AHRQ Healthcare Horizon Scanning System – Status Updates

Horizon Scanning Status Update: July 2013

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. HHSA290201000006C

Prepared by:
ECRI Institute
5200 Butler Pike
Plymouth Meeting, PA 19462

July 31, 2013

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. HHSA290201000006C). 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.

Disclaimer Regarding 508-Compliance
Persons using assistive technology may not be able to fully access information in this report. For assistance contact info@ahrq.gov.

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

Public Domain Notice

Suggested citation: ECRI Institute. AHRQ Healthcare Horizon Scanning System Status Update. (Prepared by ECRI Institute under Contract No. HHSA290201000006C) Rockville, MD: Agency for Healthcare Research and Quality. July 2013.
http://www.effectivehealthcare.ahrq.gov/reports/final.cfm.

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 emerging technologies and innovations in health care and to create an inventory of emerging 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 identifying and monitoring 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 analyzing 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 use 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 2–3 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 email to: effectivehealthcare@ahrq.hhs.gov.

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Elise Berliner, Ph.D.
Task Order Officer
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Contents

Introduction

The AHRQ Healthcare Horizon Scanning System produces reports and status updates from its activities. Two and a half years have passed since the initiation of the system. The horizon time frame focuses on identifying topics anticipated to be within 3 years of possible diffusion into clinical practice. A few surrogates are used to determine this horizon, such as clinical investigation in phase III trials for interventions subject to regulatory processes of the U.S. Food and Drug Administration (FDA). Topics with FDA orphan drug status, fast-track status, or innovation pathway designation are considered if phase II trials are ongoing. For the broad priority area of "Functional Limitations and Disability," AHRQ has designated use of the definition of disability used by the Department of Health and Human Services.

The Status Update is a summary of data elements collected from implementation of the Horizon Scanning Identification and Monitoring Protocol. Status Update reports are now produced four times a year, with each new report superseding the prior version. This Status Update is organized into three main topic-status sections and by priority condition within each section. The table of contents provides direct links to each section's priority condition tables. Topics that were already in the system are presented first as "Currently Tracked Interventions," followed by "Interventions Added Since Last Update," and then by "Interventions Tracked but Archived Since Last Update" during the prior tracking period of 12 weeks. Each table provides information under the following column headings: Topic Title, Potential Patient Population, Intervention Description (including the Developer/Manufacturer[s] and Phase of Development), Potential Comparators, and Potential Health or Other Impacts.

Criteria for including topics in the Status Update are provided in detail in the newly revised "Horizon Scanning Protocol and Operations Manual," which is available on the Effective Health Care Web site (Protocol and Operations Manual). Briefly, broad scanning is performed for each priority condition to detect "leads" to interventions and innovations that are anticipated to be within 3 years of potential diffusion into clinical practice. Sets of questions are applied to determine whether any given intervention addresses an "unmet need" such as a large 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 topic nomination meetings, 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 United States, 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 topic nomination meetings are entered into the System for tracking and appear in the Status Update report as "Currently Tracked Interventions" and "Interventions Added Since Last Update."

Topics accepted for tracking may also be designated during the meeting for further searches to collect more in-depth information about them. Such topics must be far enough along in development (typically in phase III trials for drugs, in phase II or III trials for devices, and pilot information for care delivery innovation topics) to have some preliminary efficacy and safety

data available. The horizon scanning medical librarians and analysts proceed with more in-depth and topic-specific searching for information on the topics selected for advancement.

Once topic profiles 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 United States. Over time, a topic may be archived because development has ceased because it no longer addresses an unmet need and is not novel or because the intervention has diffused past early adoption and "timed out" in the horizon scanning system (i.e., 2 years postapproval or initial diffusion).

Populating the horizon scanning system has been ongoing since December 2010. During that time, more than 15,800 leads have been uploaded into the system and reviewed by analysts, from which about 1,900 topics have been initially identified and moved through the system. This Status Update report contains 460 identified interventions we are tracking, which includes 5 new topics entered into the system during this reporting period. We archived 55 topics during this reporting period. The reason for archiving each topic is provided in its respective priority area table of archived topics. Three reasons account for the majority of archived topics: expert commenters saw no high-impact potential at this time for the parameters of interest to AHRQ; companies halted development for lack of funding or for lack of trials meeting endpoints; or topics that had been tracked met criteria for retiring from the system because they have diffused since tracking started, have shown no movement at all in over 2 years of tracking, or are 2 years past approval by the U.S. Food and Drug Administration.

In this update, four priority areas comprise about 72% of the interventions (including programs) being tracked. Interventions related to cancer account for about 35% (161/460) of tracked topics this reporting period. The other priority areas with the most tracked topics in descending order of number of topics are as follows: functional limitations and disability (17%, 80/460), cardiovascular diseases (10%, 46/460), and infectious diseases (9%, 43/460).

Interventions being tracked in each of the remaining 10 priority conditions (arthritis, dementia, depression and other mental illness, developmental delays, diabetes, obesity, peptic ulcer disease and dyspepsia, pregnancy and childbirth, pulmonary diseases, and substance abuse) plus an additional area we designate as cross-cutting, account for 4% or fewer (each priority area) of the total topics tracked, for a combined total of about 28% (130/460) of topics being tracked in the system.

In terms of overall types of interventions, about 86% (rounded to the nearest percent) fall into one of two general categories, and the proportions of topics in these categories have changed only slightly since initial reporting. About 70% of topics are pharmaceutical/biotechnology (i.e., drug, vaccine, biologic) and about 16% are devices used as implants or used externally to deliver treatments. About 4% are technologies intended to screen, diagnose, identify risk, identify blood markers or gene mutations, or monitor a disease state (these are devices, assays, imaging modalities). About 3% of topics are surgeries and procedures. About 2% are innovative programs, services, or care delivery practices, and another 2% involve information technology, information systems, or applications used in treating, managing, or monitoring patients. About 0.7% are assistive technologies (e.g., prostheses).

Section 1. Currently Tracked Interventions: 455 Interventions

Table 1. AHRQ Priority Condition: 01 Arthritis and Nontraumatic Joint Disease: 13 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Artificial cervical disc (Mobi-C) for treatment of two-level degenerative disc disease	Patients in whom 2-level degenerative disc disease (DDD) has been diagnosed	Standard of care for 2-level cervical degenerative disc disease includes anterior cervical discectomy and fusion surgery, which can reduce range of motion and lead to accelerated degeneration of adjacent discs and other complications. The Mobi-C® Cervical Disc (Mobi-C) is a metal and polyethylene mobile bearing prosthesis purportedly designed as a low-profile cervical intervertebral disc replacement for both 1- and 2-level disc replacement. Mobi-C is composed of superior and inferior cobalt/chromium/molybdenum alloy spinal plates coated with a titanium plasma spray and hydroxyapatite coating, and a polyethylene mobile insert. The controlled mobility of the insert purportedly improves restoration of the physiologic instantaneous axis of rotation of the cervical vertebrae. By restoring physiologic function and providing necessary stability, the implant can be used for patients with multi-level cervical disc disease for which there are no approved cervical disc replacement therapies. LDR Holding Corp., Austin, TX Phase II trial completed; company received an approvable letter from FDA Nov 2012; final FDA decision anticipated in 2013, though no decision date has been set	Spinal fusion	Decreased pain Improved quality of life Return to work Reduction in disability
Autologous conditioned serum for treatment of osteoarthritis (knee and spine)	Patients in whom osteoarthritis (OA) has been diagnosed	Currently no regenerative treatments are FDA approved for patients with OA. Autologous conditioned serum (ACS) consists of serum collected from the patient that has components purported to be regenerative or protective—such as interleukin (IL)-1Ra which is believed to dampen IL-1-mediated inflammation—isolated from the sample. The conditioned serum is reinjected into the arthritic joint. By specifically enriching for desired molecules, not simple fractionation/concentration, ACS purportedly has different effects than platelet-rich plasma therapy. NY Spine Medicine, Schottenstein Pain & Neurology, New York, NY Pilot studies completed; procedure currently diffusing in the U.S.	Platelet-rich plasma Mesenchymal stem-cell therapy Nonsteroidal anti-inflammatory drugs Physical therapy	Reduced pain Improved mobility Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Autologous bone-marrow-dervied mesenchymal stem cells for treatment of joint osteoarthritis	Patients in whom osteoarthritis (OA) has been diagnosed	Current conservative therapies for OA target disease symptoms such as pain and inflammation; however, they do not address the underlying pathology of the disease or halt its progression. Treatment of osteoarthritic joints with mesenchymal stem cells has the potential to be the first treatment could restore the large cartilage defects found in patients with OA. Mesenchymal stem cells are adult stem cells that progenitor cells that retain the ability to differentiate into a number of cell types, including chondrocytes, which are the cells responsible for maintaining cartilage. The stem cells can be isolated from several tissues, including bone marrow, synovium, periosteum, skeletal muscle, and adipose tissue. When first isolated from the patient, mesenchymal stem cells constitute a small fraction of the cells present in the sample and must either be concentrated by centrifugation or be passaged multiple times in vitro to expand the mesenchymal cell population. The condition of the patient may influence the attributes of the mesenchymal stem cells that are produced, and both patient age and the presence of OA have been shown to affect the ability of isolated mesenchymal stem cells to proliferate and differentiate into chondrocytes. Regenerative Sciences, Inc., Broomfield, CO Arthritis Treatment Center, Frederick, MD Phase II trials ongoing	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
Autologous platelet-rich plasma therapy for treatment of joint osteoarthritis	Patients in whom knee osteoarthritis (OA) has been diagnosed	Other than joint replacement and symptom management, effective treatment for OA to restore long-term function is not available. Viscosupplementation provides temporary relief and improves short-term function for some patients, but long-term nonsurgical treatments are needed. Platelet-rich plasma (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 re-infused in an outpatient setting at the desired anatomic site (i.e., knee). PRP contains and releases (through degranulation) at least 7 different growth factors that are intended to stimulate bone and soft-tissue healing. Orthohealing Center, Los Angeles, CA Phase III trials ongoing	Analgesics Viscosupplementation Artificial knee replacement Lifestyle modification Physical therapy	Decreased pain Increased mobility Improved quality of life

