examine its effect on face processing and response inhibition in adults receiving a diagnosis of autism. Mount Sinai School of Medicine, New York, NY Montefiore Medical Center, Bronx, NY (in collaboration with the National Alliance for Research of Schizophrenia and Depression) University of Illinois, Chicago, IL (in collaboration with the U.S. Department of Defense) Children's Hospital of Philadelphia, Philadelphia, PA Phase II trials (intranasal) ongoing; phase I trial (intravenous) ongoing	Behavioral programs N-acetylcysteine (investigational) Off-label treatments: Acetylcholinesterase inhibitors Alpha-2 adrenergic agonists Carnitine Immunomodulation and antiinflammatory treatments: Melatonin Naltrexone Oxytocin Tetrahydrobiopterin Vitamin C Risperidone	Improved Clinical Global Rating Scale and Repetitive Behavioral Scale scores Improved social cognitive behavior Improved speech and language skills Improved quality of life

Table 22. AHRQ Priority Condition: 07 Diabetes Mellitus: 7 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Docosahexaenoic acid and salicylate conjugate (CAT-1004) for treatment of type 2 diabetes mellitus	Patients in whom type 2 diabetes mellitus (T2DM) has been diagnosed	T2DM accounts for about 90% of diabetes cases globally, with incidence and prevalence rising. Many current treatments help control glucose levels, but these treatments often come with significant side effects, which include gastrointestinal (GI) effects (e.g., nausea, diarrhea), weight gain, hypoglycemia, and edema. Additionally, many patients have difficulty achieving control of blood glucose with current treatments. CAT-1004 is a conjugate of docosahexaenoic acid (DHA) and salicylate. Several studies reveal the potential therapeutic effects of omega-3 fatty acids in inflammatory and metabolic diseases. DHA exhibits cardioprotective properties and salicylate exhibits antiinflammatory properties. Studies suggest that this conjugate may improve insulin sensitivity and glucose homeostasis by simultaneously inhibiting proinflammatory pathways and activating endogenous anti-inflammatory pathways. Catabasis Pharmaceuticals, Inc., Cambridge, MA Phase I trial ongoing	Various approved drugs for T2DM treatment Various drugs currently under investigation for T2DM treatment (i.e. sodium-glucose cotransporter 2 [SGLT2] inhibitors) Behavioral and lifestyle modification	Decreased inflammation and insulin resistance Near-normal hemoglobin A_{1c} (HbA_{1c}) levels Halted or delayed acute and secondary complications
GLP1 analog (ORMD 0901) for treatment of type 2 diabetes	Patients in whom T2DM has been diagnosed	T2DM accounts for about 90% of diabetes cases globally, with incidence and prevalence rising. ORMD 0901 is an oral formulation of the approved injectable glucagon-like peptide 1 (GLP1) analog exenatide. GLP1 analogs stimulate insulin secretion, suppress glucagon release, and slow gastric emptying. An oral formulation would be expected to enhance diabetes control and patient compliance. Oramed Pharmaceuticals, Inc., Jerusalem, Israel Phase II trial ongoing	Injected exenatide Injected liraglutide	Near-normal HbA_{1c} levels Improved fasting glucose levels Improved insulin sensitivity Reduced acute and secondary complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral insulin capsule (ORMD 0801) for treatment of type 1 or type 2 diabetes	Patients in whom type 1 diabetes mellitus (T1DM) or T2DM has been diagnosed	Compliance with insulin injections is suboptimal, leading to poor blood glucose control and acute and secondary complications of diabetes. ORMD 0801 is an oral formulation of insulin. Oramed Pharmaceuticals, Inc., Jerusalem, Israel Phase II trial planned	Inhaled/intranasal insulin Injected insulin	Near-normal glucose targets Improved HbA_{1c} levels Improved patient compliance with insulin regimen Reduced acute and secondary complications
PF-04523655 (RTP801I-14) for treatment of diabetic macular edema	Patients in whom diabetic macular edema has been diagnosed	No therapies are currently FDA approved for diabetic macular edema, and 12% to 15% of patients still experience significant loss of visual acuity when using available diabetic macular edema treatments. PF-04523655 (RTP801I-14) is an siRNA directed against the *RTP-801* gene, which is believed to be involved in the development of abnormal blood vessels and vessel leakage in the eye and would represent a novel molecular target in diabetic macular edema treatment. Quark Pharmaceuticals, Inc., Fremont, CA, in cooperation with Pfizer, Inc., New York, NY Phase IIb trial completed; one phase IIb trial ongoing	Laser photocoagulation Intravitreal triamcinolone acetonide with or without laser photocoagulation Vascular endothelial growth factor antagonists: Pegaptanib Ranibizumab Bevacizumab	Improved visual acuity Halted loss of vision Improved contrast sensitivity Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Sodium-glucose cotransporter-2 (SGLT2) inhibitor (canagliflozin) for treatment of type 2 diabetes mellitus	Patients in whom T2DM has been diagnosed	T2DM accounts for about 90% of diabetes cases globally, with incidence and prevalence rising. Many current treatments help control glucose levels, but these treatments often come with significant side effects, which include GI effects (e.g., nausea, diarrhea), weight gain, hypoglycemia, and edema. Additionally, many patients have difficulty achieving control of blood glucose with current treatments. Canagliflozin is an inhibitor of SGLT2, a solute carrier predominantly found in the proximal convoluted tubule of the kidney cortex. Inhibition of SGLT2 might reduce glucose reabsorption and increase glucose excretion through urine, potentially reducing blood glucose without affecting insulin uptake and risking hypoglycemia. SGLT2 inhibitors are intended to be used with other oral agents and insulin and are without significant adverse effects. They also are believed to have potential to promote weight loss in overweight and obese patients. Johnson & Johnson, Inc., New Brunswick, NJ Phase III trials ongoing	Other SGLT2 inhibitors under investigation Various approved drugs for treatment of T2DM Behavioral and lifestyle modification	Near-normal HbA_{1c} levels Weight loss Fewer hypoglycemic events Halted or delayed acute and secondary complications
Sodium-glucose cotransporter-2 (SGLT2) inhibitor (tofogliflozin) for treatment of type 2 diabetes mellitus	Patients in whom T2DM has been diagnosed	T2DM accounts for about 90% of diabetes cases globally, with incidence and prevalence rising. Many current treatments for T2DM help control glucose levels, but these treatments often come with significant side effects, which include GI effects (e.g., nausea, diarrhea), weight gain, hypoglycemia, and edema. Additionally, many patients have difficulty achieving control of blood glucose with current treatments. Tofogliflozin inhibits SGLT2, a solute carrier predominantly found in the proximal convoluted tubule of the kidney cortex. Inhibition of SGLT2 might reduce glucose reabsorption and increase glucose excretion through urine, potentially reducing blood glucose without affecting insulin uptake and risking hypoglycemia. SGLT2 inhibitors are intended to be used with other oral agents and insulin and are without significant adverse effects. They also are believed to have potential to promote weight loss in overweight and obese patients. Chugai Pharmaceuticals Co., Ltd., Tokyo, Japan Phase III trial ongoing	Other SGLT2 inhibitors under investigation Various approved drugs for treatment of T2DM Behavioral and lifestyle modification	Near-normal HbA_{1c} levels Weight loss Decreased hypoglycemic events Halted or delayed acute and secondary complications

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Sodium-glucose cotransporter-2 (SGLT2) inhibitor (TS-071) for treatment of type 2 diabetes mellitus	Patients in whom T2DM has been diagnosed	T2DM accounts for about 90% of diabetes cases globally, with incidence and prevalence rising. Many current treatments for T2DM help control glucose levels, but these treatments often come with significant side effects, which include GI effects (e.g., nausea, diarrhea), weight gain, hypoglycemia, and edema. Additionally, many patients have difficulty achieving control of blood glucose with current treatments. TS-071 is an inhibitor of SGLT2, a solute carrier predominantly found in the proximal convoluted tubule of the kidney cortex. Inhibition of SGLT2 is purported to reduce glucose reabsorption and increase glucose excretion through urine, potentially reducing blood glucose without affecting insulin uptake and risking hypoglycemia. SGLT2 inhibitors are intended for use with other oral agents and insulin and are without significant adverse effects. They also are believed to have potential to promote weight loss in overweight and obese patients. Taisho Pharmaceutical Co., Ltd., Tokyo, Japan Phase II trial ongoing	Other SGLT2 inhibitors under investigation Various approved drugs for treatment of T2DM Behavioral and lifestyle modification	Near-normal HbA_{1c} levels Weight loss Fewer hypoglycemic events Halted or delayed acute and secondary complications