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 rheumatoid arthritis (RA) has been diagnosed	RA is a chronic inflammatory disease causing polyarthritis with frequent progression to permanent joint damage, deformity, and functional disability. Fostamatinib disodium, previously referred to as R788, is an oral spleen tyrosine kinase inhibitor that reversibly blocks lymphocyte signaling involved in inflammation and tissue degradation in RA. It is intended for treating early stage RA to reduce swelling and tissue destruction. Clinical trials dosage: 100 mg, twice daily, for four weeks followed by 150 mg, once daily. Rigel Pharmaceuticals, Inc., South San Francisco, CA Phase III trials ongoing	Disease-modifying antirheumatic drugs: methotrexate, hydroxychloroquine, sulfasalazine Monoclonal antibody inhibitors Anti-inflammatory agents: glucocorticoids, nonsteroidal anti-inflammatory drugs Analgesics	Decreased inflammation Slowed disease progression Reduced pain Improved function and activities of daily living Improved quality of life
Interleukin-17 antagonist (secukinumab) for the treatment of ankylosing spondylitis	Patients in whom ankylosing spondylitis has been diagnosed	Investigators have not found a cure for ankylosing spondylitis. Treatments are intended to reduce inflammation and improve mobility but are not effective for all patients. Secukinumab is purportedly a monoclonal antibody antagonist for interleukin-17 (IL-17). IL-17 purportedly is involved in developing delayed-type hypersensitivity reactions by increasing chemokine production, which promotes the recruitment of inflammatory cells such as monocytes and neutrophils to the local area. By blocking the effects of IL-17 localized autoimmune reactions associated with ankylosing spondylitis, pathology could be blocked while minimizing the systemic immunosuppression associated with tumor necrosis factor (TNF) blockers, which are often used in treatment. Administered subcutaneously, 75 or 150 mg, monthly. Novartis International AG, Basel, Switzerland Phase III trials ongoing	Corticosteroids Disease-modifying antirheumatic drugs Ixekizumab (in development) Nonsteroidal anti-inflammatory drugs Physical therapy Sulfasalazine (Azulfidine) TNF inhibitors	Reduced signs and symptoms Improved mobility Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ixekizumab for treatment of psoriatic arthritis	Patients in whom active psoriatic arthritis has been diagnosed	Psoriatic arthritis can progress to a stage of severe and painful symptoms in a subset of affected patients. These patients may then also experience deformity and disability of hands and fingers. Available treatment can be suboptimal. Ixekizumab is a monoclonal antibody purported to block the activity of interleukin 17, which is thought to contribute to psoriatic arthritis pathogenesis. In the ongoing UNCOVER-2 trial, ixekizumab is being given via subcutaneous injection in two 80 mg injections at week 0, followed by weekly 80 mg injections until week 12. Eli Lilly and Co. Indianapolis, IN Phase III trial ongoing	Apremilast (in development) Corticosteroids Disease-modifying antirheumatic drugs: Methotrexate, Sulfasalazine Immunosuppressants: Azathioprine, Cyclosporine Leflunomide Nonsteroidal anti-inflammatory drugs Tumor necrosis factor-alpha inhibitors: Etanercept Ustekinumab (in development)	Improved symptom scores as measured by the American College of Rheumatology 20/50/70 instruments Improved disability measures Improved quality of life measures
KIT tyrosine kinase inhibitor masitinib for treatment of rheumatoid arthritis	Patients in whom rheumatoid arthritis (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 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 purportedly targets 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. In clinical trials, masitinib is administered orally, 3 or 6 mg/kg of body weight, daily. AB Science S.A., Paris, France Phase II/III trial ongoing	Corticosteroids Disease-modifying antirheumatic drugs: hydroxychloroquine, methotrexate, sulfasalazine Nonsteroidal anti-inflammatory drugs Tocilizumab Tofacitinib (investigational) Tumor necrosis factor-alpha inhibitors	Improved symptom scores as measured by American College of Rheumatology 20/50/70 instruments Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Nitronaproxen (Naproxcinod) for treatment of osteoarthritis	Patients in whom osteoarthritis (OA) has been diagnosed	Other than joint replacement and symptom management, effective treatment for OA to restore function long-term is not available. Effective nonsteroidal anti-inflammatory drugs (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 1st-in-class cyclooxygenase inhibiting NO donators (CINODs); CINODs are intended to produce analgesic efficacy similar to traditional NSAIDs, but with fewer gastrointestinal and cardiovascular side effects because of the local effects of NO. NicOx S.A., Sophia Antipolis, France Phase III trials completed; manufacturer received FDA response letter to new drug application (NDA) requesting long-term safety data on cardiovascular effects; Apr 2012, manufacturer met with FDA to discuss additional data required for NDA resubmission; company seeking a partner to manage future development and commercialization	Celecoxib Ibuprofen Naproxen	Increased mobility Decreased pain Improved cardiovascular effects (i.e., blood pressure)
Off-label bisphosphonates for prevention of revision surgery after hip arthroplasty	Patients who have undergone knee or hip arthroplasty	Hip revision surgery is sometimes needed because of aseptic loosening of an implant. Treating a hip graft locally with an antiresorptive substance such as a bisphosphonate has been shown to decrease graft resorption in animal studies and researchers reported it led to a “remained bone density in a human series of 16 patients.” Researchers are investigating whr increased bone density of a graft in hip arthroplasty through administration of a bisphosphonate decreases “micromotion” of the implant relative to the femur to reduce aseptic loosening and need for revision surgery. Bisphosphonates are known to inhibit bone resorption by inhibiting osteoclast activity. Bone remodeling can also be responsible for the need to perform arthroplasty revision. Using bisphosphonates for this purpose might provide a low-cost solution, preventing need for hip revision surgery. Investigators are using clodronate 60 mg/mL, 10 mL as a single dose mixed into the bone graft used at the time of operation. Lund University Hospital, Lund, Sweden Phase II trial ongoing in 32 hip surgeries	Standard of care following arthroplasty	Reduced need for revision surgery Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Oral phosphodiesterase type 4 inhibitor (apremilast) for treating psoriatic arthritis	Patients in whom psoriatic arthritis has been diagnosed	In a subset of patients, psoriatic arthritis can progress to severe and painful symptoms that, without effective treatment, can lead to deformity and disability of the hands and fingers of patients. Apremilast purportedly inhibits phosphodiesterase type 4 (PDE-4). By inhibiting the PDE-4 enzyme, apremilast purportedly increases intracellular cAMP, which modulates multiple inflammatory mediators. Clinical trial dosage: 20 mg or 30 mg, twice daily, orally. Celgene Corp., Summit, NJ Phase III trials met primary endpoints Sept 2012; company plans to file new drug application in 2nd half of 2013	Corticosteroids Disease-modifying antirheumatic drugs: methotrexate, sulfasalazine Immunosuppressants: azathioprine, cyclosporine leflunomide Nonsteroidal anti-inflammatory drugs Tumor necrosis factor-alpha inhibitors	Improved symptom scores as measured by the American College of Rheumatology 20/50/70 instruments Improved scores on disability measures Improved scores on quality of life measures
Urate transport inhibitor (lesinurad) for treatment of hyperuricemia and allopurinol-refractory gout	Patients in whom hyperuricemia has been diagnosed and thus are at high risk of acute gout	Only 30% to 40% of gout patients respond adequately to the available allopurinol. Lesinurad (RDEA594) is a selective urate transporter inhibitor. Inhibition leads to uric acid excretion to reduce uric acid and crystal formation to potentially alleviate symptoms of acute gout. Clinical trials dosage: 200 mg or 400 mg once daily. Ardea Biosciences, Inc., acquired Jun 2012 by AstraZeneca, London, UK Phase III trials ongoing	Treatment: Colchicine Nonsteroidal anti-inflammatory drugs Steroids Prophylaxis: Allopurinol Febuxostat Probenecid	Reduced uric acid accumulation and crystal formation Reduced acute flares
Ustekinumab (Stelara) for treatment of psoriatic arthritis	Patients in whom active psoriatic arthritis has been diagnosed	Psoriatic arthritis can progress to a stage of severe and painful symptoms in a subset of affected patients. These patients may then also experience deformity and disability of hands and fingers. Available treatment can be suboptimal. Ustekinumab (Stelara®) is a monoclonal antibody purported to block the activity of interleukin-12 and interleukin-23, which are thought to contribute to psoriatic arthritis pathogenesis. Clinical trial dosage: 45 mg at week 0, 4, and every 12 weeks or 90 mg every 12 weeks subcutaneously injected. Janssen Biotech, Inc., Horsham, PA Phase III trial ongoing; FDA approved in 2009 for treating moderate to severe plaque psoriasis	Apremilast (in development) Corticosteroids Disease-modifying antirheumatic drugs: Methotrexate, Sulfasalazine Immunosuppressants: Azathioprine, Cyclosporine Leflunomide Nonsteroidal anti-inflammatory drugs Tumor necrosis factor-alpha inhibitors	Improved symptom scores as measured by the American College of Rheumatology 20/50/70 instruments Improved disability measures Improved quality of life measures

Table 2. AHRQ Priority Condition: 02 Cancer: 160 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
5-aminolevulinic acid fluorescence-guidance for identifying clear surgical margins glioma	Patients undergoing surgery for glioma	Complete surgical resection of glioma improves outcomes in patients who are eligible for surgery; however, the highly invasive nature of glioma and the high degree of similarity between glioma tumors and surrounding healthy brain tissue make complete surgical resection and identification of clear surgical margins difficult. 5 aminolevulinic acid (5-ALA) is a small-molecule prodrug that is converted to protoporphyrin IX (PIX) in neoplastic cells, but not in normal cells. Illuminating PIX with ultraviolet light induces fluorescence in the visible light spectrum, potentially serving as a marker for glioma tissue. Researchers postulate that surgical resection guided by the pattern of PIX fluorescence could increase the percentage of glioma tissue removed, thereby improving outcomes. 5-ALA is administered as an oral medication about 3–5 hours before surgery. Medac GmbH, Hamburg, Germany St. Joseph's Hospital and Medical Center, Phoenix 1 phase III trial completed, 1 ongoing; commercially available as Gliolan® in Europe	Standard surgical resection without fluorescence	Increased overall survival Increased progression-free survival Improved quality of life
Ado-trastuzumab emtansine (Kadcyla) for treatment of breast cancer	Patients in whom metastatic HER2-positive breast cancer has been diagnosed	Patients with advanced HER2-positive breast cancer have a poor prognosis with current treatment options. Ado-trastuzumab emtansine (formerly trastuzumab-DM1) is a combination of a HER2-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 *HER2* to produce the same (or better) results as HER2 inhibition plus chemotherapy, but with reduced side effects. This agent is administered intravenously, at 3.6 mg/ kg, every 3 weeks. F. Hoffmann-La Roche, Ltd., Basel, Switzerland FDA approved Feb 2013 for treatment of HER2-positive metastatic breast cancer; first antibody-drug conjugate approved	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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Afatinib (Tomtovok) for treatment of metastatic breast cancer	Patients in whom advanced HER2-positive breast cancer has been diagnosed	Patients with advanced HER2-positive breast cancer have a poor prognosis with current treatment options. Afatinib (BIBW 2992, Tomtovok™, previously Tovok) is a small-molecule, irreversible *ErbB* family inhibitor. It inhibits both epidermal growth factor receptor (*EGFR*; *HER1*) and *HER2* receptor tyrosine kinases; these receptor tyrosine kinases are 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. In clinical trials, afatinib is an oral medication given at a dose of 20-50 mg, daily, in combination with trastuzumab and/or various chemotherapies. 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 (Tomtovok) for treatment of head and neck cancer	Patients in whom advanced head and neck cancer has been diagnosed	Patients with advanced head and neck cancer have a poor prognosis and high recurrence rate, suggesting the need for novel treatment options. Afatinib (BIBW 2992, Tomtovok™, previously Tovok) is a small-molecule, irreversible ErbB family inhibitor. It inhibits both epidermal growth factor receptor (*EGFR*; *HER1*) and *HER2* receptor tyrosine kinases. Targeted EGFR-like receptor inhibition in head and neck cancers has a relatively high success rate. Although multiple receptor tyrosine kinase inhibitors are available, afatinib is unique in that its inhibition is irreversible. In clinical trials, afatinib is administered as a oral dose of 40-50mg, once daily. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing for 1st-line treatment and 2nd-line treatment after treatment with a platinum-based regimen	Various combination or monotherapy regimens including: 5-fluorouracil Bleomycin Cetuximab Cisplatin Docetaxel Gemcitabinel Fosfamide Methotrexate Paclitaxel Vinorelbine	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 (Gilotrif) for treatment of nonsmall cell lung cancer	Patients in whom nonsmall cell lung cancer (NSCLC) has been diagnosed and who have certain *EGFR* mutations	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. Afatinib (Gilotrif™) is a small-molecule, irreversible ErbB inhibitor. It inhibits both epidermal growth factor receptor (*EGFR*; *HER1*) and *HER2* receptor tyrosine kinases. *HER1* and *HER2* receptor tyrosine kinases are mutated and overexpressed in NSCLC in about 10% of patients; targeted EGFR-like receptor inhibition in these cancers has a relatively high success rate. Although multiple receptor tyrosine kinase inhibitors are available, afatinib is unique in that its inhibition is irreversible. EGFR gene mutations are present in about 10% of NSCLCs, with the majority of these gene mutations expressing EGFR exon 19 deletions or exon 21 L858R substitution. The product labeling indicates that afatinib is taken orally 40 mg orally, once daily. Boehringer Ingelheim, GmbH, Ingelheim, Germany FDA approved Jul 2013 for 1st–line treatment of metastatic NSCLC in patients whose tumors express specific types of *EGFR* gene mutations as detected by the FDA-approved companion diagnostic test (therascreen EGFR RGQ PCR Kit, QIAGEN, Manchester Ltd., United Kingdom)	1st-line: Combination chemotherapy (e.g., pemetrexed plus cisplatin) Targeted immunotherapy (e.g., bevacizumab, cetuximab, erlotinib) 2nd-line: Erlotinib Single agent chemotherapy (e.g., docetaxel, pemetrexed)	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 2nd-line treatments for metastatic CRC are of limited efficacy, and the median overall survival of these patients is less than 1 year. Aflibercept (Zaltrap™) is a vascular endothelial growth factor (VEGF)-signaling inhibitor that contains multiple copies of the VEGF receptor extracellular domain designed to bind VEGF. It is an antiangiogenic agent intended to reduce tumor vascularization, thereby inhibiting tumor growth. Aflibercept is indicated as an adjunct to the standard FOLFIRI regimen of leucovorin, irinotecan, and 5-fluorouracil (5-FU). This agent is administered at a dose of 4 mg/kg, intravenously, every 2 weeks. Collaboration between Regeneron Pharmaceuticals, Inc., Tarrytown, NY, and Sanofi, Paris, France Several phase III trials ongoing; FDA approved Aug 2012 for use with FOLFIRI for treating adults with CRC whose tumors have progressed after treatment with an oxaliplatin-containing regimen	5-FU-based therapy plus bevacizumab FOLFIRI FOLFIRI plus cetuximab or panitumumab Irinotecan with or without 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
Aldoxorubicin 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 a poor prognosis. Aldoxorubicin 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. Aldoxorubicin is administered at a dose of 350 mg/m2, intravenously, once every 3 weeks, for up to 6 cycles. CytRx Corp., Los Angeles, CA Phase III trial in 2nd-line setting registered, not yet recruiting; additional phase II ongoing in 1st-line setting; FDA granted orphan drug status	Doxorubicin	Increased overall survival Increased progression-free survival Improved quality of life
Algenpantucel-L (HyperAcute-Pancreas) immunotherapy for pancreatic cancer	Patients in whom non-metastatic adenocarcinoma of the pancreas has been diagnosed	Patients in whom pancreatic cancer has been diagnosed have a 5-year survival rate of about 5%; effective treatment options are needed. Algenpantucel-L immunotherapy is a treatment intended to stimulate an immune response against the patient's pancreatic cancer cells. The therapy consists of 2 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 chemoradiation. Clinical trials are testing this intervention in surgically resected and unresectable/borderline resectable pancreatic cancers. HyperAcute-Pancreas is administered at a dose of 300 million immunotherapy cells, via intradermal injection, biweekly, for up to 18 doses. NewLink Genetics Corp., Ames, IA Phase III trials ongoing under FDA special protocol assessment; trials examining use in surgically resected and unresectable disease; FDA granted fast-track and orphan drug statuses	Standard chemoradiation regimens (including systemic chemotherapy such as FOLFIRINOX, 5-fluorouracil, and/or 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
Allogeneic DNA immunotherapy (Allovectin) for treatment of melanoma	Patients in whom stage III or IV melanoma has been diagnosed	Patients with metastatic melanoma have a poor prognosis with current treatments yielding a 5-year survival rate of 15-20%. Allovectin® is a DNA-based immunotherapeutic composed of a lipid-encapsulated plasmid expressing human leukocyte antigen (HLA)-B7 and beta-2 microglobulin (required to generate a functional major histocompatibility complex ([MHC] I molecule). The therapeutic is 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. In a clinical trial, Allovectin was given in the 1st-line treatment settin. It is administered at a dose of 2 mg, by intratumoral injection, once a weekly. Vical, Inc., San Diego, CA Phase III trial ongoing, enrollment complete; FDA granted orphan drug and fast-track statuses	High dose interleukin-2 Dacarbazine Dabrafenib (if *BRAF*-positive) Ipilimumab Temozolomide Trametinib (if *BRAF*-positive) Vemurafenib (if *BRAF*-positive)	Increased overall survival Increased progression-free survival Improved quality of life
Anamorelin for treatment of cancer-related cachexia/anorexia	Patients with NSCLC in whom cancer-related cachexia/anorexia (CRCA) has been diagnosed	Although a number of treatments have been applied to CRCA, many patients do not respond to current treatment options. CRCA may limit patients' tolerance of further treatment and may 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 administered at a dose of 100 mg, orally, daily. Helsinn Healthcare S.A., Lugano/Pazzallo, Switzerland Phase III trials ongoing	Anti-cytokine antibodies Appetite stimulants: Cannabinoids Corticosteroids Cyproheptadine Progesterone derivatives Dietary counseling Melanocortin antagonists Metabolic disturbance modulators: 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
Anti-GD2 monoclonal antibody (ch14.18) for treatment of neuroblastoma	Patients with high-risk neuroblastoma who have undergone induction therapy and autologous stem cell transplantation	Current treatments for patients with high-risk neuroblastoma result in 5-year survival rates of only about 25% to 35%. A monoclonal antibody, ch14.18 is specific for a tumor-associated disialoganglioside, GD2, that exhibits low levels of expression on normal tissues (e.g., neurons, skin melanocytes, peripheral sensory nerve fibers). It purportedly targets neuroblastoma cells via antibody-dependent, cell-mediated cytotoxicity. In clinical trials, ch14.18 was administered in combination with cytokines (granulocyte macrophage colony-stimulating factor and interleukin-2) that enhance immune response and the standard neuroblastoma maintenance therapy isotretinoin. United Therapeutics Corp., Silver Spring, MD, in collaboration with the National Cancer Institute, Bethesda, MD Phase III trials ongoing; positive data from first phase III trial published in 2010	Isotretinoin	Increased overall survival Increased progression-free survival Improved quality of life
Alisertib (Aurora A kinase inhibitor) for treatment of peripheral T-cell lymphoma	Patients in whom relapsed/refractory peripheral T-cell lymphoma (PTCL) has been diagnosed	Current treatment options for relapsed/refractory PTCL are largely palliative and generate responses in fewer than 50% of patients (with the exception of brentuximab vedotin for the anaplastic large cell lymphoma [ALCL] subtype). Alisertib is an Aurora A kinase inhibitor under study for treating PTCL. Aurora A kinase is an important regulator of the mitotic spindle and is required for progression through the mitotic phase of the cell cycle. Inhibition of aurora A has been shown to cause mitotic errors, potentially leading to aneuploidy, apoptosis, and cellular senescence. Alisertib is administered orally, 50 mg, twice daily. Millennium Pharmaceuticals, Inc., subsidiary of Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trial ongoing	Alemtuzumab Brentuximab vedotin (ALCL subtype only) Bortezomib Cyclosporine (angioimmunoblastic T-cell lymphoma subtype only) Denileukin diftitox Gemcitabine Pralatrexate Radiation therapy Romidepsin	Increased overall survival Increased progression-free survival Improved quality of life
Autologous dendritic cell immunotherapy (AGS-003) for treatment of renal cell carcinoma	Patients in whom metastatic RCC (mRCC) has been diagnosed	Patients whose mRCC has progressed after targeted therapy (e.g., VEGF- or mTOR-inhibitors) have limited treatment options and a poor prognosis. 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. In clinical trials, AGS-003 is given in combination with sunitinib, following surgical resection, in patients with newly-diagnosed mRCC. Argos Therapeutics, Inc., Durham, NC Phase III trial ongoing	Axitinib Bevacizumab (with interferon alfa) Erlotinib Interleukin-2 Pazopanib Sorafenib Sunitinib Temsirolimus	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
Autologous dendritic cell immunotherapy (DCVax-L) for treatment of glioblastoma multiforme	Patients in whom unilateral glioblastoma multiforme has been diagnosed	Glioblastoma multiforme is difficult to treat and associated with a very poor patient prognosis. New therapies that improve survival and slow disease progression are needed. DCVax®-L is an autologous dendritic cell vaccine intended to promote an immune response against a patient's glioblastoma. To prepare DCVax-L, both a tumor isolate and a blood draw to obtain immune cells are required. Dendritic cells (antigen-presenting cells of the immune system) are expanded from the patient's isolated immune cells and exposed to tumor lysate. These activated dendritic cells are then injected back into the patient intradermally every 2–6 months for up to 3 years. Northwest Biotherapeutics, Inc., Bethesda, MD Phase III trial ongoing	Bevacizumab (under investigation) Other immunotherapeutics (in development, e.g., HSPPC-95, ICT107) Radiation therapy Surgical resection (with or without carmustine wafer) Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life
Automated breast ultrasound (somo.v automated breast ultrasound system) for breast cancer screening of patients with dense breast tissue	Women with dense breast tissue who are undergoing screening mammography	The presence of dense breast tissue limits the accuracy of screening mammography, and screening mammography's sensitivity for tumors in women with dense breast tissue is as low as 30% to 50%. Ultrasound imaging has been used for some time in breast imaging; however, it is not routinely used in screening of asymptomatic women in the U.S. The somo.v automated breast ultrasound system generates 3-dimensional images of the breast in an automated fashion. The system is under study as an adjunct to conventional mammographic screening in women with dense breast tissue. U-Systems, Inc., acquired Nov 2012 by General Electric Co., Fairfield, CT Sept 2012, FDA approved for screening indication; previously FDA cleared for diagnostic use	Screening mammography alone Screening magnetic resonance imaging Manual breast ultrasound	Increased breast cancer sensitivity and specificity Improved positive predictive and negative values for breast cancer