Table 23. AHRQ Priority Condition: 08 Functional Limitations and Disability: 24 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
ACE-536 for treatment of anemia in myelodysplastic syndromes	Patients in whom anemia secondary to myelodysplastic syndromes (MDS) has been diagnosed	Anemia is one of the most common and debilitating complications of MDS, often significantly reducing the number of red blood cells (RBC) and preventing RBC production. Anemia is sometimes treated with therapies targeting the erythropoietin pathway; however, therapies targeting this pathway have exposed patients to increased risk of tumor stimulation and progression, as well as increased risk of thrombosis. In MDS, defects in RBC production occur in the latter stages of red cell maturation, whereas current therapies target earlier stages of RBC production. ACE-536 is a ligand trap therapy that inhibits signaling of several members of the transforming growth factor-beta protein super family, responsible for stimulation of RBC production, late cell-type differentiation, and inhibition of tumor growth and metastasis. Essentially, ACE-536 affects late RBC maturation, effectively increasing RBC production for treatment of anemia in MDS. Celgene Corp., Summit, NJ, in collaboration with Acceleron Pharma, Inc., Cambridge, MA Phase I trial has been suspended	Erythropoiesis-stimulating agents	Decreased risk of thrombosis and tumor stimulation Increased hemoglobin Reduced fatigue and inflammation Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Amygdala retraining program for treatment of chronic fatigue syndrome	Patients in whom chronic fatigue syndrome (CFS) has been diagnosed	CFS has no cure and no single therapy provides symptom relief in all patients; new therapies are needed. The amygdala retraining program (ARP) is based on the hypothesis that following a traumatic event involving acute psychological stress, the brain's amygdala may become conditioned to be chronically sensitized to signals arising in the body (i.e., physiological, chemical, dietary stressors). This conditioned response leads to overstimulation of the sympathetic nervous system eventually resulting in chronic fatigue; it is purported that the development of neuronal pathways from the medial prefrontal cortex to the amygdala in the brain can extinguish this fear response. The ARP attempts to develop these "safety neurons" by a program tailored to the patient consisting of holistic dietary, lifestyle, stress management, and self-awareness treatments. Stress tools and techniques are performed for a minimum of 30 minutes a day in one sitting (meditation, "soften and flow," and alternate nostril breathing), along with some neurolinguistic-programming, 30-second tools used throughout the day when required. The intent of these techniques is to recognize and interrupt fearful responses, replacing them with a relaxation response. Ashok Gupta, holistic medicine practitioner, London, UK Ann Vincent, M.D., Mayo Clinic, Rochester, MN Trial ongoing (unphased); sold as a proprietary program; currently clinically implementable	Dietary restrictions Gentle stretching Lifestyle changes Nutritional supplementation Pharmacotherapies to treat sleep disorders Prevention of overexertion Stress reduction	Improved ability to perform daily activities Reduced symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Amygdala retraining program for treatment of fibromyalgia	Patients in whom fibromyalgia has been diagnosed	Fibromyalgia is poorly understood and lacking effective treatment options for many patients. The amygdala retraining program (ARP) is based on the hypothesis that following a traumatic event involving acute psychological stress, the brain's amygdala may become conditioned to be chronically sensitized to signals arising in the body (i.e., physiological, chemical, dietary stressors). This conditioned response leads to overstimulation of the sympathetic nervous system eventually resulting in neurologic disorders such as fibromyalgia; it is purported that the development of neuronal pathways from the medial prefrontal cortex to the amygdala in the brain can extinguish this fear response. The ARP attempts to develop these "safety neurons" by a program tailored to the patient consisting of holistic dietary, lifestyle, stress management, and self-awareness treatments. Stress tools and techniques are performed for a minimum of 30 minutes a day in one sitting (meditation, "soften and flow," and alternate nostril breathing), along with some neurolinguistic-programming, 30-second tools used throughout the day when required; the intention of these techniques is to recognize and interrupt fearful responses, replacing them with a relaxation response. Ashok Gupta, holistic medicine practitioner, London, UK Ann Vincent, M.D., Mayo Clinic, Rochester, MN Sold as a proprietary program; currently clinically implementable	Duloxetine Fluoxetine Gabapentin Lorazepam Milnacipran Pregabalin Stress reduction Tricyclic antidepressants	Improved ability to perform daily activities Reduced symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Atacicept for treatment of systemic lupus erythematosus	Patients in whom systemic lupus erythematosus (SLE) has been diagnosed	There is no permanent cure for SLE, and current treatments provide only partial relief of symptoms. Atacicept is a biologic that is purported to decrease the activity of autoreactive B cells, which may play a key role in the pathogenesis of SLE. Atacicept is a recombinant protein that consists of domains from the proteins B-lymphocyte stimulator (BLyS) and a proliferation-inducing ligand (APRIL), which are involved in the maintenance, proliferation, and antibody production of B cells, fused to the constant domain of immunoglobulin. Because BLyS and APRIL bind the TACI (transmembrane activator and calcium-modulating and cyclophilin ligand [CAML] interactor) receptor, atacicept is also called TACI-Ig. Atacicept is purported to be an antagonist for the TACI receptor. Atacicept is hypothesized to selectively impair mature B cells and plasma cells more than memory B cells or progenitor cells. Atacicept is administered subcutaneously, 75 or 150 mg, once weekly. EMD Serono, Inc., Rockland, MA Phase II/III trial ongoing	AGS-009 Belimumab Rituximab Rontalizumab	Delayed disease progression Reduced symptoms Fewer flares Improved quality of life
CM2489 calcium release-activated calcium channel inhibitor for treatment of psoriasis	Patients in whom moderate to severe plaque psoriasis has been diagnosed	CM2489 is a first-in-class inhibitor of calcium release-activated calcium (CRAC) channels. CRAC channels are central mediators of immune cell response through calcineurin/NFAT, which leads to cytokine production and lymphocyte proliferation. Downregulation of these proinflammatory signals is proposed as a treatment for psoriasis. CalciMedica, La Jolla, CA Phase I trial ongoing	Topical ointments such as: Anthralin Calcineurin inhibitors Coal tar Corticosteroids Phototherapy Systemic medications: Cyclosporin, Hydroxyurea Immunomodulators Methotrexate Retinoids, Thioguanine	Improved psoriasis severity index scale scores Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
CNV2197944 for treatment of chronic neuropathic pain	Patients in whom chronic neuropathic pain has been diagnosed	Current pain medications are not effective in all patients and are associated with significant side effects such as the potential for addiction and gastrointestinal complications. CNV2197944 is a novel, small-molecule, calcium-channel blocker specific for the cav2.2 ion channel, which has been implicated in the pathogenesis of pain. Convergence Pharmaceuticals, Ltd., Cambridge, UK Phase I trial ongoing	Nonsteroidal antiinflammatory drugs (NSAIDs) Opioid analgesics	Reduced pain Improved quality of life
Concussion management system for treatment of concussion and prevention of second impact syndrome	Patients in whom a concussion has been diagnosed	Athletes or participants in recreational activities who return too soon to action after concussion and before accurate and proper assessment are at increased risk of second impact syndrome, a condition involving second trauma to the head before the concussion has resolved and the brain is fully healed. The Concussion Management System involves the use of a dual-function mouth guard, which acts as a dosimeter to record each hit to an athlete's head and serves as a monitoring device, recording energy activity during head hits and reporting the data via Bluetooth technology. This might enable more accurate assessment of cognitive and motor function for athletes, compared with existing concussion assessment tools and software. Cleveland Clinic, Cleveland, OH Pilot trial ongoing	Axon Sports' CCAT Biodex Balance System SD CNS Vital Signs™ CSMi's ImPACT™ Sport Concussion Assessment Tool 2 SportsWare™ Concussion HeadMinder™ Standardized Assessment of Concussion tool	Decreased recurrence of concussions Improved management of concussions Prevention of second impact syndrome Improved quality of life
Cyclic pyranopterin monophosphate enzyme replacement therapy for molybdenum cofactor deficiency type A	Patients in whom molybdenum cofactor deficiency (MoCD) type A has been diagnosed	No current treatments are available for MoCD type A, which results from a deficiency in cyclic pyranopterin monophosphate activity leading to accumulation of sulfite and death within weeks or months of birth. Cyclic pyranopterin monophosphate enzyme replacement therapy is intended to restore the enzymatic activity missing in patients with MoCD type A. Alexion Pharmaceuticals, Inc., Cheshire, CT Early phase trials ongoing	No treatments currently available	Improved urine sulfite levels Improved neurological symptoms Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Dopamine stabilizer pridopidine (ACR16, Huntexil) for treatment of Huntington's disease	Patients in whom Huntington's disease (HD) has been diagnosed	There is no cure for HD, and current therapies only help to manage emotional and motor symptoms associated with the disease. Pridopidine (ACR16, Huntexil®) is a small-molecule, dopamine stabilizer that is purported to increase or decrease dopamine to healthy levels in patients with HD. Pridopidine is purported to contrast with neuroleptics that reduce dopamine activity regardless of baseline level. Administered orally, 45 and 67.5 mg, twice daily. NeuroSearch a/s, Ballerup, Denmark Phase II/III trial completed	Antidepressants Antipsychotics Tetrabenazine	Improved clinical global impression of change (CGI-C), cognitive function, behavior, and symptoms of depression and anxiety Improved voluntary motor function
Drug-releasing implant (Propel system) to prevent occlusion of sinuses after surgery for chronic sinusitis	Patients in whom chronic sinusitis has been diagnosed	Chronic sinusitis affects approximately one in seven adults in the U.S. and can lead to complications such as headaches, breathing difficulties, facial pain, and reduced olfactory and gustatory senses. Current treatment for chronic sinusitis are medical treatments that may lack efficacy for some patients or surgical interventions that may be too invasive and associated with high rates of recurrence of symptoms. The Propel™ system is a springlike implant that is surgically implanted during endoscopic sinus surgery to maintain open sinuses after surgery and to prevent complications by delivering advanced corticosteroids directly to the sinus. It is intended to prevent obstruction of the ethmoid sinus. Intersect ENT, Inc., Palo Alto, CA FDA approved Aug 2011 under premarket approval (PMA) process	Antibiotics Decongestants Immunotherapy Nasal corticosteroids NSAIDs Oral or injected corticosteroids Saline nasal spray Sinus surgery	Reduced sinus inflammation Improved breathing Decreased headaches and facial pain Improved gustatory and olfactory senses Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Electrical Nerve Block system for treatment of chronic amputation pain	Patients who have had an amputation who experience chronic amputation pain	There is no currently approved treatment for chronic amputation pain, and many patients do not experience pain relief with the current treatment options. The Electrical Nerve Block system uses high frequency stimulation of peripheral nerves to prevent transmission of pain signals to the central nervous system (CNS). The Electrical Nerve Block system consists of a pacemaker-like implanted device that transmits electrical pulses through an electrode attached to a peripheral nerve. Neuros Medical, Inc., Willoughby, OH Pilot trials ongoing	Acupuncture Anticonvulsants Electrical spinal cord stimulation Intrathecal catheter-delivered drugs Analgesics Stump revision/neurectomy Transcutaneous electrical nerve stimulation Tricyclic antidepressants	Reduced pain Improved quality of life
Enzyme replacement therapy (ENB-0040) for treatment of hypophosphatasia in infants and children	Infants and children receiving a diagnosis of hypophosphatasia	Hypophosphatasia is a rare metabolic disorder caused by deficiency of the tissue-nonspecific isoenzyme of alkaline phosphatase (TNSALP). No other pharmacologic therapy is available currently. TNSALP is a phosphomonoesterase that plays a key role in regulation of bone mineralization. Alterations in the *TNSALP* gene results in extracellular accumulation of inorganic pyrophosphate, leading to inhibition of bone mineralization and resultant rickets, osteomalacia, or both. Incidence has been estimated at 1 per 100,000 births. ENB-0040 is an enzyme that is a form of recombinant human TNSALP. This enzyme is fused to the Fc portion of human immunoglobulin G and attaches to a deca-aspartate bone-targeting peptide derived from osteopontin and bone sialoprotein. This enzyme has a high affinity for bone, allowing it to exert its effects with limited systemic effect and at a half-life 30% longer in bone, compared with serum. Enobia Pharma, Cambridge, MA Phase II trials ongoing; phase II/III trial ongoing; FDA granted fast track status and orphan drug status	Cortisone Magnesium Plasma Vitamin B_6 Zinc	Restoration of bone mineralization Decreased risk of rickets and osteomalacia Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Enzyme replacement therapy (SBC-102) for treatment of lysosomal acid lipase deficiency	Patients in whom lysosomal acid lipase deficiency has been diagnosed	Lysosomal acid lipase deficiency is a rare genetic syndrome for which no treatment is FDA approved. SBC-102 is a recombinant protein intended to be used as an enzyme replacement therapy for this disease. Synageva BioPharma, Lexington, MA Phase II/III trial ongoing; FDA granted orphan drug status	Palliative treatments	Improved cholesteryl ester and triglyceride levels Improved quality of life
Epratuzumab for treatment of systemic lupus erythematosus	Patients in whom SLE has been diagnosed	There is no permanent cure for SLE and currently available treatments provide only partial relief of symptoms, so better treatments are needed. Epratuzumab is a fully humanized monoclonal antibody that is purported to bind and modulate the activity of CD22, an antigen found on B cells purported to prevent autoreactive responses. Autoreactive B cells are believed to play a major role in SLE pathogenesis. The drug is administered as a subcutaneous injection once monthly in clinical trials. UCB S.A., Brussels, Belgium Phase III trials ongoing	Belimumab Rituximab Rontalizumab	Delayed progression of disease Reduced symptoms Fewer flares Improved quality of life
Gel polymer (LeGoo) for prevention of blood loss in vascular surgery	Patients undergoing vascular surgical procedure	Vascular surgery often requires the anastomosis, or joining, of two or more blood vessels for the creation of a bypass. A primary adverse event for this surgical procedure is blood loss, which may also obstruct a surgical team's field of view. Elastic loops and surgical clamps are devices used to temporarily block blood flow, but the damaging and weakening of blood vessels has been a complication. LeGoo is a thermosensitive gel polymer that works paradoxically by solidifying at high temperature and liquefying at room temperature or below. The gel polymer is injected into the preferred suture site of the blood vessel, where a plug is formed in the shape of the blood vessel, blocking blood flow for 15 minutes. After 15 minutes, the gel polymer dissolves and passes through the microcirculation before being passed in urine. If a surgeon is finished in less than 15 minutes, a cold pack of ice or cold saline can be used to dissolve the gel polymer. This device is specifically indicated for blood vessels below the neck, 4 mm or less in diameter. This device is also specifically contraindicated for vessels supplying blood to the brain. Pluromed, Inc., Woburn, MA FDA approved Oct 2011 under PMA process	Elastic vessel loops Surgical clamps	Effective temporary blood vessel block Minimized blood loss Decreased damage to blood vessels