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 2nd deadliest cancer after pancreatic cancer; no new 1st-line treatment options have been made available in the past decade. Bevacizumab (Avastin®) is a monoclonal antibody that binds vascular endothelial growth factor (VEGF) and prevents 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. This agent is on the market for several other indications and is being tested in the 1st- and 2nd-line settings in combination with standard chemotherapy. In clinical trials, bevacizumab is administered at 15 mg/kg, intravenously, on day 1 of each 3-week cycle. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland, and National Cancer Institute, Bethesda, MD Multiple phase III trials ongoing; manufacturer anticipates U.S. regulatory submission during 2013; U.K. National Institute for Clinical Excellence announced in May 2013 it would not recommend use for ovarian cancer	Combination chemotherapy including one or more of the following: Carboplatin Gemcitabine Paclitaxel Pegylated liposomal doxorubicin Topotecan Paclitaxel monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Blinatumomab (bispecific T-cell-engager [BiTE] anti-CD19 antibody) 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 2 separate antibody-antigen binding domains: (1) the domain specific for CD19, an antigen expressed by the immature lymphocytes expanded in ALL, and (2) the domain specific for CD3 a molecule expressed on the surface of cytotoxic T cells. Blinatumomab purportedly leads to leukemic cell apoptosis by bridging an interaction between leukemic cells and T cells. Amgen, Inc., Thousand Oaks, CA Phase II trials 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
Brivanib (multikinase inhibitor) for treatment of hepatocellular carcinoma	Patients in whom hepatocellular carcinoma (HCC) has been diagnosed	Patients with HCC that cannot be surgically resected have few treatment options and a poor prognosis. Brivanib is a novel multikinase inhibitor that inhibits multiple tyrosine kinases including vascular endothelial growth factor (VEGF) receptors and fibroblast growth factor receptors (FGFRs). Brivanib's activity against FGFRs differentiates it from multikinase inhibitors available for treating HCC. Research has demonstrated that signaling through FGFR may be a mechanism by which resistance to VEGF-targeted therapy occurs; therefore, simultaneous inhibition of the VEGF and fibroblast growth factor pathways may have synergistic anticancer effects. Brivanib is under study in 3 HCC indications: 1st- and 2nd-line chemotherapy after treatment with sorafenib and adjunctive therapy with transarterial chemoembolization (TACE). In late-stage clinical trials, brivanib is administered orally, 800 mg, daily. Bristol-Myers Squibb, New York, NY Phase III trials ongoing, enrollment completed; phase III trial in the 2nd-line setting failed to meet its primary endpoint in Jul 2012; however, additional phase III trials continue	Sorafenib alone TACE alone	Increased overall survival Increased progression-free survival Improved quality of life
Buparlisib for treatment-refractory metastatic breast cancer	Patients with aromatase inhibitor or mTOR inhibitor-refractory, hormone receptor positive, *HER2*-negative metastatic breast cancer	Patients with hormone receptor–positive breast cancer typically develop resistance to 1st-line therapy with estrogen receptor–targeted therapies. The phosphoinositide 3 kinase (PI3K)/mTOR pathway is a cell signaling pathway that is frequently activated in a wide range of cancers and in particular may underly tumor resistance to estrogen receptor-targeted therapies. Buparlisib (BKM120) is an orally administered pan-PI3K inhibitor (i.e., an inhibitor of all PI3K isoforms) that is intended to block the PI3K/mTOR pathway. In clinical trials, buparlisib is being administered in combination with the anti-estrogen drug fulvestrant. It is an oral agent administered at a dose of 100mg, daily. Novartis International AG, Basel, Switzerland Phase III clinical trials ongoing; drug also under study for endometrial cancer, glioblastoma, HER2-positive breast cancer, melanoma, nonsmall cell lung cancer, prostate cancer, and urothelial cancer	Everolimus plus exemestane Fulvestrant 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
Cabozantinib (Cometriq) for treatment of castration-resistant prostate cancer	Patients with castration-resistant prostate cancer (CRPC) that may include bone metastases	Median overall survival for patients with CRPC is only about 18 months. No treatments for CRPC are available that target MET, which may be responsible for prostate cancer drug resistance in patients treated with current receptor tyrosine kinase inhibitors. Cabozantinib (Cometriq™) is an oral, small-molecule, receptor tyrosine kinase inhibitor that targets MET and vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2). MET plays key roles in proliferation, migration, invasion, and angiogenesis; overexpression of the hepatocyte growth factor ligand of MET and activation of the MET pathway supports tumors; VEGFR2 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. In trials, it is administered at a 100 mg dose, once daily. Exelixis, Inc., South San Francisco, CA Phase II and phase III trials ongoing	Abiraterone Cabazitaxel Denosumab Docetaxel Enzalutamide Radium-223	Reduced bone metastasis Reduced bone pain Increased overall survival Increased progression-free survival Improved quality of life
Carfilzomib (Kyprolis) for treatment of multiple myeloma	Patients in whom recurrent or treatment-refractory multiple myeloma has been diagnosed	Patients in whom relapsed/refractory multiple myeloma has been diagnosed have few treatment options and median survival of less than 1 year. Carfilzomib (Kyprolis™) 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. Product labeling states that it is administered intravenously over 2–10 minutes on 2 consecutive days each week for 3 weeks (days 1, 2, 8, 9, 15, and 16), followed by a 12-day rest period (days 17–28) with a recommended cycle 1 dose of 20 mg/m2 of body surface area/day and if tolerated increased for cycle 2 and subsequent cycles doses to 27 mg/m2/day. Onyx Pharmaceuticals, Inc., South San Francisco, CA FDA granted accelerated approval Jul 2012 for treating patients “with multiple myeloma who have received at least two prior therapies, including bortezomib and an immunomodulatory agent, and have demonstrated disease progression on or within 60 days of completion of the last therapy.”	Combination therapies Cytotoxic chemotherapies (bendamustine, cyclophosphamide, doxorubicin, melphalan, vincristine) Immunomodulatory drugs (lenalidomide, pomalidomide, 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
CD34-positive cell selection system (CliniMACS) for treatment of acute myeloid leukemia	Patients with acute myeloid leukemia (AML) who are undergoing allogeneic stem cell transplantation (SCT)	Allogeneic SCT is the most effective treatment for AML; however, its use is complicated by potential adverse events including the development of graft-versus-host disease (GVHD), in which donor immune cells mount an immune response against recipient tissues. Patients with acute GVHD typically exhibit damage to the skin, liver, and gastrointestinal tract, and GVHD is lethal in up to 80% of patients with severe forms of the disease. Methods to prevent GVHD include pretransplant depletion of the donor T cells thought to be the cause of GVHD. However, no FDA-approved device is available to perform T-cell depletion, and its use has been hampered by the potential for poor engraftment and/or AML relapse in patients treated with processed grafts. The CliniMACS® CD34 reagent system is intended to prepare T-cell depleted stem cell grafts. The system uses CD34 monoclonal antibodies coupled to magnetic particles to isolate CD34-positive hematopoietic stem cells while simultaneously passively removing differentiated T cells. Miltenyi Biotec GmbH, Bergisch Gladbach, Germany Phase II trial complete; company filed for humanitarian use device exemption with FDA, so phase III trials may not be required for clinical use	Noncommercial, manual methods of T-cell depletion	Improved engraftment rate Increased duration of disease-free survival Improved rates of acute and chronic GVHD
Cilengitide for treatment of glioblastoma	Patients in whom glioblastoma has been diagnosed	Median survival of patients with glioblastoma is only about 14 months with current therapies. Integrins are transmembrane proteins that are widely expressed in both glioblastomas and tumor vasculature and mediate cell processes such as cell survival and migration and tumor angiogenesis. Cilengitide is a 1st-in-class, small-molecule antagonist of integrins (specifically alpha-v-beta3 and alpha-v-beta5), which may have antiglioblastoma activity. Treatment is intended for use against newly diagnosed glioblastoma that exhibits methylation of the methylguanine-DNA methyltransferase gene (a marker of temozolomide sensitivity). In clinical trials, cilengitide is administered in a twice-weekly, intravenous dose of 2,000 mg in combination with standard therapy using temozolomide and radiation therapy. EMD Serono, Inc., Rockland, MA, subsidiary of Merck KGaA, Darmstadt, Germany Phase III trial ongoing, trial failed to meet endpoints; several phase II trial in newly diagnosed GBM ongoing; also in trials for nonsmall cell lung cancer	Temozolomide plus 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
Cobimetinib (MEK inhibitor) for treatment of melanoma	Patients in whom *BRAF* mutation-positive metastatic melanoma has been diagnosed	Patients with *BRAF* mutation–positive melanoma frequently demonstrate a response to *BRAF* inhibitors; however, these responses are typically short in duration. MEK is a kinase that functions downstream of *BRAF* in the pathway driving melanoma pathogenesis in *BRAF* mutation–positive melanoma. Dual inhibition of *BRAF* and MEK may increase the duration of response to agents targeting the RAS/RAF/MEK/ERK pathway. Cobimetinib is an orally administered MEK inhibitor under study in combination with the *BRAF* inhibitor vemurafenib. F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trial ongoing	Dabrafenib Ipilimumab Trametinib Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life
Computer-assisted system (Sedasys) for automated propofol sedation during gastrointestinal endoscopy procedures	Patients who are undergoing propofol-induced sedation during colonoscopy or upper gastrointestinal (GI) procedures	Propofol-induced sedation can be associated with risk of oversedation and decreased oxygen saturation. 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 oversedation) for delivering propofol. The system is intended to enable nonanesthesiologists (i.e., other physicians or nurses) to administer sedation for endoscopic GI procedures. Ethicon Endo-Surgery unit of Johnson & Johnson, New Brunswick, NJ After repeated premarket approval applications, FDA approved May 2013	Propofol sedation administered and monitored by anesthesiologist	Successful and safe propofol sedation without need for an anesthesiologist
Custirsen (OGX-011) for treatment of advanced nonsmall cell lung cancer	Patients in whom nonsmall cell lung cancer (NSCLC) has been diagnosed	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. Custirsen (OGX-011) is an antisense RNA molecule intended for treating advanced, unresectable NSCLC. An ongoing clinical trial is testing custirsen in the 2nd-line setting following 1st-line treatment with a platinum-based chemotherapy. It is given intravenously in combination with docetaxel: 3 loading doses of custirsen 640 mg are given over 2 hours in 5–9 days prior to day 1 of cycle 1; then custirsen 640 mg weekly every 21-day cycle. OncoGenex Pharmaceuticals, Inc., Bothell, WA Teva Pharmaceutical Industries, Ltd., Petach Tikva, Israel Phase III trials ongoing	Docetaxel Erlotinib Pemetrexed Platinum doublet (plus or minus bevacizumab)	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
Custirsen (OGX-011) for treatment of metastatic castration-resistant prostate cancer	Patients in whom castration-resistant prostate cancer (CRPC) has been diagnosed	Median overall survival for patients with CRPC is only about 18 months. 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., Petach Tikva, Israel Phase III trials (AFFINITY and SYNERGY) ongoing; FDA granted fast-track status	Abiraterone Cabazitaxel Docetaxel Enzalutamide Radium-223 (in development) Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life
Dabrafenib (Tafinlar) for treatment of metastatic melanoma	Patients in whom metastatic melanoma characterized as having activated *BRAF* mutations has been diagnosed	Patients with metastatic melanoma have a poor prognosis with current treatments yielding a 5-year survival rate of 15-20%. Dabrafenib (Tafinlar) is an activated *BRAF* kinase inhibitor. The developer describes it as "a highly potent and selective adenosine triphosphate competitive *BRAF* inhibitor with more than 100-fold selectivity for mutant (mut) *BRAF*. It displays dose-dependent inhibition of MEK and extracellular signal-regulated kinase phosphorylation in mut *BRAF* cell lines and tumor regression in xenograft models." Dabrafenib is an oral medication administered at a dose of 150 mg, twice daily. Clinical trials are also examining dabrafenib as part of a combination therapy regimen with trametinib to prevent acquired *BRAF* inhibitor drug resistance. GlaxoSmithKline, Middlesex, UK Dabrafenib monotherapy FDA approved May 2013 in conjunction with companion diagnostic test to detect *BRAF* ^{V600}E/K mutations (THxID BRAF, bioMerieux); phase III trial ongoing for combination therapy with the MEK inhibitor trametinib; Jun 2013, company announced a supplemental new drug application had been submitted for dabrafenib plus trametinib combination therapy	High dose interleukin-2DacarbazineIpilimumabTemozolomideTrametinib 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
Dendritic cell immunotherapy (ICT-107) for treatment of glioblastoma multiforme	Patients in whom glioblastoma multiforme (GBM) has been diagnosed who have undergone surgical debulking	GBM is difficult to treat and associated with a very poor patient prognosis. 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, HER2, gp-100, melanoma antigenic epitope-1, TRP-2, and interleukin-13Ra2 for the potential intradermal treatment of glioblastoma. ICT-107 is under investigation in newly-diagnosed GBM. It is administered as an adjuvant to surgical resection and chemoradiation therapy; 4 induction doses are followed by a maintenance regimen that continues until disease progression. ImmunoCellular Therapeutics, Ltd., Woodland Hills, CA Phase IIb trial ongoing, enrollment completed with interim data analysis in 2013; FDA granted orphan drug status in 2010; drug expected to have abbreviated regulatory pathway	Bevacizumab (under investigation) Other immunotherapeutics (in development, e.g., DCVax-L, HSPPC-95) Radiation therapy Surgical resection (with or without carmustine wafer) Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life
Denosumab (Xgeva) for prevention of bone metastasis in breast cancer	Patients with early-stage breast cancer at high risk for recurrence	Breast cancer patients who have cancer in the lymph nodes, large tumors, or locally advanced disease have a high risk of disease recurrence. Metastasis to the bone represents 40% of all initial recurrences. Denosumab is a monoclonal antibody that inhibits RANKL, a protein that stimulates bone removal. This agent is already approved for preventing skeletal-related events in patients with established bone metastases from solid tumors. Preclinical data suggest that RANKL inhibition may also prevent skeletal tumor formation. In an ongoing trial, denosumab is being tested in the adjuvant setting for prolonging bone metastasis–free survival and disease-free survival. In this setting denosumab is administered at 120 mg once monthly for 6 months followed by 120 mg once every three months for up to five years. Amgen, Inc., Thousand Oaks, CA Phase III trial ongoing	Exemestane RaloxifeneTamoxifen	Increased overall survival Increased bone metastasis–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