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
IGF-2 peptide conjugated alpha-glucosidase (BMN-701) enzyme replacement therapy for Pompe disease	Patients in whom late-onset Pompe disease has been diagnosed	Pompe disease, which is a genetic disease that results in a deficiency in alpha-glucosidase activity; current enzyme replacement therapies for the disease do not adequately address disease impact on skeletal muscle. Insulin-like growth factor 2 (IGF-2) peptide conjugated alpha-glucosidase (BMN-701) is an enzyme replacement therapy. Current enzyme replacement therapies have poor uptake in skeletal muscle, potentially due to low level skeletal muscle expression of the key transporter required for cellular entry of the enzyme. BMN-701 purports to circumvent this problem through the addition of the IGF-2 peptide, which is recognized by the transporter. BioMarin Pharmaceuticals, Inc., Novato, CA Phase I/II trial ongoing	Alpha-glucosidase enzyme replacement therapies: Lumizyme Myozyme	Improved muscle strength, functional status, pulmonary function and/or ventilation Improved quality of life
Integrin agonist (SAR 1118) for treatment of dry eye disease	Patients in whom dry eye disease has been diagnosed	About 20 million people in the U.S. are affected by dry eye disease. There are numerous causal factors for dry eye, with most diseases secondary to dry eye disease causing T-cell inflammation and proliferation and cytokine production. This may result in ocular surface damage and degradation of tear film. Several behavioral and pharmacologic therapies are available for treatment of dry eye but can work with limited efficacy or may be too invasive with resultant complications. SAR 1118 is a lymphocyte-associated antigen-1 (LFA-1) antagonist that binds to intercellular adhesion molecule-1, the LFA-1 cognate ligand, purportedly inhibiting cell adhesion, cytokine production, and cell proliferation. SARcode Bioscience, Inc., Brisbane, CA Phase III trial ongoing	Artificial tears Hot compresses Lubricating ointments Proper eyelid cleaning and sanitary behavior modification Tetracycline and doxycycline Topical azithromycin Topical corticosteroids	Reduced occurrence and recurrence of dry eye Decreased incidence of blindness from chronic dry eye Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mu-opioid agonist (NKTR-181) for treatment of chronic pain	Patients experiencing chronic pain	Current opioid analgesics have the potential for addiction and dangerous suppression of CNS activity leading to respiratory distress. NKTR-181 is a novel mu-opioid agonist formulation that modifies the opioid by pegylation, which is intended to reduce the rate at which the drug crosses the blood-brain barrier, thereby limiting high CNS concentrations that could lead to respiratory distress or feelings of euphoria. Nektar Therapeutics, San Francisco, CA Phase Ia trial complete; phase Ib trial ongoing	Conventional mu-opioid agonists	Improved pain relief Reduced adverse effects Reduced risk of addiction Improved quality of life
NuQu injectable cell-therapy for spinal disc regeneration	Patients with severe chronic lower back pain that is refractory to conservative treatment	Conservative treatment (physical therapy, pain medication) is not effective in a small proportion of patients with chronic low back pain from degenerative disc disease. Invasive surgical options such as spinal fusion have significant risks and can adversely affect adjacent discs; less invasive, effective options are needed. NuQu® treatment involves the injection of culture-expanded juvenile knee cartilage cells into the intervertebral disc, where they are intended to restore nucleus structure and disc height and prevent further degeneration. The procedure is performed under fluoroscopic guidance in an outpatient setting. ISTO Technologies, Inc., St. Louis, MO Phase I trial ongoing	Artificial disc replacement Discectomy Spinal fusion	Reduced back pain Increased function Improved quality of life
Off-label rifampicin for treatment of multiple system atrophy	Patients in whom multiple system atrophy (MSA) has been diagnosed	MSA is a progressive neurodegenerative disorder characterized by cytoplasmic inclusions containing abnormally aggregated alpha-synuclein proteins, which are purported to be associated with the neurodegeneration observed in MSA. Current MSA treatments are aimed at controlling symptoms rather than treating the underlying cause of neurodegeneration. The antibiotic rifampicin is purported to reduce the aggregation of alpha-synuclein and the associated neurodegeneration in a preclinical models, as well as disaggregate preformed alpha-synuclein fibrils. Mayo Clinic, Minneapolis, MN Phase III trial ongoing	Blood pressure medications Impotence drugs Incontinence drugs Levodopa and carbidopa	Improved symptoms based on Unified Multiple System Atrophy Rating Scale (UMSARS) Reduced neurodegeneration Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral growth hormone secretagogue (AEZS-130) for diagnosis of adult growth hormone deficiency	Patients in whom adult growth hormone deficiency (AGHD) has been diagnosed	AGHD affects about 35,000 adults in the U.S., leading to complications such as reduced muscle mass and bone mass, reduced energy levels, increased body fat, cardiac dysfunction, and increased insulin resistance. Current diagnostic measures for growth hormone (GH) deficiency are blood screenings without provocation by an agent, intravenous application of pharmacologic agents to stimulate GH production, or MRI detection of pituitary dysfunction. These current diagnostic tests have been deemed invasive, inconclusive, or have unwanted adverse effects. AEZS-130 is an orally active molecule, ghrelin agonist that purportedly stimulates the secretion of GH. Stimulation of GH secretion, which normally occurs in the body during sleep, is believed to allow a clinician to observe the body's response to AEZS-130. If GH levels remain low after administration of AEZS-130, this might confirm a diagnosis of AGHD. Growth hormone secretagogues are potent regulators of lipid, sugar, and protein metabolism that directly stimulate GH secretion from the pituitary gland without the involvement of growth-hormone-releasing hormone or somatostatin. AEZS-130 is administered once, orally, for the stimulation of GH secretion. AEterna Zentaris, Inc., Quebec, Quebec, Canada Phase III trial completed; FDA granted orphan drug status; company expects NDA filing in 2012	Blood GH testing IGF level testing Insulin tolerance testing MRI of pituitary to detect dysfunction	Increased sensitivity and specificity Improved diagnostic accuracy Increased patient compliance with recommended diagnostic strategy Reduced risk of adverse events from invasive tests
Oral short-chain fatty acid derivative compound (HQK-1001) for treatment of sickle cell disease	Patients in whom sickle cell disease (SCD) has been diagnosed	SCD is an autosomal recessive disorder that affects about 100,000 people in the U.S. and Europe. There is increased prevalence of disease in people of African and Mediterranean descent; about 1 in 500 African-American children born have sickle cell anemia. Despite advancements in management of complications of SCD (i.e., pain crises), the only drug currently FDA approved for treatment is hydroxyurea. HQK-1001 is a short chain fatty acid derivative (SCFAD) compound that purportedly reduces the frequency of pain crises and hospitalizations related to SCD. SFCAD has been shown to stimulate expression of fetal hemoglobin and production of red blood cells. HQK-1001 is administered orally at 10, 20 or 30 mg/kg of body weight, once a day (on dosing days). HemaQuest Pharmaceuticals, Inc., San Diego, CA Phase I/II trial completed; FDA granted orphan drug status	Allogeneic hematopoietic stem cell transplantation Antioxidant therapy Azacitidine Decitabine butyrate Gene therapy Gardos channel inhibition Hydroxyurea Lenalidomide Nitrous oxide and vasodilators Statins	Reduced severity and duration of vaso-occlusive crises Reduced health disparities (African Americans) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PN1/Nav1.7 sodium channel blocker for treatment of pain	Patients with any form of pain (e.g., pain associated with cancer, arthritis, migraine headaches; muscle pain; pain from burns)	This agent is intended to block PN1/Nav1.7, a sodium channel expressed on peripheral neurons that research has demonstrated is essential for transmitting pain signals to the CNS. Unlike CNS-acting opioids, PN1/Nav1.7 blockers would terminate pain signals peripherally, potentially avoiding CNS-based side effects such drowsiness and respiratory distress. Icagen, Inc., Durham, NC, in collaboration with Pfizer, Inc., New York, NY Phase I trial ongoing	NSAIDs Opioids	Reduced pain Maintained alertness Improved quality of life
THR-184 for treatment of acute kidney injury postsurgery	Patients in whom acute kidney injury (AKI) postsurgery has been diagnosed	Acute kidney injury (AKI) is characterized by a rapid, temporary loss of kidney function resulting in a failure to maintain fluid, electrolyte, and acid-base homeostasis. AKI is diagnosed in about 1 million patients each year in the U.S., all of whom experience some permanent loss of kidney function. Causal factors for AKI include cardiac and/or vascular surgery, sepsis, inflammatory disease, trauma, or the administration of contrast dye for imaging. AKI is common in hospitalized patients and has a poor prognosis with mortality ranging from 10% to 80%. Treatment options for AKI are limited, with no pharmacological therapy approved for treatment of AKI. THR-184 is a peptide that selectively activates the bone morphogenetic protein type II receptor and type I activin-like kinase (ALK) receptors, responsible for regulation of growth, differentiation, chemotaxis, and apoptosis (programmed cell death) of various cell types such as epithelial, mesenchymal, hematopoietic, and neuronal cells. Through activation of these receptors, this therapy might serve as a preventive and therapeutic option for patients in whom AKI has been diagnosed. Thrasos, Inc., Montreal, Quebec, Canada Phase I trial ongoing	Cincor™ system (in development) Deferoxamine Deferiprone (in development) Hydration	Reduced incidence and complications Improved quality of life

Table 24. AHRQ Priority Condition: 09 Infectious Disease including HIV-AIDS: 12 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
AVI-6002 for treatment of Ebola virus exposure	Patients who have been exposed to Ebola virus	Ebola infection has an 80% mortality rate with no effective treatments. AVI-6002 is a drug that uses phosphorodiamidate morpholino oligomer (PMO) antisense technology; PMOs are synthetic structures modeled after RNA, but with modifications purported to improve pharmacologic properties. PMOs have the same nucleic acid bases found in RNA or DNA, but they are bound to morpholine rings instead of ribose rings and are linked through phosphorodiamidate rather than phosphodiester or phosphorothioate groups, which are purported to eliminate ionization in physiologic pH, making PMOs uncharged. AVI-6002 utilizes the manufacturer's PMOplus™ technology to add position-specific, molecular charges to the PMO backbone, which is purported to improve targeted cell penetration to improve efficacy in the presence of viral mutations. PMOs could be created in a very short (i.e., days or weeks) timeframe. AVI BioPharma, Inc., Bothell, WA Phase I trial ongoing; manufacturer to file for approval through the animal efficacy rule after completing studies in healthy human subjects	Supportive care	Increased symptom resolution Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
AVI-6003 for treatment of Marburg virus	Patients who have been exposed to Marburg virus	Marburg infection has an 80% mortality rate with no effective treatments. AVI-6003 uses phosphorodiamidate morpholino oligomer (PMO) antisense technology; PMOs are synthetic structures modeled after RNA, but with modifications purported to improve pharmacologic properties. PMOs have the same nucleic acid bases found in RNA or DNA, but they are bound to morpholine rings instead of ribose rings and are linked through phosphorodiamidate rather than phosphodiester or phosphorothioate groups, which are purported to eliminate ionization in physiologic pH, making PMOs uncharged. AVI-6003 utilizes the manufacturer's PMOplus™ technology to add position-specific, molecular charges into the PMO backbone, which is purported to improve targeted cell penetration to improve efficacy in the presence of viral mutations. PMOs could be created in a very short (i.e., days or weeks) timeframe. AVI BioPharma, Inc., Bothell, WA, with support from the U.S. Army Medical Research Institute for Infectious Diseases, Frederick, MD Phase I trial ongoing; manufacturer to file for approval through the animal efficacy rule after completing studies in healthy human subjects	Supportive care	Improved symptom resolution Reduced mortality
Crofelemer for treatment of HIV-1-associated diarrhea	Patients on HIV antiretroviral therapy with chronic diarrhea	Approximately 40% of patients in the U.S. with HIV-1 have chronic diarrhea, which can reduce adherence to antiretroviral regimens. Effective antidiarrheals that do not cause adverse reactions with antiretrovirals are needed. Crofelemer purported to treat diarrhea by inhibiting the cystic fibrosis transmembrane conductance regulator ion channel, which is responsible for the transport of chloride ions into the intestinal lumen, which subsequently draws water into the bowel. Crofelemer is purported to have poor systemic absorption, thus limiting the development of adverse events. In trials, crofelemer has been administered orally, 125 mg, twice daily. Napo Pharmaceuticals, Inc., San Francisco, CA Phase III trials ongoing; FDA granted fast track approval	Absorbents containing attapulgite or polycarbophil Antibiotics Diphenoxylate Loperamide	Reduced number of watery bowel movements Relief of diarrhea

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Disinfection of high-touch surfaces with peracetic acid disinfectant to prevent transmission of hospital-acquired infections	Patients at risk for developing a hospital-acquired infection (HAI)	HAIs are the fourth leading cause of death in the U.S. after heart disease, stroke, and cancer. About one of every 20 hospitalized U.S. patient acquires an HAI, resulting in 100,000 deaths each year. Bacteria on surfaces in intensive care units are said to be responsible for 35% to 80% of HAIs. Cleaning the most frequently touched surfaces (i.e., bed rails, bedside tables, call buttons, telephones) in patient rooms daily with a surface sporicidal and disinfectant containing peracetic acid is purported to reduce the transmission of the bacteria *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus* more than standard terminal-cleaning procedures using bleach. Cleveland VA Medical Center, Cleveland, OH	Antimicrobial copper touch surfaces Terminal cleaning procedures using bleach and cleaning of visibly soiled surfaces as necessary	Reduced infection rates Reduced bacteria isolated from surfaces Reduced morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
INSTI rapid HIV antibody test for the detection of HIV-1 and HIV-2 infection	Patients who wish to determine their HIV-1 or HIV-2 status	Current HIV-infection diagnostics require 15 to 30 minutes for preliminary results, which must be later confirmed by more costly and time-consuming Western blot and indirect fluorescent antibody tests. Using a multi-test rapid algorithm may eventually provide quick and definitive HIV testing at the point of care. INSTI™ rapid HIV antibody test includes a unique antigen construct comprised of recombinant transmembrane proteins from HIV-1 (gp-41) and HIV-2 (gp-36), which is purported to provide greater than 99% sensitivity and specificity and can add to the predictive power of any rapid testing algorithm currently in use. INSTI uses a novel flow-through technology which purportedly allows more rapid detection of HIV, within 60 seconds, compared with the lateral-flow technology currently used in rapid HIV detection kits. INSTI also includes a unique procedural control using a true human immunoglobulin G which purportedly will allow the test to react only when the correct quantity of human blood is added, which may reduce user error. The test is purported to be highly stable and does not require refrigeration or specialized storage. By combining pretest and posttest counseling into one visit, INSTI may increase the capacity of a health care facility to provide HIV testing to more patients and promote prompt treatment. BioLytical™ Laboratories, Inc., Richmond, British Columbia, Canada FDA approved December 2010 under premarket approval application for detection of antibodies to HIV-1 in whole blood, finger stick blood, or plasma specimens	OraQuick Advance® Uni-Gold Recombigen® Clearview® Complete HIV 1/2 and Clearview® HIV 1/2 Stat-Pak Reveal™ HIV	Improved HIV counseling Improved HIV detection Improved treatment outcomes Increased rates of HIV testing
Live attenuated rabies virus vaccine for treatment and prevention of rabies	Patients at risk for rabies or who are suspected to be infected with rabies	Rabies can be effectively treated or prevented only if it has not infected the central nervous system (CNS), after which time survival outcomes are poor. Live attenuated rabies vaccine is purported to prevent rabies infection. It is also purported to generate effective cellular immune responses to the virus in patients infected with rabies virus even after it has infected the CNS and progressed to the brain. Thomas Jefferson University, Philadelphia, PA Pilot trial ongoing	Prophylactic rabies vaccine Rabies immune globulin	Improved survival following exposure

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Polymerase inhibitor INX-189 for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	Current standard of care for HCV infection cures the infection in less than half of treated patients, and newly approved protease inhibitors are associated with frequent adverse events. Effective and more tolerable treatments are needed. INX-189 is an orally administered prodrug and 2'-C-methylguanosine analog. It is purported to inhibit the HCV NS5B protease activity, which may limit viral replication by inhibiting viral genome replication. INX-189 is intended to be used in combination with pegylated interferon (INF) and ribavirin for this indication. Administered orally at a dose of 100 to 200 mg. Manufacturer states trial data supports INX-189's potential for once-daily dosing. Inhibitex, Inc., Alpharetta, GA Phase I/II trials ongoing; FDA granted fast track status	Boceprevir NS5B polymerase inhibitors (in phase II trials) Pegylated INF and ribavirin Telaprevir	Rapid virologic response (HCV RNA undetectable at week 4) Sustained virologic response (HCV RNA undetectable after 24 weeks of followup) Reduced need for liver transplantation Reduced symptoms
Modified vaccinia virus Ankara vector-encoding influenza nucleoprotein and matrix protein 1 for prevention of influenza	Patients at risk for influenza	Influenza strains mutate each year, requiring a new vaccines annually for protection. A long-lasting, effective, universal vaccine is sought. Modified vaccinia virus Ankara (MVA) vector vaccine encoding nucleoprotein and matrix protein 1 (MVA-NP+M1) of influenza virus has been designed to induce broad T-cell responses in patients. The NP and M1 antigens are naturally expressed inside viruses and virus-infected cells and do not mutate annually, unlike the neuraminidase and hemagglutinin antigens targeted in traditional antibody-based influenza vaccines. Thus, the investigators purport, this vaccine is not expected to need annual reformulations. The MVA vector is purported to express NP and M1 proteins resulting in the generation of T-cell based immunity in the absence of a productive viral infection. Jenner Institute (a partnership between Oxford University and the Institute for Animal Health), Oxford, UK Phase I trial completed against the H3N2/Wisconsin strain	Seasonal influenza vaccines	Prevention of influenza infections Reduced hospitalizations Reduced length of hospitalization Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label neurokinin-1 receptor antagonist aprepitant (Emend) for treatment of HIV infection	Patients in whom HIV infection has been diagnosed	HIV infection remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments. HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy continue to suggest that improved therapeutic options be pursued to treat patients. Additionally, patients with successfully managed HIV infection frequently develop neurocognitive impairment that is associated with residual chronic inflammation. Aprepitant (Emend®), a drug already approved for treatment of chemotherapy-induced nausea and vomiting (CINV), is purported to have immunomodulator and antiviral activity. That activity is intended to target residual inflammation by acting on host cells and not the virus, thus leading to prevention of inflammatory and neurocognitive events associated with HIV infection. Aprepitant is purported to be a neurokinin-1 receptor (NK1R) antagonist, inhibiting HIV replication in macrophages by decreasing expression of the chemokine receptor type 5 (CCR5) coreceptor which is needed for HIV to infect cells and possibly other mechanisms. Aprepitant is also purported to improve natural killer cell function, which may help patients better control the virus. Aprepitant is purported to act synergistically with HIV protease inhibitors. In trials, aprepitant was administered orally, 125 or 250 mg, once daily. University of Pennsylvania, Philadelphia, PA, and National Institute of Mental Health, North Bethesda, MD (trial sponsors) Merck & Co., Inc., Whitehouse Station, NJ (manufacturer) Phase I trials ongoing for HIV-1 treatment; FDA approved in 2003 for prevention of acute and delayed CINV and prevention of postoperative nausea and vomiting	Antiretroviral therapy Bavituximab Therapeutic vaccines	Delayed onset of AIDS Increased T-cell counts Reduced cognitive impairment Reduced viral load

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Patient-centered signage to improve hand washing among health care workers	Patients attending health care facilities	Hand-washing compliance by health care workers is only around 40% in many health care settings, leading to the transmission of deadly and costly infections. It is purported that many health care workers have expressed that because they are frequently exposed to infections, they are more immune to infection and thus do not wash their hands. Signage where hand washing should occur stating "Hand Hygiene Prevents Patients from Catching Diseases" may be more effective than "Hand Hygiene Prevents You from Catching Diseases" or a generic catchy message such as "Gel In, Wash Out." A patient-centered message may appeal to the "do no harm" precept of the Hippocratic oath. University of North Carolina at Chapel Hill	Standard hand-washing practices Radiofrequency identification hand-washing systems	Reduced costs associated with HAIs Reduced HAI incidence Reduced HAI morbidity and mortality
Vacc-4x for treatment of chronic HIV-1 infection	Patients in whom chronic HIV-1 infection has been diagnosed	HIV infection remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments. HIV drug resistance, poor tolerance to existing treatments, and high lifelong cost of therapy suggest that new therapeutic options are needed. Vacc-4x is a therapeutic vaccine comprised of four synthetic peptides with slight modifications to increase immunogenicity. Vacc-4x is believed to encode two conserved regions from the HIV Gag (p24) protein in which mutations in these regions lead to defective virus. Sustained immune responses to p24 have been associated with delayed disease progression. Investigators purport that Vacc-4x may be the first HIV treatment that is not vulnerable to viral escape mutants. Bionor Pharma ASA, Oslo, Norway Phase II trial ongoing	Highly active antiretroviral therapy Personalized vaccination Therapeutic vaccination	Reduced viral load Reduced medication regimen Reduced morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
VPM1002 vaccine for prevention of tuberculosis infection	People at risk for tuberculosis (TB) infection	Antibiotic resistance and long duration of TB treatment can lead to poor treatment outcomes; better methods of TB prevention are needed. VPM1002 TB vaccine is a genetically modified form of the bacterium *Mycobacterium bovis* Bacillus Calmette-Guérin (BCG) strain TB vaccine that has been modified to express the altered *a* gene from the *Listeria* bacterium. This allows the vaccine to escape the phagosome, gain access to the cytosol of the antigen-presenting cell, and potentially improve immunogenicity. Vakzine Projekt Management GmbH, Hannover, Germany Phase I trial ongoing	Antibacterial therapy Current BCG vaccine	Protection against multidrug-resistant TB Reduced infection rates

Table 25. AHRQ Priority Condition: 10 Obesity: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Melanin concentrating hormone 1 antagonist (ALB-127158[a]) for treatment of obesity	Patients who are overweight	Only one long-term weight-loss drug is currently on the market in the U.S., and this drug results in 5% weight loss in only 50% of patients. The melanin concentrating hormone 1 (MCH-1) signaling pathway is a neuropeptide-based pathway that promotes food intake; and ALB-127158(a) is an MCH-1 antagonist that purportedly acts as an appetite suppressant. AMRI, Albany, NY Phase I trial completed	Orlistat Antiobesity drugs in development: Contrave®, Qnexa®	Excess weight loss Total weight loss Reduced obesity-related comorbidities (e.g., cardiovascular, diabetes)