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; FDA granted fast-track status	5-Fluorouracil/ leucovorin monotherapy Gemcitabine monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Dovitinib (multikinase inhibitor) for treatment of metastatic renal cell carcinoma	Patients in whom metastatic renal cell carcinoma (RCC) has been diagnosed	Metastatic RCC that has progressed after VEGF-targeted and mTOR inhibitor therapies has not been treatable, and patients have a poor prognosis. Dovitinib is a novel multikinase inhibitor that inhibits multiple tyrosine kinases including VEGF receptors, platelet-derived growth factor receptors, and fibroblast growth factor receptors (FGFRs). Dovitinib's activity against FGFR differentiates it from multikinase inhibitors available for treating RCC. Research has demonstrated that signaling through FGFR may be a mechanism by which resistance to VEGF-targeted therapy occurs; therefore, simultaneous inhibition of the VEGF and FGF pathways may generate responses in disease that is refractory to VEGF-targeted therapy. In clinical trials, dovitinib is an oral medication administered at a dose of 500 mg per day, for 5 out of 7 days each week to patients previously treated with both vascular endothelial growth factor (VEGF) targeted therapy (e.g., axitinib, bevacizumab, pazopanib, sunitinib, tivozanib) and mTOR inhibitor therapy (e.g., everolimus, ridaforolimus, temsirolimus). Novartis International AG, Basel, Switzerland Phase III trial ongoing, enrollment complete; phase I/II trials ongoing in breast, endometrial, and hepatocellular carcinomas	Sorafenib	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
Doxepin oral rinse for the treatment of radiation therapy-associated oral mucositis	Patients experiencing oral mucositis resulting from radiation therapy for head or neck cancer	Oral mucositis is a complication commonly experienced by patients undergoing radiation therapy for head or neck cancers. Significant mouth pain is associated with oral mucositis, and it causes difficulty eating and drinking and impairs quality of life. Current treatments for oral mucositis such as narcotics and lidocaine are associated with significant side effects and limited efficacy. In a phase III trial, a daily oral rinse containing doxepin, a tricyclic antidepressant, significantly improved mouth pain associated with oral mucositis. North Central Cancer Treatment Group (National Cancer Institute and Mayo Clinic), Rochester, MN Phase III trial ongoing	Lidocaine Narcotics	Decreased pain and oral side effects Improved ability to eat and drink Improved treatment adherence Improved quality of life
EGEN-001 gene threapy for recurrent or persistent ovarian cancer	Patients with recurrent or persistent ovarian, primary peritoneal, or fallopian tube cancer who have received at least 1 round of treatment with a platinum-based regimen	Patients in whom platinum-resistant ovarian cancer has been diagnosed have a poor prognosis and few treatment options. EGEN-001 is a novel gene therapy intended to induce the expression of interleukin-12 (IL-12) in tumor cells; IL-12 expression purportedly leads to 3 antitumor activities: (1) activation and proliferation of natural killer (NK) cells, leading to an innate immune response against the tumor; (2) maturation and 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, which has antiangiogenic properties. EGEN-001 is formulated with the TheraPlas™ delivery system that forms active nanoparticles that transfect cells with IL-12; this formulation is optimized for delivery into the tumor microenvironment by intraperitoneal catheter. This agent is currently being tested in platinum-refractory ovarian cancer. In clinical trials, EGEN-001 is administered at a dose of 24 mg/m2, weekly. EGEN, Inc., Huntsville, AL Phase II trial ongoing, enrollment complete; FDA granted orphan drug status; early-stage trials in other treatment settings and disease indications ongoing	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
Elotuzumab (anti-CS1 monoclonal antibody) for treatment of multiple myeloma	Patients in whom newly diagnosed multiple myeloma or relapsed/refractory multiple myeloma has been diagnosed	Although treatments for multiple myeloma have improved, the median life expectancy for patients in whom multiple myeloma is diagnosed is only 5–7 years. Immunotherapeutic options for multiple myeloma are not available. CS1 has been identified as a glycoprotein expressed preferentially on multiple myeloma cells, and elotuzumab is a humanized, monoclonal antibody specific for CS1. It purportedly has 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; FDA granted orphan drug status	For stem cell transplant eligible patients, 1st-line therapy such as: Bortezomib/ dexamethasone Cyclophosphamide/ dexamethasone For patients ineligible for stem cell transplant, 1st-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
Enzalutamide (Xtandi) for treatment of castration-resistant prostate cancer	Patients in whom metastatic castration-resistant prostate cancer (mCRPC) has been diagnosed	Median overall survival for patients with CRPC is only about 18 months. 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 metastatic prostate cancers do not respond to these therapies or develop resistance. Enzalutamide (Xtandi) is an androgen receptor antagonist that purportedly inhibits androgen signaling at 3 levels by blocking testosterone binding to the androgen receptor, inhibiting nuclear translocation of the activated androgen receptor and inhibiting DNA binding of activated androgen receptor. By more completely inhibiting androgen signaling, enzalutamide may overcome limitations of current antiandrogen therapies. Enzalutamide is an oral drug being tested in both chemotherapy-naïve patients and patients who have previously been treated with docetaxel. Enzalutamide is administered at a dose of 160 mg (four 40-mg capsules) orally, once daily. Medivation, Inc., San Francisco, CA Astellas Pharma, Inc., Tokyo, Japan FDA approved Aug 2012 for patients with mCRPC who have previously been treated with docetaxel; trials ongoing for patients with chemotherapy-naïve prostate cancer	Abiraterone Cabazitaxel Docetaxel Radium-223 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
Etirinotecan pegol for treatment-refractory breast cancer	Patients with metastatic breast cancer whose disease has progressed after 2 systemic chemotherapy regimens including anthracycline-, taxane-, and capecitabine-containing regimens	Patients with breast cancer that is refractory to standard systemic chemotherapy regimens have few treatment options and a poor prognosis. Etirinotecan pegol (NKTR-102) is a novel formulation of the topoisomerase I inhibitor irinotecan. Although approved for treating colorectal cancer, irinotecan is not indicated for treating breast cancer. Etirinotecan pegol is a modified version of irinotecan in which the drug is linked to a macromolecule core. The linkage purportedly renders the drug inert in the bloodstream and allows 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. In clinical trials, etirinotecan pegol is administered at an intravenous dose of 145 mg/m2, once every 21 days. Nektar Therapeutics, San Francisco, CA Phase III trial ongoing; FDA granted fast-track designation; trials also investigating use in ovarian, colorectal, and other cancers	Eribulin Gemcitabine Ixabepilone Nab-paclitaxel Pemetrexed Vinorelbine	Increased overall survival Increased progression-free survival Improved quality of life
Everolimus (Afinitor) for treatment of estrogen-receptor-positive breast cancer	Patients with metastatic estrogen receptor–positive breast cancer that has progressed after treatment with 1st-line aromatase inhibitors	For patients whose breast cancer progresses after 1st-line treatment with antiestrogen therapy, therapies with improved response rates are needed. Everolimus (Afinitor®) is a small-molecule inhibitor of the protein mTOR, which is a central regulator of cell growth. Inhibition of mTOR by everolimus has been demonstrated to be effective in treating multiple cancer types (e.g., renal cell carcinoma, astrocytoma). Everolimus is approved for treating HR+, HER2- breast cancer in addition to several other disease indications; it is administered at a dose of 10 mg, orally, once daily. Novartis International AG, Basel, Switzerland FDA approved Jul 2012 for treating postmenopausal women with advanced hormone receptor–positive, HER2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole; positive phase III data recently reported for use of everolimus in HER2-positive breast cancers, regulatory filings for HER2 indications expected in 2013/2014	Exemestane 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
Everolimus (Afinitor) for treatment of hepatocellular carcinoma	Patients with recurrent advanced hepatocellular carcinoma	Sorafenib is the only systemic treatment that has demonstrated improvement in survival for patients with HCC. Patients whose disease progresses after sorafenib treatment have few treatment options. The mTOR/PI3K pathway is a central regulator of cell growth, proliferation, death, and migration. Inhibition of mTOR has exhibited anticancer activity in a number of disease settings. Everolimus (Afinitor®) is an mTOR inhibitor approved for treating multiple cancer types and is under study for treating patients who have HCC. In treating HCC, everolimus is administered at a thrice-daily oral dose of 2.5 mg. Novartis International AG, Basel, Switzerland Phase III trial ongoing	Best supportive care	Increased overall survival Increased progression-free survival Improved quality of life
Everolimus (Afinitor) for treatment of renal angiomyolipoma	Patients with tuberous sclerosis complex or sporadic lymphangioleio-myomatosis who develop angiomyolipomas	Angiomyolipomas are benign tumors that typically arise in the kidneys of patients with tuberous sclerosis complex or the lung disease lymphangioleiomyomatosis. Large angiomyolipomas may lead to renal failure and/or hemorrhage. No pharmacotherapies are available to treat angiomyolipomas. Loss-of-function mutations in the tuberous sclerosis complex (TSC) genes are thought to give rise to angiomyolipomas. A consequence of TSC loss of function is activation of the protein mTOR; therefore, using an mTOR inhibitor such as everolimus may be beneficial in treating these patients. Everolimus is taken once daily, as an oral tablet. Novartis International AG, Basel, Switzerland Received FDA approval for angiomyolipoma Apr 2012; everolimus is marketed as Afinitor® for multiple cancer indications	Angiomyolipoma embolization	Tumor size reduction 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
Ex vivo expanded cord blood (StemEx) for allogeneic bone marrow transplant for hematologic malignancies	Patients with hematologic malignancies who need a bone marrow transplant and for whom no suitable matched donor is available	Suitably-matched bone marrow donors are not available for all patients with hematologic malignancies who could benefit from a transplant because of the difficulty in identifying suitably matched donors. An exact match is needed for adult marrow transplants to avoid complications from graft-versus-host disease (GVHD), and cord blood is associated with a lower risk of GVHD. However, the number of stem cells in cord blood is not sufficient to provide complete bone marrow engraftment. StemEx is a graft of stem cells and progenitor cells isolated from a single unit of cord blood. Stem cells and progenitor cells are enriched ex vivo by means of copper chelation, which reduces the availability of copper and purportedly promotes cell proliferation over differentiation. The enriched cell population is then infused to the patient along with the remainder of the cord blood unit. Gamida Cell, Ltd., Jerusalem, Israel in partnership with Teva Pharmaceutical Industries, Ltd., Petah-Tikva, Israel Phase II/III trial ongoing; FDA granted orphan drug status for hematopoietic support in patients with relapsed or refractory hematologic malignancies who are receiving high-dose therapy, in patients with chronic myeloid leukemia, and in patients with myelodysplastic syndromes	Pooled unexpanded cord blood transplant Unexpanded cord blood transplant	Increased overall survival Improved bone marrow engraftment rate Improved neutrophil recovery rate Improved platelet recovery rate
Exemestane for prevention of breast cancer in postmenopausal women at elevated risk of breast cancer	Postmenopausal women at risk for developing invasive breast cancer	The available therapies for preventing breast cancer in patients who have not developed the disease but are at elevated risk, tamoxifen and raloxifene, have limited patient acceptance because of persistent, undesirable side effects. Better-tolerated therapies are needed to prevent breast cancer in women at higher risk of developing the disease. Exemestane (Aromasin) is an aromatase inhibitor that blocks estrogen production. Exemestane is approved for treating advanced breast cancer that has progressed after tamoxifen therapy and as an adjuvant therapy after 2–3 years of tamoxifen treatment in women with estrogen receptor–positive breast cancer. A large phase III (n=4,560) trial reported that women who took exemestane as a primary preventive therapy were 65% less likely to develop breast cancer. At 3-year followup, no toxicities were observed and the drug had minimal impact on quality of life. However, further analyses revealed increased loss of bone density in women taking exemestane, which is the focus of ongoing studies. In ongoing trials, the drug is administered 25 mg, orally, once daily in the morning. Pfizer, Inc., New York, NY Phase III trial ongoing; approved for other breast cancer indications; could be prescribed off-label. Phase III trial on implications of bone density effects ongoing.	Raloxifene Tamoxifen	Decreased risk of developing breast cancer Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Farletuzumab (antifolate receptor monoclonal antibody) for treatment of ovarian cancer	Patients with recurrent ovarian cancer who are candidates for platinum and taxane-based therapy	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's action purportedly leads 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. Morphotek, Exton, PA, a subsidiary of Eisai Co., Ltd., Tokyo, Japan Phase III trial in platinum-sensitive disease failed to meet primary endpoint of progression-free survival in Jan 2013. Company reported trend towards improved PFS in subset of patients and that it would "determine a new development strategy based on discussion with external experts and the relevant health authorities."	Platinum-sensitive ovarian cancer: combination chemotherapy including one or more of the following:CarboplatinDocetaxelGemcitabinePaclitaxelPegylated liposomal doxorubicinTopotecan Platinum-refractory ovarian cancer: Docetaxel Etoposide Gemcitabine Paclitaxel Pegylated liposomal doxorubicin Topotecan	Increased overall survival Increased progression-free survival Improved quality of life
Ganetespib (hsp90 inhibitor) for treatment of nonsmall cell lung cancer	Patients with advanced or metastatic nonsmall cell lung cancer (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 treating NSCLC, ganetespib is being tested as an adjunct to the cytotoxic agent docetaxel. Ganetespib is administered at a dose of 150 mg/m2, intravenously, once weekly for 3 weeks followed by 1 week of rest. Synta Pharmaceuticals Corp., Lexington, MA Phase III trial ongoing; data reported from phase IIb/III trial	2nd-line: Crizotinib (if ALK+) Erlotinib Single agent chemotherapy (e.g., docetaxel, 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
Gemtuzumab ozogamicin (antibody-drug conjugate) for treatment of acute myeloid leukemia	Patients in whom acute myeloid leukemia (AML) has been diagnosed	With current treatments, the 5-year survival rate for patients with AML ranges from 20% to 70%, depending on disease subtype. Gemtuzumab ozogamicin is an AML treatment that conjugates a highly toxic chemotherapy agent to a monoclonal antibody specific for a cell surface marker expressed on most AML cells (CD33). The conjugate is intended to preferentially target AML cells with the toxic chemotherapy. Gemtuzumab ozogamicin is administered intravenously; various dosing schedules have been reported. During a recently completed phase III trial, investigators administered gemtuzumab ozogamicin in combination with a standard chemotherapy regimen using daunorubicin and cytarabine. Pfizer, Inc., New York, NY FDA approved in 2000 for treating AML; drug withdrawn from U.S. market in 2010 after negative study results and high toxicity observed in postmarket trials. Drug remains available in Europe, where trials have shown benefit using an altered dosing scheme. Pfizer is analyzing data to determine whether to make new FDA submission. The drug is available in the U.S. only to patients already taking it.	Standard chemotherapy with daunorubicin and cytarabine	Increased overall survival Increased progression-free survival Improved quality of life