Table 26. AHRQ Priority Condition: 11 Peptic Ulcer Disease and Dyspepsia: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Allogeneic precultured adult bone-marrow-derived mesenchymal stem cells remestemcel-L (Prochymal) for treatment of Crohn's disease	Patients in whom Crohn's disease has been diagnosed	Patients with Crohn's disease frequently suffer damage to their bowel and require surgery; no regenerative therapies are currently approved for Crohn's disease. Remestemcel-L (Prochymal®) consists of allogeneic, bone-marrow-derived human mesenchymal stem cells, which are purported to reduce inflammation and promote crypt regeneration in damaged intestine. The manufacturer has developed a specific "expansion" process for these cells, which are intended to be used off the shelf and delivered as an intravenous infusion. Administered in a clinical trial three times, 200 million cells per infusion, 42 days apart. Osiris Therapeutics, Inc., Columbia, MD Phase III trials ongoing; FDA granted fast track designation	Autologous bone marrow-derived mesenchymal stromal cells Teduglutide	Increased disease remission Improved disease symptoms Improved quality of life
Plecanatide (SP-304) for treatment of chronic idiopathic constipation	Patients in whom chronic idiopathic, constipation has been diagnosed	Current treatments for constipation are ineffective or poorly tolerated in some patients. Effective, well tolerated therapies are needed. Plecanatide is a synthetic peptide uroguanylin analog that targets guanylate cyclase C receptors in the gastrointestinal (GI) tract. Uroguanylin is a natural peptide hormone that regulates ion and fluid transport in the GI tract. Plecanatide is purported to be more potent than uroguanylin. It may be used to treat chronic constipation or constipation-predominant irritable bowel syndrome. In trials, it is being administered orally, 0.3 to 9 mg, once daily. Synergy Pharmaceuticals, Inc., New York, NY Phase II/III trial initiating	Linaclotide Lubiprostone	Decreased straining and abdominal discomfort Increased frequency of bowel movements Improved stool consistency Improved quality of life

Table 27. AHRQ Priority Condition: 12 Pregnancy, including Preterm Birth: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral androgen (dimethandrolone undecanoate) for male contraception	Male patients pursuing contraception	Dimethandrolone undecanoate (DMAU) is a potent, orally active androgen with progestational activity that might act as a single-agent oral hormonal contraceptive (given its dual androgenic and progestational activity). DMAU purportedly suppresses the hypothalamic-pituitary-gonadal axis, resulting in severe oligospermia. DMAU purportedly decreases levels of follicle-stimulating hormone, luteinizing hormone, and testosterone. DMAU may be administered orally at 25, 50, 100, 200, 400 or 800 mg per dose. Los Angeles Biomedical Research Institute, Los Angeles, CA in collaboration with the National Institutes of Health, Bethesda, MD, and University of Washington, Seattle, WA Phase I trial ongoing	Combination hormone implant (under development) Condoms Reverse inhibition of sperm under guidance copolymer (under development in India) Vasectomy	Long-acting male contraception Decreased risk of unplanned pregnancy Changes in use of condoms

Table 28. AHRQ Priority Condition: 13 Pulmonary Disease, Asthma: 5 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Imatinib (Gleevec) for treatment of pulmonary arterial hypertension	Patients in whom pulmonary arterial hypertension (PAH) has been diagnosed	PAH has no cure and can result in heart failure and death. Imatinib (Gleevec®) is a small-molecule, ABL kinase inhibitor that is purported to inhibit cellular processes that are responsible for uncontrolled growth of arterial smooth muscle cells. Imatinib has been administered orally, 200 to 400 mg, once daily in clinical trials. Novartis AG, Basel, Switzerland Phase III trials ongoing	Anticoagulants Bosentan Calcium channel blockers Epoprostenol Nitric oxide inhalation Sildenafil Treprostinil	Improved exercise capacity Reduced mortality Reduced hospitalization
Interleukin-5 antagonist (mepolizumab, Bosatria) for treatment of eosinophilic asthma	Patients in whom eosinophilic asthma has been diagnosed	Eosinophilic asthma occurs in approximately 30% of patients with severe uncontrolled asthma. Uncontrolled asthma can lead to hospitalization or death. Patients with severe asthma must take systemic corticosteroids that can lead to adverse events. Mepolizumab (Bosatria®) is a humanized monoclonal antibody designed to bind and inhibit the activity of interleukin-5 (IL-5). IL-5 is purported to play a crucial role in the maturation, growth, and chemotaxis (movement) of eosinophils, inflammatory white blood cells implicated in asthma and not found in the lungs under normal circumstances. Administered intravenously, 75, 250, and 750 mg, every 4 weeks. GlaxoSmithKline, Middlesex, UK Phase II trials ongoing	Masitinib Omalizumab Oral corticosteroids Reslizumab	Improved asthma control Improved asthma exacerbation rate Reduced emergency room visits Reduced hospitalization Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Interleukin-5 antagonist (reslizumab, Cinquil) for treatment of eosinophilic asthma	Patients in whom eosinophilic asthma has been diagnosed	Eosinophilic asthma occurs in approximately 30% of patients with severe uncontrolled asthma. Uncontrolled asthma can lead to hospitalization or death. Patients with severe asthma must take systemic corticosteroids that can lead to adverse events. Reslizumab (Cinquil™) is a humanized monoclonal antibody designed to bind and inhibit the activity of IL-5. IL-5 is purported to play a crucial role in the maturation, growth, and chemotaxis (movement) of eosinophils, inflammatory white blood cells implicated in asthma and not found in the lungs under normal circumstances. Cephalon, Inc., Frazer, PA Phase III trials ongoing	Masitinib Mepolizumab Omalizumab Oral corticosteroids	Improved asthma control Improved asthma exacerbation rate Reduced emergency room visits Reduced hospitalization Improved quality of life
KIT tyrosine kinase inhibitor masitinib for treatment of severe asthma	Patients in whom severe persistent asthma has been diagnosed	Approximately 10% of patients with asthma do not respond to high doses of inhaled corticosteroids and long-acting beta-2 antagonists. Uncontrolled asthma can lead to hospitalization or death. Patients with severe asthma must take systemic corticosteroids that can lead to adverse events. Masitinib is an orally administered tyrosine kinase inhibitor that is purported to target the activity of mast cells, which are involved in triggering asthma attacks. Masitinib purportedly targets mast cells through selectively inhibiting KIT, platelet-derived growth factor receptor, Lyn, and to a lesser extent, fibroblast growth factor receptor 3. Masitinib is administered orally, 6 mg/kg of body weight daily, in clinical trials. AB Science S.A., Paris, France Phase III trial ongoing	Omalizumab Oral corticosteroids	Improved asthma control Improved asthma exacerbation rate Reduced emergency room visits Reduced hospitalization Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label azithromycin for prevention of chronic obstructive pulmonary disease exacerbations	Patients in whom chronic obstructive pulmonary disease (COPD) has been diagnosed	Patients experiencing severe acute exacerbations of COPD have a greater 30-day mortality rate than patients experiencing acute myocardial infarction. Acute exacerbations of COPD dramatically change the course of the disease and are associated with a rapid decline in lung function and worsening quality of life; better treatments are needed. Antibiotics have been used to prevent COPD exacerbations; however, they were shown to be ineffective. Recently macrolide antibiotics have been selected to prevent COPD exacerbations because of their purported antibacterial action combined with immunomodulatory and antiinflammatory properties. Administered orally, 250 mg, once daily, for 1 year to prevent COPD exacerbations. University of Colorado Denver Health Sciences Center, Denver, CO Phase III trials ongoing; FDA approved in 1992 for treatment of community-acquired respiratory infections and skin infections	Glucocorticoids Long-acting anticholinergic agents Long-acting beta2-agonists Phosphodiesterase-4 inhibitors	Reduced cost due to exacerbations Reduced incidence of exacerbations Increased survival Improved quality of life

Table 29. AHRQ Priority Condition: 14 Substance Abuse: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
GABA transaminase inhibitor (CPP-109, vigabatrin) for treatment of cocaine dependence	Patients in whom cocaine dependence has been diagnosed	No pharmacotherapies for cocaine dependence have been approved by FDA. CPP-109 (vigabatrin) is a gamma aminobutyric acid (GABA) transaminase inhibitor. By inhibiting GABA transaminase, GABA levels in the brain are increased, thereby suppressing dopamine release and reducing the pleasurable feelings associated with cocaine use. Vigabatrin is approved for use in patients with epilepsy, but is being redeveloped for cocaine-addiction treatment by a different company. For this indication, the drug is intended to be administered dissolved in orange juice. Catalyst Pharmaceutical Partners, Inc., Coral Gables, FL Phase II/III trial ongoing	Antabuse Beta blockers TA-CD vaccine Tiagabine Topiramate	Reduced reward associated with cocaine use Prevented relapse Long-term abstinence Improved health outcomes associated with abstinence

Table 30. AHRQ Priority Condition: 15 Cross-cutting and Other: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Primary care house calls by paramedics	Patients in need of primary care appointments who have barriers to obtaining primary care	Several factors have converged in recent years that pose barriers in certain patient groups (e.g., incapacitated elderly) to going out to obtain primary care at a primary care office. Furthermore, part of the Federal Health Reform Act was intended to enable establishment of innovative primary care programs, which could include emergency medical service workers as providers of primary care. Several states have repurposed their emergency paramedics to make primary care house calls to patients who otherwise would not be able to seek care in a clinical setting. Patients are referred to paramedic personnel by their primary care physicians to receive services at home. Paramedics see patients during the downtime when they are not responding to emergency calls. Services include hospital discharge followup, blood draws, medication reconciliation, and wound care. Some of these initiatives are being funded by State grants, but eventually are intended to be services covered by third-party payers. Pilot programs ongoing in several states, including Colorado, Texas, and Minnesota	No care due to lack of access House calls by physicians Care in a clinical setting	Improved access to care Lower morbidity Improved health outcomes Increased survival Improved patient satisfaction

Section 3. Interventions Tracked but Archived Since Last Update: 38 Interventions

Table 31. AHRQ Priority Condition: 01 Arthritis and Nontraumatic Joint: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Chemokine receptor antagonist novarixin (SCH 527123) for treatment of psoriasis	Patients in whom psoriasis has been diagnosed	Novarixin is an oral CXCR2 receptor antagonist that is purported to have anti-inflammatory effects, such as inhibiting the mirgration of neutrophils to sites of inflammation, which is believed to be involed in the development of psoriasis plaques. Merck & Co., Inc., Whitehouse Station, NJ Phase II trial completed	Alefacept Ustekinumab TNF blockers: Adalimumab Etanercept Infliximab	Reduced symptoms on Psoriasis Activity and Severity Index	No evidence that Merck is pursuing further development of this drug for this indication anymore.