Gene-mediated cytotoxic immunotherapy (ProstAtak) for prostate cancer	Patients in whom intermediate to high-risk localized prostate cancer has been diagnosed	Prostate cancer recurrence rates after front-line treatment range between 10% and 60% depending on whether tumor pathology indicates that the tumor is low risk or high risk; therefore, therapies that could reduce this recurrence rate are highly sought. A gene-mediated cytotoxic immunotherapy (GMCI), ProstAtak™ is being tested for preventing recurrence after conventional therapy. GMCI purports to lead to direct tumor cytotoxicity as well as a protective immune response. The treatment consists of an adenovirus vector that contains a herpes simplex virus (HSV) thymidine kinase gene (Adv-tk). After 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 dendritic cells and produce a systemic immune response. In treating prostate cancer, GMCI is being administered in combination with radiation therapy. Advantagene, Inc., Auburndale, MA Phase III trial ongoing under FDA special protocol assessment	Androgen deprivation therapy Radiation therapy Surgical resection	Increased overall survival Increased disease-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
Glembatumumab vedotin for treatment-refractory breast cancer	Patients with metastatic, glycoprotein NMB (GPNMB)-overexpressing triple negative breast cancer	Therapies with improved efficacy are needed for patients with metastatic triple negative breast cancer, as these patients have limited treatment options and a poor prognosis. Glembatumumab vedotin is an antibody-drug conjugate that links a highly toxic chemotherapy drug to a monoclonal antibody specific for GPNMB, a protein known to be overexpressed in some breast tumors. GPNMB has been implicated in enhancing the metastatic potential of breast cancer cells, particularly the triple-negative breast cancer subtype. A companion diagnostic test to determine whether a patient's cancer expresses GPNMB will be used to determine patient eligibility for treatment with glembatumumab vedotin. In a phase III trial, this agent will be compared to capecitabine in patients previously treated with anthracycline and taxane chemotherapy. Glembatumumab vedotin is an intravenous medication given at a dose of 1.88 mg/kg, once every 3 weeks. Celldex Therapeutics, Inc., Needham, MA Phase IIb trial complete; FDA granted fast -track status for treating treatment-resistant or refractory breast cancer; phase III trial to begin late 2013	Albumin-bound paclitaxe Capecitabine Docetaxel Doxorubicin Eribulin Gemcitabine Ixabepilone Liposomal doxorubicin Paclitaxel Vinorelbine	Increased overall survival Increased progression-free survival Improved quality of life
Gonadotropin-releasing hormone analogs for prevention of ovarian failure in women receiving gondaotoxic chemotherapy	Women undergoing gonadotoxic systemic chemotherapy for cancer	About 25% of women undergoing systemic chemotherapy for conditions such as breast cancer experience premature menopause as a side effect of treatment. No consensus on treatment exists for preventing this side effect. Ovarian suppression using gonadotropin-releasing hormone analogs (e.g., goserelin, triptorelin) may protect ovarian function against the effects of chemotherapy through several mechanisms, including decreasing the number of primordial follicles entering the relatively chemotherapy-sensitive differentiation stage; decreasing ovarian perfusion, thereby reducing ovarian exposure to chemotherapy; upregulating intragonadal antiapoptotic molecules (e.g., sphingosine-1-phosphate); and protecting ovarian germline stem cells. In clinical trials, gonadotropin-releasing hormone analogs (i.e., goserelin or triptorelin) are administered concomitantly with standard cytotoxic chemotherapy regimens. SWOG, Ann Arbor, MI, and International Breast Cancer Study Group IBCSG, Bern, Switzerland Phase III trials ongoing, enrollment complete; agents could be prescribed off-label	Other fertility preservation techniques (e.g., embryo, ovarian tissue, or oocyte cryopreservation)	Decreased rate of amenorrhea at 12 months post-chemotherapy Preserved fertility Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
High-intensity focused ultrasound (Ablatherm-HIFU system) for treatment of localized prostate cancer	Patients in whom localized prostate cancer has been diagnosed	High-intensity focused ultrasound (HIFU) is a noninvasive treatment under study for treating prostate cancer. HIFU ablates tissue by using sound waves to generate heat within a small, focused area, leaving surrounding tissue unaffected. The noninvasive and targeted nature of HIFU has the potential to reduce side effects associated with invasive procedures and radiation therapy and, unlike these procedures, may also be repeated in the event of local recurrence. HIFU ablation is performed in a 1–3 hour outpatient procedure. The most advanced clinical trial of the Ablatherm®-HIFU system in the U.S. is studying its use in treating patients who have localized prostate cancer and have not undergone previous prostate cancer treatment. EDAP TMS S.A., Lyon, France Phase II/III trial met primary endpoint; PMA accepted by FDA in Mar 2013; system available in Europe since 2000	Brachytherapy External beam radiation Observation Radical prostatectomy Other HIFU systems (in development)	Increased overall survival Increased progression-free survival Improved patient quality of life
High-intensity focused ultrasound (Sonablate system) for treatment of localized prostate cancer	Patients in whom localized prostate cancer has been diagnosed	High-intensity focused ultrasound (HIFU) is a noninvasive treatment under study for treating prostate cancer. HIFU ablates tissue by using sound waves to generate heat within a small, focused area, leaving surrounding tissue unaffected. The noninvasive and targeted nature of HIFU has the potential to reduce side effects associated with invasive procedures and radiation therapy and, unlike these procedures, may also be repeated in the event of local recurrence. HIFU ablation is performed in a 1–3 hour outpatient procedure. The most advanced clinical trial of the Sonablate system in the U.S. is studying its use in treating patients with localized prostate cancer that has recurred after initial therapy with external beam radiation therapy. SonaCare Medical, LLC (formerly USHIFU, LLC), Charlotte, NC Phase III trial ongoing; system available in Europe since 2001	Brachytherapy External beam radiation Observation Radical prostatectomy Other HIFU systems (in development)	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 (panobinostat) for treatment of recurrent multiple myeloma	Patients with recurrent multiple myeloma	Although treatments for multiple myeloma have improved, the median life expectancy for patients with multiple myeloma is only 5–7 years. Additionally, as several newer treatments for multiple myeloma have been moved into the frontline setting as combination therapies, additional salvage treatments are needed. Histone deacetylase (HDAC) inhibitors are a class of anticancer drugs whose exact mechanism of action is unclear but might be related to inhibition of DNA-damage repair or modification of cell-cycle proteins. Although 2 HDAC inhibitors (vorinostat and romidepsin) have been approved for treating cutaneous T-cell lymphoma, no HDAC inhibitor is approved for treating multiple myeloma. In an ongoing registration-phase clinical trial, panobinostat is being tested in combination with the proteasome inhibitor bortezomib and the glucocorticosteroid dexamethasone in patients whose disease requires retreatment after at least 1 round of chemotherapy. Novartis International AG, Basel, Switzerland Phase III trial ongoing; FDA granted orphan drug status	Chemotherapy at standard or high doses including one or more of the following: Bendamustine Bortezomib Cisplatin Cyclophosphamide Dexamethasone Doxorubicin Etoposide Lenalidomide Thalidomide	Increased overall survival Increased progression-free survival Improved quality of life
Hypoxia-activated DNA alkylating agent (TH-302) for treatment of pancreatic cancer	Patients in whom metastatic pancreatic adenocarcinoma has been diagnosed.	About 5% of patients with pancreatic cancer respond to the current standard of care (gemcitabine chemotherapy), and the prognosis for these patients is very poor. 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. Thus, new options are needed. TH-302 is a novel cytotoxic agent purported to be preferentially activated in hypoxic conditions. In its activated form, TH-302 is said to be a potent DNA alkylating agent (dibromo isophoramide mustard). Selective activation of TH-302 in hypoxic conditions might target alkylating activity to tumors. TH-302 is administered intravenously, and in clinical trials for pancreatic cancer, it is being administered in combination with gemcitabine. Threshold Pharmaceuticals, South San Francisco, CA, in partnership with Merck KGaA, Darmstadt, Germany Phase III trial ongoing	Various chemotherapies including 1 or more of the following: 5-Fluorouracil Capecitabine Erlotinib Gemcitabine Leucovorin Oxaliplatin	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 soft tissue sarcoma	Patients in whom locally advanced, unresectable or metastatic soft tissue sarcoma has been diagnosed	Until recently, doxorubicin was the only FDA-approved treatment option for soft tissue sarcomas (excluding GIST and liposarcomas), and no consensus treatment exists for patients who have progressed on doxorubicin chemotherapy. 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 purportedly is 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 1st-line therapy in combination with doxorubicin to try to target both the hypoxic and normoxic regions of the tumor. TH-302 is an intravenous medication administered at a dose of 300 mg/m2, on days 1 and 8 of a 21-day cycle. Threshold Pharmaceuticals, South San Francisco, CA, with Merck & Co., Inc. Whitehouse Station, NJ Phase III trial ongoing in soft tissue sarcoma; also under late-stage study in pancreatic cancer; companies signed agreement in Feb 2012 to codevelop and commercialize TH-302	Doxorubicin 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
Ibrutinib (Bruton's tyrosine kinase inhibitor) for treatment of chronic or small lymphocytic leukemia	Patients in whom chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL) has been diagnosed	Ibrutinib is a small molecule kinase inhibitor with activity against Bruton's tyrosine kinase (Btk). Many B-cell malignancies, including CLL and SLL, purportedly depend on B-cell receptor (BCR) signaling for survival, and Btk is essential for transduction of the BCR signaling pathway. Therefore, its inhibition may be of therapeutic benefit in patients with CLL or SLL. Ibrutinib is orally administered at a once-daily dose of 560 mg in trials. Ibrutinib is under study in patients with various stages of CLL or SLL, including recurrent/refractory CLL or SLL and in patients aged 65 years or older with newly diagnosed CLL or SLL Pharmacyclics, Sunnyvale, CA, in partnership with the Janssen Biotech, Inc., a unit of Johnson & Johnson, New Brunswick, NJ Phase III trials ongoing; FDA granted orphan drug status and breakthrough therapy designation; new drug application submitted Jul 2013	For patients with recurrent/refractory CLL/SLL: Various chemotherapy regimens, including: Bendamustine plus rituximab Ofatumumab For patients aged 65 years or older with CLL/SLL: 1 or more of the following: Alemtuzumab Bendamustine Chlorambucil Cladribine Cyclophosphamide Prednisone Also: Fludarabine Lenalidomide Rituximab	Increased overall survival Increased progression-free survival Improved quality of life
Ibrutinib (Bruton's tyrosine kinase inhibitor) for treatment of mantle cell lymphoma	Patients in whom recurrent/refractory mantle cell lymphoma (MCL) has been diagnosed	Although patients with MCL frequently respond to initial chemotherapy treatment, the disease eventually progresses in most patients. Median overall survival is between 5 and 7 years. Ibrutinib is a small-molecule kinase inhibitor with activity against Bruton's tyrosine kinase (Btk). Many B-cell malignancies (including MCL) purportedly depend on B-cell receptor (BCR) signaling for survival, and Btk is essential for transduction of the BCR signaling pathway. Therefore, its inhibition may be of therapeutic benefit in patients with MCL. In trials, ibrutinib has been orally administered at a once-daily dose of 560 mg. Pharmacyclics, Sunnyvale, CA, in partnership with the Janssen Biotech unit of Johnson & Johnson, New Brunswick, NJ Phase III trial ongoing; FDA granted orphan drug status in Dec 2012; in Feb 2013, FDA granted breakthrough therapy designation; new drug application submitted Jul 2013	Various chemotherapies including 1 or more of the following: Bendamustine Bortezomib Cyclophosphamide Etoposide Fludarabine Lenalidomide Mitoxantrone Pentostatin Procarbazine Rituximab Temsirolimus	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
Ibrutinib (Bruton's tyrosine kinase inhibitor) for treatment of Waldenström's macroglobulinemia	Patients in whom Waldenström's Macroglobulinemia has been diagnosed	Although several off-label treatments are in use for Waldenström's macroglobulinemia, no treatments are FDA-approved for this indication, and no standard treatment exists. Ibrutinib is a small-molecule kinase inhibitor with activity against Bruton's tyrosine kinase (Btk). Many B-cell malignancies (including Waldenström's macroglobulinemia) purportedly depend on B-cell receptor (BCR) signaling for survival, and Btk is essential for transduction of the BCR signaling pathway. Therefore, its inhibition may be of therapeutic benefit in patients with Waldenström's macroglobulinemia. In clinical trials, ibrutinib has been orally administered at a once-daily dose of 560 mg. Pharmacyclics, Sunnyvale, CA, in partnership with the Janssen Biotech, Inc., a unit of Johnson & Johnson, New Brunswick, NJ Phase II trial ongoing; FDA granted breakthrough therapy designation Feb 2013	Various chemotherapy regimens, including: Bendamustine Bortezomib Cladribine Cyclophosphamide Dexamethasone Doxorubicin Fludarabine Prednisone Rituximab Thalidomide Vincristine	Increased overall survival Increased progression free survival Improved quality of life
Inotuzumab ozogamicin (antibody-drug conjugate) for treatment-refractory acute lymphoblastic leukemia	Patients in whom recurrent or treatment-refractory acute lymphoblastic leukemia (ALL) has been diagnosed	Among patients who experience an ALL relapse, only about 30% will achieve long-term remission with subsequent therapies. Inotuzumab ozogamicin is an antibody-drug conjugate that links the cytotoxic antibiotic calicheamicin to an antibody specific for CD22, a marker highly expressed by ALL cells. In clinical trials, inotuzumab ozogamicin monotherapy is being administered once weekly, by intravenous infusion. Pfizer, Inc., New York, NY Phase III trial ongoing; FDA granted orphan drug status	Various combinations of the following chemotherapy agents: Anthracyclines Asparaginase Cyclophosphamide Cytarabine (ara-C) Epipodophyllotoxins Vincristine	Increased overall survival Increased progression-free survival Improved quality of life
I-124 girentuximab (Redectane) positron-emission tomography for detection of clear cell renal cell carcinoma	Patients with uncharacterized renal masses; patients undergoing treatment for renal cell carcinoma	cG250 is a monoclonal antibody specific for carbonic anhydrase IX, a protein that is expressed by the majority of clear cell renal cell carcinomas (ccRCCs) and few normal tissues. Redectane® is a modified version of cG250 that incorporates a radioisotope that can be visualized by positron emission tomography (iodine-124). In combination with computed tomography (CT). Imaging using Redectane could potentially be used in diagnosing ccRCC and to monitor ccRCC treatment efficacy and screen patients for ccRCC recurrence and metastasis. Redectane is administered by intravenous infusion. Wilex AG, Munich, Germany Phase III trial complete; 2nd phase III trial scheduled to begin in Jul 2013	CT imaging alone	Increased sensitivity and specificity for ccRCC