Table 32. AHRQ Priority Condition: 02 Cancer: 7 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Cancer vaccine (MKC1106-MT) for treatment of advanced melanoma	Patients who are positive for *HLA-A2* gene in whom treatment-resistant advanced regional or metastatic melanoma confined to skin, subcutaneous tissue, and/or lymph nodes has been diagnosed	MKC1106 is a two-part cancer vaccine strategy in which immune stimulants are introduced directly into lymph nodes, which have a large concentration of antigen presenting cells and T cells. The first part of the vaccine is a DNA plasmid that encodes fragments of cancer-specific Melan-A and tyrosinase; second portion of vaccine involves injection of human leukocyte antigen-A2 specific peptides into the lymph nodes MannKind Corp., Valencia, CA Phase II trial terminated by company for business reasons	Standard of care	Improved overall survival Improved progression-free survival Improved quality of life	Company halted development for business reasons
EL625, cenersen (Aezea) for treatment of acute myelogenous leukemia	Patients in whom acute myelogenous leukemia has been diagnosed	EL625, cenersen (Aezea®) inhibits the translation of p53 protein, reducing p53 expression; proposed to sensitize cancer cells and protect noncancer cells from effects of chemotherapy. Eleos, Inc., Omaha, NE Phase II trial complete; FDA granted orphan drug status for malignant melanoma, CLL, and acute myelogenous leukemia.	Standard chemotherapy	Increased overall survival Increased progression-free survival Improved quality of life	Development appears halted; most recent study was withdrawn prior to patient enrollment because of insufficient funding

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Erwinia chrysanthemi-derived asparaginase (Erwinase) for treatment of acute lymphoblastic leukemia	Patients in whom acute lymphoblastic leukemia (ALL) has been diagnosed and who have developed hypersensitivity to *Escherichia coli*-derived asparaginase	One of the mainstays of ALL treatment is the use of asparaginase; however, up to 60% of patients treated with asparaginase develop an antibody response and/or hypersensitivity reactions to the *E. coli*-derived drug. Erwinase® is a preparation of asparaginase derived from *Erwinia chrysanthemi* that is immunologically distinct and could allow continued asparaginase treatment of patients who have developed immune reactions to the *E. coli*-derived drug. EUSA Pharma, Ltd., Oxford, UK Phase III trials completed; biologic license application submitted to FDA in Nov 2010. Erwinase is currently available in U.S. under treatment investigational new drug exemption; FDA granted orphan drug status	Anthracyclines (doxorubicin, daunorubicin) Cyclophosphamide Cytarabine (ara-C) Epipodophyllotoxins (etoposide, teniposide) Vincristine	Increased progression-free survival Increased overall survival Improved quality of life	While drug has been granted orphan drug status and a biologic license application was recently submitted to FDA, this product has been available to clinicians for many years under FDA-approved expanded access programs. References to its use date back to the 1970s. Approval seems unlikely to make a significant impact on the health care system.
Exelbine (ANX-530) for treatment of nonsmall cell lung cancer (NSCLC)	Patients in whom NSCLC has been diagnosed who would normally be treated with Navelbine or its generic equivalents	Exelbine™ is an emulsion formulation of Navelbine® (vinorelbine); proposed to result in fewer side effects associated with venous injection of Navelbine (e.g., injection site reactions such as phlebitis, erythema, pain). ADVENTRX Pharmaceuticals, Inc., San Diego, CA New drug application submitted to FDA through a 505(b)(2) application that relies on FDA's findings of safety and effectiveness of a reference drug. FDA issued response letter Aug 9, 2011, requesting a bioequivalence trial be redone. In Sept 2011, ADVENTRX announced that it had discontinued development of Exelbine.	Navelbine or generic monotherapy Navelbine or generic in combination with cisplatin	Reduced injection-site side effects Improved patient compliance	In Oct 2011, the company stated it "has discontinued making significant additional capital investments into the Exelbine program and is seeking a partner or outside investor for the program."

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
OncoVex (GM-CSF) for treatment of locally advanced head and neck cancer	Patients in whom locally advanced head and neck cancer has been diagnosed	Advanced head and neck cancer has a poor prognosis and high recurrence rate, suggesting a need for novel treatment options. OncoVex (GM-CSF) is an oncolytic virus purported to replicate only in tumor cells; OncoVex is engineered to lyse tumors cells as well as to express tumor-specific antigens and GM-CSF, which help to generate tumor-specific immune responses for additional benefit. Administered intratumorally up to 4 mL of 10^8 pfu/mL per node and up to 8mL total of OncoVex^GM-CSF and cisplatin (100 mg/m^2) following radiation and OncoVex^GM-CSF in trials. Amgen, Inc., Thousand Oaks, CA Phase III trial terminated	Surgical resection Radiation therapy with adjuvant chemotherapy (cisplatin) Reolysin (in clinical development)	Increased overall survival Increased progression-free survival Improved quality of life	Amgen seem to have halted development in head and neck cancer. Phase III trial is listed as terminated on clinical trials.gov.
Respiragene test for smokers at high risk of lung cancer who would benefit from computed tomography screening	Smokers and ex-smokers being screened for lung cancer	The Respiragene™ test examines a patient's genotype at 20 markers and considers those results and family and smoking/health history to predict likely lifetime risk of lung cancer. This is purported to be useful to determine who should receive computed tomography screening. Molecular Diagnostics Laboratories, LLC , Covington, KY, clinical lab division of PhD Diagnostics, part of the larger BioLOGIC LLC network Available as laboratory-developed test	Chest radiographic screening for high-risk population Computed tomography screening for high-risk population	Increased sensitivity and specificity Increased predictive values Earlier cancer detection Increased overall survival due to earlier diagnosis and treatment	No longer meets horizon scanning system criteria to include only tests being developed as commercial test kits (i.e., laboratory-developed tests excluded from system)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Thymidylate synthase level determination to predict response to 5-fluorouracil chemotherapy in colorectal cancer	Patients in whom nonresectable CRC has been diagnosed who are undergoing chemotherapy with a 5-fluorouracil regimen	5-Fluorouracil is a thymidylate synthase inhibitor (TSI). Pretreatment determination of tumor thymidylate synthase levels might be useful to predict response to 5-fluorouracil monotherapy versus combination therapy with irinotecan, which has higher toxicity. Phase II trial complete	Chemotherapy without predetermination of TSI level	Improved tumor response Increased survival Reduced side effects	No longer meets horizon scanning system criteria to include only tests being developed as commercial test kits (i.e., laboratory-developed tests excluded from system)

Table 33. AHRQ Priority Condition: 03 Cardiovascular: 6 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
B vitamin supplementation for treatment of stroke-related depression	Patients in whom stroke-related depression has been diagnosed	Of patients who survive stroke, depression occurs in approximately 40% to 50%, and major depression occurs in about 20%. Consuming certain B vitamins through diet or supplementation is known to decrease total plasma concentration of homocysteine (tHcy) and is proposed to improve response to standard antidepressant therapy. Researchers are studying whether daily B-vitamin supplementation reduces long-term prevalence of depression in patients who survive a stroke. Royal Perth Hospital, Perth, Western Australia, led the investigation Large international trial (VITATOPS-DEP) completed at 111 participating centers in U.S., Australia, New Zealand, Europe, Asia, Russia, and other locations; results published Oct 2010	Antidepressant therapy with and without B supplementation	Symptom improvement Decreased depression Improved quality of life	Initially identified as an injected supplement requiring physician administration; confirmed it is an oral vitamin supplement and does not meet horizon scanning system criteria
Bucindolol hydrochloride (Gencaro) for treatment of heart failure in beta-1 389 Arg/Arg positive patients	Patients in whom advanced HF has been diagnosed and have genotype-defined (beta-1 389 Arg/Arg positive)	Bucindolol hydrochloride (Gencaro™) is first cardiovascular drug for which genetic testing will have to be performed to identify patients who are likely to respond to it. Laboratory Corp. of America (LabCorp) is developing and commercializing a companion genetic diagnostic to aid in identifying patients best suited for bucindolol. ARCA biopharma, Inc., Broomfield, CO NDA not approved by FDA in 2009; FDA granted Special Protocol Assessment in May 2010 on design of new trial to assess safety and efficacy for chronic HF in patients with genotype that appears to respond best to bucindolol. Trial has not yet begun.	Optimal medical management	Improved heart function Delayed progression of HF Reduced hospital admissions to treat HF	Experts identified as very low impact “me-too” drug for this indication; company also appears to have halted development

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Cardio3KG for diagnosis of left bundle branch block abnormality in suspected heart attack	Patients in whom MI is suspected	Cardio3KG™ is electrocardiogram software called the QRS-T Loop ratio, intended to help determine whether left bundle branch block (LBBB) is new or old through identification of a diffuse 12-lead electrocardiogram abnormality that makes it difficult or impossible to read an electrocardiogram; intended to determine whether a new LBBB is producing signs of an acute heart attack. NewCardio, Inc., Santa Clara, CA Company intends file for FDA 510(k) clearance in 2011 or early 2012	Electrocardiogram readings without Cardio3KG software Computed tomography angiography Angiography	More accurate discrimination between old and new LBBB Reduced unnecessary invasive procedures	Expert commenting stated that this technology will never be high impact because it's an "incremental" benefit over currently available technology
Everolimus-eluting (Promus Element) stent for treatment of coronary artery disease in patients with diabetes or acute myocardial infarction	Patients in whom coronary artery disease associated with diabetes or acute MI has been diagnosed and who are eligible for stenting	Everolimus-eluting stent (Promus® Element™) purports to be made of a novel platinum chromium alloy and to have an innovative stent design intended to offer greater radial strength and flexibility while reducing stent recoil, which the company asserts is important for patients with coronary artery disease associated with diabetes or in the setting of acute MI. Boston Scientific, Inc., Boston, MA Late-phase U.S. trials; anticipating FDA premarket approval (PMA) application submission by 2012; CE marked; launched in India Feb 2011	Other DESs used in patients with diabetes or acute MI Bypass graft surgery Optimal medical management	Consistent lesion coverage and drug distribution	In-depth searches showed this to be an incremental development; does not address unmet need

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Galectin-3 blood test for assessing prognosis in heart failure	Patients in whom chronic HF has been diagnosed	The Galectin-3 test is intended to be used in conjunction with clinical evaluation as an aid to assess the prognosis of patients. Elevated galectin-3 levels in HF patients have been associated with a higher risk of adverse events, including mortality or hospitalization. BG Medical, Waltham, MA in partnership with Abbott Laboratories, Abbott Park, IL, BioMerieux SA, Marcy l'Etoile, France, and Alere, Inc., Waltham, MA FDA 510(k) clearance granted Nov 2010	Blood pressure Other blood tests (urea nitrogen; brain natriuretic peptide; sodium levels)	Accurate detection of Galectin-3 levels Sensitive/specific identification of HF patients at high risk of adverse events or mortality	Expert comments deemed this low impact; also is not a test kit, only a laboratory developed test which does not meet current horizon scanning system criteria for inclusion
PCSK9 inhibitor (SPC5001) for treatment of hyper-cholesterolemia	Patients in whom hyper-cholesterolemia has been diagnosed	Despite available therapies, most patients with high cholesterol levels are not getting the treatment they need to reduce their risk of cardiovascular events, the World Health Organization recently reported. This drug represents a new mechanism of action for this disease state; SPC5001 is a mRNA-targeted drug that is intended to inhibit proprotein convertase subtilisin/kexin type 9 (PCSK9), a protein involved in removing LDL cholesterol from the bloodstream (inhibiting PCSK9 increases degradation of LDL). Santaris Pharma a/s, Hoersholm, Denmark Phase I trial terminated	Omega-3 fatty acids Statins	Improved lipid parameters Improved cardiovascular outcomes	Development appears to have been halted

Table 34. AHRQ Priority Condition: 04 Dementias (including Alzheimer's Disease): 3 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
ApoA-1 production agent (RVX-208) for treatment of Alzheimer's disease	Patients in whom AD has been diagnosed	RVX-208 is a first-in-class ApoA-1 production agent, originally developed as a lipid modifying drug. High levels high-density lipoprotein cholesterol are associated with prevention of AD, low plasma Abeta40 is a risk factor for developing AD, and Abeta40 (biomarker for AD) binds to ApoA-1. Thus, increasing ApoA-1 may clear Abeta40 from the brain, decreasing the Abeta40 load in the brain, which may have disease-modifying effects to slow or halt progression of AD. Resverlogix Corp., Calgary, Alberta, Canada; collaborating with Sun Health Research Institute, Sun City, AZ Phase I trial completed	No comparators approved for disease modification Symptom treatment comparators: Galantamine Rivastigmine Donepezil Memantine	Decreased Abeta40 load in brain Reduced symptoms Reduced incidence Improved quality of life Improved long-term outcomes	Development appears to be halted
Docosahexaenoic acid (DHA) for treatment of mild to moderate Alzheimer's disease	Patients in whom mild to moderate AD has been diagnosed	Docosahexaenoic acid (omega-3 fatty acid); epidemiological studies have shown that omega-3 fatty acid consumption reduces AD risk; docosahexaenoic acid modifies the expression of Alzheimer-like brain pathology in mouse models. Funded by Martak Biosciences Corp., Columbia, MD Phase III trial completed	Memantine Cholinesterase inhibitors	Delayed or halted progression of disease Preserved memory and cognitive ability Preserved independence Less need for assistance with activities of daily living	Current horizon scanning criteria exclude tracking of over-the-counter supplements

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Wearable camera (SenseCam) to improve episodic memory in Alzheimer's disease	Patients who are experiencing memory loss secondary to mild Alzheimer's disease (AD)	A retrospective memory aid (SenseCam) that is a wide angle digital camera on a lanyard worn around the neck with automatic capture and additional sensing capability (temperature level, audio level, etc.), plus viewer software for personal computer; takes pictures passively without user intervention to create a frontal and peripheral view of patient experiences throughout the day; patients review photos on computer several times over the course of 2 weeks to strengthen episodic memory. Microsoft Research, Redmond, WA Vicon® Industries (licensee), Hauppauge, NY Available commercially as Vicon Revue as of 2010	Diary-keeping Digital cameras/recorders (require user intervention) Medication (has limited success)	Improved recall of episodic memory (without having to review images) Improved sense of self Reduced anxiety in social situations	Experts commenting did not foresee potential for high impact.

Table 35. AHRQ Priority Condition: 05 Depression and Other Mental Health Disorders: 4 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Agomelatine (Valdoxan) for treatment of major depressive disorder	Patients in whom major depressive disorder (MDD) has been diagnosed	Agomelatine (Valdoxan®) is a novel melatonin (MT1 and MT2 receptors) and selective serotonin agonist (5-HT2C antagonist) that is approved for treatment of MDD in Europe and under development in the U.S. Effects in obsessive-compulsive disorder (OCD) may have to do with melatonin modulation playing a role in circadian rhythm restoration; treatment is proposed as either a switch therapy or a treatment for patients with OCD who have never had drug therapy for the disorder. Novartis AG, Basel, Switzerland (licensed to pursue development in the U.S.) Servier Laboratories, Neuilly-sur-Seine, France Two phase III trials completed	Selective serotonin reuptake inhibitors Atypical antipsychotic drugs (off-label)	Improved scores on MDD scales (HAM-D; MADRS) Improved quality of life	Novartis announced in its financial report on Oct 25, 2011, discontinuation of the development program for agomelatine
Micronutrients for treatment of bipolar disorder and major depression	Patients in whom bipolar disorder or major depression has been diagnosed	EMPowerPlus is a micronutrient formula consisting of 16 minerals, 14 vitamins, 3 amino acids, and 3 antioxidants; taken with current psychiatric medications or as a stand-alone therapy. Truehope Nutritional Support, Ltd., Raymond, Alberta, Canada Not yet available in U.S.; commercially available in Canada	Drug therapy for bipolar disorder and depression Psychotherapy Cognitive behavioral therapy Combination therapy	Reduction in symptoms Improved quality of life	Current horizon scanning criteria exclude tracking of over-the-counter supplements and micronutrients

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Multianalyte biomarker panel for diagnosis of major depressive disorder	Patients in whom MDD diagnosis is suspected	First-in-class blood test for diagnosis of MDD; measures metabolic response, inflammatory response, hypothalamic-pituitary-adrenal axis factors, and neurochemical factors; intended for use in conjunction with physician interview and rating scales. Ridge Diagnostics, San Diego, CA Phase II trials ongoing	Physician interviews and observations Depression rating scales	Increased sensitivity and specificity Improved negative and positive predictive values Objective means of diagnosis Ability to differentiate MDD from other psychiatric disorders	Current horizon scanning system criteria exclude laboratory-developed tests not intended for development of commercial test kit
Radiosurgery for treatment of obsessive-compulsive disorder	Patients in whom severe, treatment-resistant OCD has been diagnosed	Effective therapy for treatment-resistant OCD is needed. Radiosurgery has been used infrequently for treatment of OCD for more than 20 years; this is proposed as a new approach to a different part of the brain. University of Pittsburgh, Pittsburgh, PA Pilot trial completed late 2010	DBS Surgical anterior capsulotomy	Reduced objective symptom scores Improved social and thought behaviors and physical manifestations Improved quality of life	Determined to be very incremental to prior radiosurgery approaches

Table 36. AHRQ Priority Condition 06: Developmental Delays including Autism and ADHD: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Weighted blanket for treatment of attention-deficit/hyper-activity disorder	Patients in whom ADHD has been diagnosed	ADHD is the behavioral disorder most commonly diagnosed in children, affecting about 3% to 5% of children in the U.S. ADHD may cause lack of sleep, depression, learning disabilities, and other behavioral abnormalities. The Ball Blanket is intended to stimulate the sensory system, improving body consciousness. Weight from balls integrated into the blanket press certain points of the body, stimulating the sensory system. Inhibitory impulses are transmitted to the CNS, theoretically increasing the sense of the body and its limits and purportedly providing a feeling of tranquility. Various manufacturers, including Protac a/s, Aarhus, Denmark Unphased studies under way; some completed	Behavioral therapies Combination therapies Drug therapies	Improved sleep Improved attentiveness and academic performance Reduced behavioral abnormalities	Experts commenting identified this as very low to no potential for high impact

Table 37. AHRQ Priority Condition: 07 Diabetes: 4 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Calanus oil for reducing intra-abdominal fat	Patients with body mass index (BMI) of 25 to 30	Diet supplement of Calanus® oil (a crustacean similar to krill; not for patients with allergies to shellfish); intended to reduce intra-abdominal fat, improve glucose tolerance and lipid profile. Administered 1 g, two times per day. University of Tromso, Tromso, Norway Phase II/III trial ongoing	Olive oil Exercise Diet	Reduced intra-abdominal fat Weight loss Improved lipid status Improved blood glucose levels Improved systolic and diastolic blood pressure	Current horizon scanning criteria exclude over the counter dietary suppplements
Dogs to detect hypoglycemic and hyperglycemic events in juvenile diabetes	Children in whom T1DM has been diagnosed	Diabetes-alert dogs are trained to alert parents and caregivers when children have low blood sugar. Diabetes Friendly Foundation, Dallas, TX No trials identified; foundation is fund-raising	Blood sugar monitors	Decrease or eliminate hypoglycemic events Increased independence for children Improved quality of life for parents and children	No indication this is being pursued further at this time

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Olmesartan (Benicar) to prevent microalbuminuria associated with type 2 diabetes	Patients in whom T2DM has been diagnosed and who have normal urine albumin levels and at least one cardiovascular risk factor	ACE inhibitors and angiotensin-receptor blockers (ARBs) have been shown to slow progression of diabetic nephropathy; while studies on use of ACE inhibitors to control hypertension have been performed and found that the drugs delayed onset of microalbuminuria (a marker of early kidney damage and a cardiovascular risk factor), studies in diabetic patients with normal blood pressure and studies on use of ARBs to prevent microalbuminuria have not been performed. Olmesartan (Benicar®) is and ARB being studied as an agent to prevent microalbuminuria in patients with diabetes and normal blood pressure or hypertension controlled by medications that do not impact the renin-angiotensin system. Daiichi Sankyo, Tokyo, Japan Phase III trial completed 2009	ACE inhibitors Other ARBs	Delay in development of microalbuminuria Reduced percentage of T2DM patients who present with microalbuminuria Prevention of diabetic nephropathy	Development appears to have been halted
Vascular endothelial growth factor A transcriptional activator (SB-509) for treatment of diabetic neuropathy	Patients in whom diabetic neuropathy has been diagnosed	SB-509 is a rationally designed zinc finger transcription factor that fuses a DNA binding domain specific for a DNA sequence in proximity to the vascular endothelial growth factor A (*VEGF-A*) gene to a transcriptional activation domain; designed to upregulate expression of VEGF-A, which has neuroproliferative, neuroregenerative, and neuroprotective properties. Sangamo Biosciences, Inc., Richmond, CA Phase IIb trial did not meet its primary or secondary clinical endpoints	Agents to maintain tight glycemic control Analgesics Lidocaine patches Duloxetine [antidepressant], Pregabalin [anticonvulsant])	Reduced pain	Company announced Oct 2011 halting development program for SB-509

Table 38. AHRQ Priority Condition: 08 Functional Limitations and Disability: 6 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Enzyme replacement therapy (CM - 4612) for treatment of attention deficit hyperactivity disorder	Children in whom attention deficit hyperactivity disorder (ADHD) has been diagnosed	CM - 4612 is a drug intended to address the lack of protein digestion seen in ADHD; compound is given with meals and intended to increase protein digestion and availability of essential amino acids. Curemark, LLC, Rye, NY Phase III trials ongoing	Medications for ADHD Behavioral therapy Combination therapy	Reduced behavioral symptoms Improved focus Improved academic achievement Improved quality of life	Development of drug by this name appears no longer in development; company has drug by a different name in development for ADHD
Carbidopa-levodopa (IPX 066) for treatment of early-stage Parkinson's disease	Patients in whom early-stage PD has been diagnosed	New formulation as extended-release carbidopa-levodopa (IPX066) aimed at producing a rapid and sustained concentration of levodopa; intended to improve symptom management and potentially reduce off time in patients; extended-release formulation could reduce dosing frequency. Impax Laboratories, Inc., Hayward, CA Phase III trials ongoing	Regular formulation of carbidopa-levodopa	Improvement from baseline on Unified Parkinson's Disease Rating Scale	New formulation determined to be too incremental to existing treatment
Ibutamoren mesylate for treatment of decreased appetite in end-stage renal disease	Patients with end stage renal disease (ESRD) at risk of malnutrition due to decreased appetite	Orally administered ibutamoren mesylate (MK-0677), a synthetic form of ghrelin, an endogenous growth hormone (GH) receptor secretagogue shown to raise endogenous growth hormone levels and improve food intake. Merck & Co., Inc., Whitehouse Station, NJ Phase II trials to raise insulin-like growth factor-1 (IGF-1) in ESRD ongoing; MK-0677 previously studied in phase II trials for other indications	Parenteral administration of GH and IGF-1 to improve muscle mass, quality of life, nutritional parameters, immune and physical function in ESRD patients	Reduction in malnutrition leading to muscle loss due and functional disability in ESRD patients	Company no longer lists drug in its development pipeline

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Neurostimulation (Aura6000) for treatment of obstructive sleep apnea	Patients in whom OSA has been diagnosed	Compliance with current mechanical OSA therapies (e.g., CPAP delivered while asleep) is low and current surgical alternatives permanently alter facial/airway anatomy. Aura6000™ represents a novel surgical treatment as an implant designed to deliver physiologically timed, mild stimulation to the hypoglossal nerve on each breathing cycle; intended to restore tone to the muscles that control the base of the tongue, preventing it from collapsing and obstructing the airway; implant is controlled by patients via a handheld programmer and the purported advantage of this treatment is that it doesn't permanently alter facial or airway anatomy. ImThera Medical, Inc., San Diego, CA Phase I/II trials completed in Europe; company intends to pursue an IDE with FDA in 2011 to start trials in U.S.	CPAP Oral appliances Positional therapy Weight loss Surgery	Improved compliance with therapy Improved airway muscle tone Improved long-term cardiovascular outcomes Improved quality of life Improved sleep quality	Experts commenting on topic considered this very low potential impact
Neurostimulation (Inspire) for treatment of obstructive sleep apnea	Patients in whom OSA has been diagnosed	Inspire™ Upper Airway Stimulation (UAS) is an implant designed to deliver physiologically timed, mild stimulation to hypoglossal nerve on each breathing cycle; intended to restore tone to the muscles that control the base of the tongue, preventing it from collapsing and obstructing the airway; controlled by patients via handheld programmer; purported advantage of this potential treatment for OSA is that it doesn't permanently alter facial or airway anatomy. Inspire Medical Systems, Minneapolis, MN Phase III trial initiated; CE marked	CPAP Oral appliances Positional therapy Weight loss Surgery	Improved airway muscle tone Improved long-term cardiovascular outcomes Improved quality of life Improved sleep quality	Experts commenting on topic considered this very low potential impact