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Immature PSA ([-2]proPSA) assay as a decision aid regarding prostate cancer biopsy	Patients with elevated levels of serum prostate-specific antigen (PSA) levels of 4–10 ng/mL but normal results on digital rectal examination who must decide whether to undergo prostate biopsy	Prostate cancer screening using serum PSA is problematic because of its inability to distinguish between benign prostate conditions and prostate cancer. This exposes many men without prostate cancer to unneccesary prostate biopsies. [-2]proPSA is a partially processed form of PSA purported to be elevated in patients with prostate cancer that has the potential to improve upon the specificity of existing PSA-based screening. The [-2]proPSA test measures levels of the analyte using an immunoassay. Results of the assay are combined with total PSA and free PSA measurements obtained from the same sample to generate a "Prostate Health Index," which purportedly indicates the likelihood of prostate cancer. Beckman Coulter, Inc., Brea, CA FDA approved Jul 2012 as "an aid in distinguishing prostate cancer from benign prostatic conditions, for prostate cancer detection in men aged 50 years and older with total PSA ≥4.0 to ≤10.0 ng/mL, and with digital rectal examination findings that are not suspicious for cancer"; available in Europe since 2010	PSA testing alone Free PSA testing alone Percent-free-PSA testing Prostate cancer antigen 3 (PCA3) testing	Improved positive and negative predictive values Improved sensitivity Improved specificity Reduced number of unnecessary biopsies
Immunomodulator (Imprime PGG) for treatment of advanced colorectal cancer	Patients in whom recurrent or metastatic KRAS wild type colorectal cancer (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 that purportedly induces an antitumor response by binding complement receptors 1-3 and stimulating neutrophils. Imprime PGG purportedly works synergistically with monoclonal antibody therapy such as cetuximab. In clinical trials, this agent is being examined as part of a combination therapy with cetuximab. Imprime PGG is administered at a dose of 4 mg/kg of body weight, by injection, weekly. Biothera, Eagan, MN Phase III trial ongoing	Cetuximab monotherapy Regorafenib	Increased overall survival Increased progression-free survival Improved quality of life
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 becomes solid in the body and is intended for use during radiation therapy to create distance between the targeted tumor and organs at risk of collateral radiation damage (e.g., displace the rectum from the prostate). Augmenix, Inc., Waltham, MA Phase III trial ongoing, no longer recruiting; CE marked; in May 2011, Varian Medical Systems, Inc., Palo Alto, CA, invested in Augmenix with option to buy company	Radiation therapy without normal-tissue spacer	Reduced radiation-associated side effects to healthy tissue