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Synthetic bone graft (Augment) for foot and ankle fusion surgery	Patients who have been referred for foot and ankle bone fusion surgery	Obviating need for autologous graft harvesting from patients undergoing foot and ankle fusion surgery could reduce surgical times and quicken patient recovery by reducing pain and risk of infection from bone harvesting. Recombinant human platelet-derived growth factor (rhPDGF-BB) is a synthetic form of platelet-derived growth factor (PDGF) used to augment healing during foot and ankle bone fusion procedures. Augment™ is injected during bone graft surgery. BioMimetic Therapeutics, Inc., Franklin, TN Premarket approval application (PMA) submitted to FDA; FDA advisory panel gave positive recommendation for approval in May 2011	Autologous bone grafts	Reduced pain by obviating need for harvesting bone for autologous bone grafts Reduced complications associated with autologous bone harvest Faster recovery	In-depth searches showed this to be similar to other products available already

Table 39. AHRQ Priority Condition: 09 Infectious Disease: 8 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Blood test for distinguishing respiratory viral infections from bacterial infections	Patients with symptoms of a respiratory infection	Blood test is purported to seek out the "signature" of the microbe that caused the patient symptoms; it is intended to be more accurate and consistent than looking for the microbes themselves. University researchers; U.S. Department of Defense Early phase trials ongoing	Physical examination Laboratory cultures	More accurate diagnosis and faster triage to appropriate treatment of colds, flu, respiratory illness Reduced inappropriate antibiotic and antiviral use Reduced antimicrobial and antiviral resistance Reduced transmission of serious respiratory infections	Does not meet current horizon scanning criteria for inclusion; laboratory-developed test not being developed as a test kit at this time

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Collaborative patient safety program to eliminate central-line-associated bloodstream infections	Hospitals with sub-optimal rates of central-line-associated bloodstream infections (CLABSIs)	Comprehensive Unit-Based Safety Program (CUSP) is a model for using evidence, rigorous measurement, and collaboration to reduce CLABSIs; it combines use of three existing programs: (1) Quality and Safety Research Group (QSRG) model to translate research into practice; (2) CUSP, to improve safety culture at a hospital and learn from mistakes; (3) ongoing measuring, reporting of data, and performance improvement. Johns Hopkins School of Medicine and QSRG, Baltimore, MD First state-wide program implemented in Michigan; then Rhode Island and in Adventist healthcare system; early clinical data available	Checklist-based patient safety measures and programs	Reduced incidence of CLBASIs Reduced mortality for CLBASIs Improved work culture and teamwork	In-depth searches found program to be diffused
Oritavancin for treatment of acute bacterial skin and skin structure infection	Patients in whom acute bacterial skin and skin structure infection has been diagnosed	Oritavancin is a semisynthetic lipoglycopeptide antibiotic for treatment of serious gram-positive infections, with similar structure to vancomycin; however oritavancin may be administered as a single 1,200 mg intravenous injection instead of 7 to 10 days of intravenous vancomycin. Oritavancin could offer a simpler, easier-to-administer dosing regimen that may reduce hospital costs by shortening stays and reducing nosocomial infection rates. The Medicines Co., Parsippany, NJ Phase III trials ongoing	Daptomycin Linezolid Quinupristin/ dalfopristin Vancomycin	Resolution of fever Clinical cure	Too incremental (potential improvement to vancomycin)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Automated monitoring system to improve nurses' hand hygiene	Nurses in hospitals	Hand-washing compliance is difficult to achieve and maintain; noncompliance results in serious consequences for patients (morbidity and mortality) and the health care system. The automated hand hygiene (HH) monitoring system (iDAPT program) is a wearable monitor that tracks HH rates, times, and locations, transmits alerts to improve compliance, and aggregates performance data. It works with both wearable hand sanitizer dispensers and wall-mounted dispensers, notes when hands should be washed (e.g., when entering or leaving patient rooms, while in utility areas, bathrooms, etc.), and alerts caregivers if they don't comply. Can be implemented entirely on its own, without tapping into hospital infrastructure. Developed by Toronto Rehabilitation Institute, Toronto, Ontario, Canada Feasibility and acceptability trials completed; larger efficacy trial being designed (Sept 2011)	Other monitoring systems, for which no clinical data is available (e.g., visual reminders using motion sensors when entering patient rooms)	Improved HH and HH compliance Reduced nosocomial infections Reduced morbidity and mortality	Too similar to other tracking systems for handwashing compliance
Influenza virus vaccine (Fluzone Quadrivalent) for prevention of influenza	People at risk of contracting viral influenza	Influenza virus vaccine (Fluzone® Quadrivalent) consists of a quadrivalent inactivated influenza vaccine; two strains of type A (H1N1 and H3N2) and two strains of type B (one each from the Yamagata and Victoria lineages) influenza viruses; designed to give the broadest protection against flu variants (even emergent strains), more broad than existing vaccines. Sanofi-Aventis, Bridgewater, NJ Phase III trials ongoing	Trivalent influenza vaccine	Improved protection against the flu Decreased transmission rates	Experts commenting considered this to be too incremental with very low potiential for high impact

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Live intranasal quadrivalent influenza vaccine (FluMist) for prevention of seasonal influenza	Patients at risk for contracting seasonal influenza	Quadrivalent live attenuated influenza vaccine (Q/LAIV, FluMist®) is a vaccine formulation that consists of four live attenuated strains of H1N1, H3N2, B/Yamagata and B/Victoria influenza virus, which is intended to provide broad spectrum coverage against seasonal influenza strains; the quadrivalent vaccine is purported to be as immunogenic and safe as trivalent formulations containing either B strain; if approved, it could be the first quadrivalent vaccine on the market. Administered intranasally in eligible individuals 2 to 49 years of age. MedImmune, LLC, Gaithersburg, MD Supplemental biologics license application filed with FDA in Jul 2011	FLU Q-QIV (GSK2282512A) Fluzone Quadrivalent Other quadrivalent vaccines In development	Increased protection against influenza infection Reduced morbidity Reduced mortality	Experts commenting considered this to be too incremental with very low potiential for high impact
Quadrivalent vaccine (FLU Q-QIV) for prevention of viral influenza	People at risk for viral influenza	Vaccine (FLU Q-QIV GSK2282512A) consists of a quadrivalent inactivated influenza vaccine, other flu vaccines address fewer than four viruses. GlaxoSmithKline, Middlesex, UK Phase III trials ongoing	Trivalent influenza vaccine	Improved protection against the flu Decreased transmission rates of viral influenza	Experts commenting considered this to be too incremental with very low potiential for high impact
Sodium fusidate (Taksta) for treatment of methicillin-resistant *Staphylococcus aureus*	Patients in whom a diagnosis of methicillin-resistant *S. aureus* (MRSA) infection is suspected	Sodium fusidate (Taksta™; formerly CEM-102) antibiotic is intended to be administered through a unique oral dosing regimen. Cempra Pharmaceuticals, Inc., Chapel Hill, NC Phase II trials completed in U.S.; available in Europe	Clindamycin Linezolid Minocycline	Resolution of MRSA infection	Experts commenting considered this to be too incremental with very low potiential for high impact

Section 4. Interventions Identified and Not Tracked: 2 Interventions

Table 40. AHRQ Priority Condition: 03 Cardiovascular: 1 Intervention

Topic Title	Potential Patient Population	Intervention Manufacturer(s) Phase of Development	Potential Comparators	Reason Not Tracked
Fibrogen-based cell preparation (HP802-247) for treatment of venous leg ulcers	Patients in whom venouse leg ulcers have been diagnosed	Venous stasis wounds are caused by poor blood circulation in the lower extremities due to weakening of venous valves. Venous stasis ulcers are slow to heal and often recur after treatment, progressing to rapidly eroding and deep wounds. HP802-247 is an allogeneic living cell suspension consisting of two components that are sprayed sequentially on the wound bed: a fibrinogen solution and a cell preparation containing a mixture of growth arrested, living, allogeneic epidermal keratinocytes and dermal fibroblasts. This compound is purported to release angiogenic factors into the wound through living, metabolically active, but nonproliferating cells trapped in the wound surface via the created fibrin matrix. This mechanism of action purportedly stimulates the patient's cells to heal the venous leg wound. One dose of HP802-247 consists of 260 uL containing keratinocytes and fibroblasts totaling 0.5 x 10^6 or 5.0 x 10^6 power cells per mL plus fibrin. Healthpoint Biotherapeutics, Inc., Fort Worth, TX Phase IIb trial completed	Hyperbaric oxygen therapy Negative wound pressure therapy Other platelet-derived growth factors (PDGFs) Standard wound therapy (debridement and dressing)	Many other preparations available; too incremental

Table 41. AHRQ Priority Condition: 07 Diabetes: 1 Intervention

Topic Title	Potential Patient Population	Intervention Manufacturer(s) Phase of Development	Potential Comparators	Reason Not Tracked
Fibrogen-based cell preparation (HP802-247) for treatment of venous leg ulcers	Patients in whom venouse leg ulcers have been diagnosed	Venous stasis wounds are caused by poor blood circulation in the lower extremities due to weakening of venous valves. Venous stasis ulcers are slow to heal and often recur after treatment, progressing to rapidly eroding and deep wounds. HP802-247 is an allogeneic living cell suspension consisting of two components that are sprayed sequentially on the wound bed: a fibrinogen solution and a cell preparation containing a mixture of growth arrested, living, allogeneic epidermal keratinocytes and dermal fibroblasts. This compound is purported to release angiogenic factors into the wound through living, metabolically active, but nonproliferating cells trapped in the wound surface via the created fibrin matrix. This mechanism of action purportedly stimulates the patient's cells to heal the venous leg wound. One dose of HP802-247 consists of 260 uL containing keratinocytes and fibroblasts totaling 0.5 x 10^6 or 5.0 x 10^6 power cells per mL plus fibrin. Healthpoint Biotherapeutics, Inc., Fort Worth, TX Phase IIb trial completed	Hyperbaric oxygen therapy Negative wound pressure therapy Other platelet-derived growth factors (PDGFs) Standard wound therapy (debridement and dressing)	Many other preparations available; too incremental
Topical platelet-derived growth factor (KUR-211) for treatment of diabetes-related foot ulcers	Patients in whom diabetic foot ulcers have been diagnosed	Approximately 3 million patients a year suffer from diabetic foot ulcers, and an estimated 15% will require amputation. Current treatments for diabetic foot ulcers achieve complete healing less than 30% of the time; therefore, effective treatments are intended to accelerate and complete the wound healing process. KUR-211 is a bioactive material that consists of a modified variant of PDGF incorporated into a fibrin sealant. This material is applied to the foot ulcer as a foam and has a "TG-hook" technology that allows PDGF to remain at the ulcerated site to stimulate granulation tissue formation through sustained delivery of PDGF. KUR-211 is applied topically twice a week for a maximum of 16 weeks. Kuros Biosurgery AG, Zurich, Switzerland Phase IIb trial ongoing	Hyperbaric oxygen therapy Negative wound pressure therapy Other PDGFs Standard wound therapy (debridement and dressing)	Many other PDGFs available; too incremental