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ipilimumab (Yervoy) for treatment of advanced nonsmall cell lung cancer	Patients with recurrent or metastatic nonsmall cell lung cancer (NSCLC) who have not received previous systemic therapy	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. Ipilimumab (Yervoy™) is a 1st-in-class, cytotoxic T-lymphocyte antigen 4 (CTLA-4)-targeted immunotherapy. By blocking the activity of CTLA-4, ipilimumab may increase antitumor cytotoxic activity (reduce immune tolerance to tumor cells). This agent is being tested as 1st-line treatment as part of combination therapy with carboplatin and paclitaxel. ipilimumab is administered at a dose of 10 mg/kg, intravenously, once every 3 weeks for 4 doses, then once every 12 weeks beginning at week 24. Bristol-Myers Squibb, New York, NY Phase III trial ongoing	Combination chemotherapy (e.g., pemetrexed plus cisplatin) Targeted immunotherapy (e.g., bevacizumab, cetuximab, crizotinib [if ALK+], erlotinib)	Increased overall survival Increased progression-free survival Improved quality of life
Ipilimumab (Yervoy) for treatment of metastatic hormone-refractory prostate cancer	Patients in whom metastatic, chemotherapy-naïve or docetaxel-treated castration-resistant prostate cancer (CRPC) has been diagnosed	Men with progressive metastatic CRPC have a poor prognosis and few treatment options. Ipilimumab (Yervoy™) is a 1st-in-class targeted anticytotoxic T-lymphocyte antigen 4 therapy; it is intended to block the activity of cytotoxic T-lymphocyte antigen 4, which could lead to increased antitumor cytotoxic activity (reduce immune tolerance to tumor cells). Bristol-Myers Squibb, New York, NY Phase III trials ongoing	Abiraterone Cabazitaxel Docetaxel Enzalutamide Radium-223 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
Irreversible electroporation (NanoKnife) for treatment of hepatocellular carcinoma	Patients with early-stage hepatocellular carcinoma (HCC) that is not surgically resectable	Surgical resection and/or ablation of locally advanced tumors is the only potentially curative treatment option for patients with HCC. 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 presence 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 [RF] ablation, cryotherapy), irreversible electroporation does not induce 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 treating HCC, irreversible electroporation is performed in a minimally invasive laparoscopic procedure. AngioDynamics, Latham, NY Phase II trial ongoing; FDA cleared for surgical ablation of soft tissue but not for any cancer indication; under investigational device exemption status for a premarket approval application for liver cancer	Cryotherapy RF 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 with pancreatic cancer. 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 presence 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 [RF] ablation, cryotherapy), irreversible electroporation does not induce 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 treating pancreatic cancer, irreversible electroporation is performed in a minimally invasive laparoscopic procedure. AngioDynamics, Latham, NY Phase II trial ongoing; FDA cleared for surgical ablation of soft tissue but not for any cancer indication; under investigational device exemption status for a premarket approval application for liver cancer	Cryotherapy RF ablation	Increased overall survival Increased rate of clinical downstaging to surgically tumor Improved adverse event profile Improved quality of life
JAK2 inhibitor (pacritinib) for treatment of myelofibrosis	Patients in whom myelofibrosis has been diagnosed	Few treatment options are available for myelofibrosis. The kinase JAK2 appears to play a central role in the majority of myelofibrosis pathophysiology; therefore, inhibition of JAK2 is seen as a promising intervention for myelofibrosis, as demonstrated by the recent marketing approval of a dual JAK1/JAK2 inhibitor (ruxolitinib, Jakafi™) for this indication. Pacritinib is a novel JAK kinase inhibitor that is selective for JAK2, potentially altering the drug's efficacy and/or side effect profile. Pacritinib is administered orally at a dose of 400 mg, once daily. Cell Therapeutics, Inc, Seattle, WA Phase III trial ongoing	Ruxolitinib	Increased overall survival Increased progression-free survival Reduced spleen size Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Lenvatinib for treatment of differentiated thyroid cancer	Patients with differentiated thyroid cancer that is resistant to radioiodine therapy	Differentiated thyroid cancer (e.g., papillary, follicular) comprises the majority of diagnosed thyroid cancers. Although many differentiated thyroid cancers are treated successfully with radioiodine, patients with disease that is resistant to radioiodine have few treatment options and a poor prognosis. Lenvatinib is a small-molecule multikinase inhibitor with activity against multiple tyrosine kinases involved in signaling pathways that regulate cell growth and proliferation and angiogenesis (e.g., vascular endothelial growth factor receptors 2 and 3). In a late-phase clinical trial, lenvatinib is an oral medication administered as a once-daily dose of 24 mg. Eisai Co., Ltd., Tokyo, Japan Phase III trial ongoing; FDA granted orphan drug status Feb 2013; Eisai reported 2013 target date for regulatory submission	Pazopanib (off label) Sorafenib (off label) Sunitinib (off label)	Increased overall survival Increased progression-free survival Improved quality of life
Leukocyte/interleukin (Multikine) immune therapy for head and neck cancer	Patients in whom head and neck cancer has been diagnosed	Advanced head and neck cancer has a poor prognosis and high recurrence rate, suggesting the need for novel treatment options. Multikine (leukocyte interleukin injection) is a mix of immune stimulators (tumor necrosis factor, interleukin-1, other cytokines) that is intended to be delivered before conventional treatment (surgery, radiotherapy, chemotherapy). In a clinical trial, Multikine is administered prior to standard of care therapy in treatment-naive patients. The manufacturer asserts that this is when the immune system is best able to mount an immune response. Multikine will be administered at a dose of 400 IU, delivered by injection directly to the tumor and nearby lymph nodes, 5 times a week for 3 weeks. This agent will be administered in combination with low non-chemotherapeutic doses of cyclophosphamide, indomethacin, and zinc (CIZ). CEL-SCI Corp., Vienna, VA; in partnership with Ergomed Clinical Research Ltd., London, UK, for development aborad Phase III trial ongoing; interim review of safety data in Oct 2012 raised no safety concerns	Surgical resection and chemoradiation 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
Linsitinib for treatment of adrenocortical carcinoma	Patients in whom locally advanced or metastatic adrenocortical carcinoma has been diagnosed	Current 2nd- and 3rd-line treatments for adrenocortical carcinoma are largely ineffective, and only about 10% of patients with metastatic disease survive 5 years after the disease is diagnosed. Insulin-like growth factor (IGF) signaling has been implicated in adrenocortical carcinoma pathogenesis through the finding that IGF-2 is often upregulated in these tumors. Linsitinib is an orally administered, small-molecule inhibitor of an IGF-2 target, the IGF-1 receptor (IGF-1R). IGF-1R signaling purportedly regulates multiple cancer-related properties in cells, including growth, energy metabolism, differentiation, and apoptosis; therefore, its inhibition may have anticancer activity. In clinical trials, linsitinib is being administered twice daily, at a dose of 150 mg. Astellas Pharma, Inc., Tokyo, Japan (previously developed by Osi Pharmaceuticals, which was acquired by Astellas) Phase III trial complete	Etoposide/doxorubicin/cisplatin plus mitotane Streptozotocin plus mitotane	Increased overall survival Increased progression-free survival Improved quality of life
Liposome encapsulated irinotecan (MM-398) for treatment of pancreatic cancer	Patients with metastatic pancreatic cancer previously treated with gemcitabine	Only about 25% of patients with metastatic pancreatic cancer have disease that responds to 1st-line therapy with gemcitabine; patients have a poor prognosis with current 2nd-line treatment options. MM-398 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 2nd-line treatment. Liposomal encapsulation of irinotecan has 3 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. Combination therapy with 5-FU and leucovorin is being investigated, as well as MM-398 monotherapy, in the 2nd-line setting. In clinical trials, MM-398 is being administered by intravenous infusion at a dose of 120 mg/m2, every 3 weeks. Merrimack Pharmaceuticals, Inc., Cambridge, MA Phase III trial (NAPOLI-1) ongoing, topline data expected late 2013/early 2014; FDA granted orphan drug status for treating 2nd-line pancreatic cancer	Capecitabine Capecitabine/ oxaliplatin FOLFOX (folinic acid [leucovorin], 5-fluorouracil, oxaliplatin)	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
Liposome encapsulated vincristine (Marqibo) for treatment of acute lymphoblastic leukemia	Adult patients with recurrent Philadelphia chromosome–negative acute lymphoblastic leukemia (ALL)	Adult patients with recurrent ALL have a poor prognosis and few treatment options. The microtubule-assembly inhibitor vincristine is a mainstay of ALL treatment both in the frontline and salvage settings. However, the effectiveness of vincristine is limited by the inability to maintain therapeutic levels of the drug for long periods of time and the inability to further escalate the dose because of toxicity. Marqibo® is a novel liposomal formulation of vincristine that purportedly allows the slow release of vincristine, potentially maintaining therapeutic levels of vincristine and improving efficacy. It is administered as a once-weekly injection. The labeling includes a boxed warning that it must be administered intravenously because other injection methods, such as injection into spinal fluid, could result in death. Talon Therapeutics, Inc., San Mateo, CA FDA approved Aug 2012 for patients whose leukemia has recurred 2 or more times, or whose leukemia has progressed after 2 or more therapy regimens; phase III confirmatory study ongoing	Combination chemotherapy including 1 or more of the following: Anthracyclines Asparaginase Methotrexate High-dose cytarabine Steroids Vincristine	Increased overall survival Increased disease-free survival Improved quality of life
Lorvotuzumab mertansine for treatment of small cell lung cancer	Patients in whom advanced small cell lung cancer (SCLC) has been diagnosed; patients must have no previous systemic chemotherapy exposure	The 5-year survival rate for patients in whom small cell lung cancer is diagnosed is only about 15%. Lorvotuzumab mertansine (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 SCLC. In current clinical trials, Lorvotuzumab mertansine is being given as an adjunct to a conventional cytotoxic chemotherapy regimen of carboplatin plus etoposide in the 1st-line setting. Lorvotuzumab mertansine is administered on days 1 and 8 of every 3-week cycle. ImmunoGen, Inc., Waltham, MA Phase II trial ongoing, following interim safety analysis, dose reduction recommended; FDA granted orphan drug status	Carboplatin plus etoposide	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
MABp1 (Xilonix) for treatment of cancer-related cachexia	Patients in whom cancer-related cachexia has been diagnosed	While a number of treatments have been developed to address cancer-related cachexia (wasting of skeletal muscle mass), many patients do not respond to current treatment options. Cancer-related cachexia may limit the ability of patients to tolerate further treatment and/or directly affect survival. Cancer-related cachexia is caused by metabolic and neurochemical alterations in the body that lead to the wasting of skeletal muscle mass. While the mechanism by which tumors induce cachexia is poorly understood, one hypothesis states that interleukin-1α-mediated pro-inflammatory signals to the central nervous system may induce systemic cachexia. MABp1 (Xilonix™) is a monoclonal antibody that acts as an interleukin-1α antagonist potentially disrupting this pro-inflammatory signaling. It is administered intravenously. XBiotech, Austin, Texas Phase III trial ongoing; FDA granted fast-track status	Appetite stimulants: Cannabinoids Corticosteroids Cyproheptadine Progesterone derivatives Dietary counseling Melanocortin antagonists Metabolic disturbance modulators: Anti-cytokine antibodies Pentoxifylline Thalidomide	Increased body weight Increased lean body mass Increased muscle strength Increased overall survival Improved quality of life
MAGE-A3-specific cancer immunotherapeutic (GSK2132231A) for treatment of melanoma	Patients with resectable stage IIIB or IIIC cutaneous melanoma that expresses melanoma antigenic epitope (MAGE)-A3 antigen	Patients with advanced melanoma 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 being tested in the adjuvant setting for treating melanoma. In a multicenter, international phase III trial of 1,349 patients, GSK2132231A is being administered as a course of 13 injections over 27 months. GlaxoSmithKline, Middlesex, UK Phase III trial ongoing; phase III trial also ongoing in NSCLC; initial results expected late 2013	Granulocyte-macrophage colony stimulating factor Interferon-alpha Interleukin-2 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
Magnetic resonance imaging-ultrasound image fusion for image-guided prostate biopsy	Patients who are suspected of having prostate cancer based on elevated prostate-specific antigen (PSA) or abnormal digital rectal exam	Transrectal ultrasound (TRUS)-guided biopsy has been the standard of care for many years. However, TRUS cannot discriminate normal tissue from cancerous tissue; therefore, a random sampling procedure is used and some cancers may be missed. MRI has the potential to identify prostate tissue that may be cancerous, and some institutions have adopted the use of MRI-guided biopsy. Although this procedure may improve cancer detection rates, MRI-guided biopsy is expensive, time consuming, and cumbersome because of the need to perform the biopsy within the MRI machine gantry. A new procedure uses MRI data to guide prostate biopsies performed in an office setting by a urologist—rather than by a radiologist—followed by fusion of MRI image data with TRUS image data. It might enable evaluation of areas of suspicion that were identified using MRI to be targeted using TRUS-guided biopsy. Philips Healthcare unit of Royal Philips Electronics, Amsterdam, the Netherlands Phase III trial ongoing. Pilot studies completed by multiple institutions (e.g., Kyoto Prefectural University of Medicine, Kyoto, Japan; University of Regensburg, Regensburg, Germany)	MRI-guided biopsy TRUS-guided biopsy	Improved positive and negative predictive values Improved sensitivity Improved specificity
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 2nd 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, allowing the surgeon to resect additional tissue during the same surgical procedure; the system uses radiofrequency spectroscopy to discern differences in the electromagnetic signature of cancerous cells relative to normal tissue. Dune Medical Devices, Inc., Framingham, MA FDA approved Jan 2013 for intra-operative tissue assessment of surgical margins during surgery for early-stage breast cancer; system has been available in Europe since 2008	No marketed comparator in the U.S.	Reduced number of reexcision 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
Masitinib (multikinase inhibitor) for treatment of activating c-KIT mutation-positive melanoma	Patients with unresectable, advanced 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. Although KIT kinase inhibitors have been developed for other cancers dependent on KIT activity (e.g., imatinib for treating gastrointestinal stromal tumors), no KIT kinase inhibitor is approved for treating c-KIT mutation-positive melanoma. Masitinib is an orally administered, kinase inhibitor with activity against KIT as well as platelet-derived growth factor receptors, the intracellular kinase Lyn, and to a lesser extent, fibroblast growth factor receptor 3. Masitinib is under study as a monotherapy for treating melanoma at a dose of 7.5 mg/kg, daily. AB Science S.A., Paris, France Phase III trial ongoing	Dacarbazine Interleukin-2 Ipilimumab Nilotinib (in development)	Increased overall survival Increased progression-free survival Improved quality of life
Masitinib (multikinase inhibitor) for treatment of pancreatic cancer	Patients in whom advanced/ 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. Masitinib is an orally administered multikinase inhibitor under study for treating patients who have pancreatic cancer. Masitinib inhibits several tyrosine kinases that have been shown to be overexpressed in pancreatic cancers (e.g., platelet-derived growth factor receptors, fibroblast growth factor receptor-3) or whose expression is associated with chemotherapy resistance (e.g., focal adhesion kinase). Additionally, masitinib inhibits mast cell differentiation, proliferation, and granulation through its activity on stem cell growth factor receptor (KIT) and Lyn kinase. Tumor infiltration by mast cells has been associated with increased tumor growth and spread. In clinical trials, masitinib (at a dosage of 9 mg/kg/day) has been used in combination with gemcitabine. AB Science S.A., Paris, France Phase III trial complete; positive data reported for 2 specific patient populations with poor prognoses; FDA granted orphan drug status for treating pancreatic cancer; regulatory submission made to European Medicines Agency; companion diagnostic test intended to identify likely responders to masitinib on the basis of an RNA-based blood test in development in conjunction with Skuldtech (Montpellier, France)	Various chemotherapies including 1 or more of the following: 5-Fluorouracil Capecitabine Erlotinib Gemcitabine Leucovorin Oxaliplatin	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
Methylated septin 9 plasma DNA test (Epi proColon) for colorectal cancer screening	All patients undergoing routine colorectal cancer (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, Berlin, Germany Epigenomics submitted premarket approval application Jan 2013; FDA granted priority review status; available in Europe as Epi ProColon 2.0 CE since 2011	Colonoscopy Computed tomographic colonography Fecal DNA tests Sigmoidoscopy	Increased sensitivity and specificity Increased predictive values Avoided unnecessary followup procedures Improved adherence with CRCl screening Earlier intervention for identified cancer
Midostaurin (multikinase inhibitor) for treatment of acute myeloid leukemia bearing FLT3 mutations	Patients with newly diagnosed acute myeloid leukemia (AML) bearing an internal tandem duplication in the FLT3 gene (ITD-FLT3)	The presence of activating FLT3 mutations in AML is associated with a poor prognosis, and patients identified as having disease bearing such a mutation more often experience disease recurrence after initial therapy. Midostaurin is a small-molecule kinase inhibitor that has activity against FLT3 and additional tyrosine kinases (e.g., c-KIT). Addition of midostaurin's anti-FLT3 activity to conventional 1st-line therapy (cytarabine and daunorubicin) might improve response rates and decrease recurrence. Treatment is intended for patients younger than 60 years of age who are able to tolerate high-dose cytarabine consolidation therapy. In a late-stage clinical trial, midostaurin is being given in a twice-daily oral dose for 2 weeks. Patients are administered midostaurin after both induction therapy with cytarabine and daunorubicin and consolidation therapy with high-dose cytarabine. Novartis International AG, Basel, Switzerland Phase III trial ongoing; FDA granted orphan drug status	Cytarabine/ daunorubicin	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 disruptor (CPI-613) for treatment of various cancers	Patients with an advanced malignancy, in particular pancreatic cancer or acute myeloid leukemia (AML)	The metabolic activity of cancer cells is altered significantly compared with noncancerous cells; therefore, therapies targeting aspects of cellular metabolism specific to cancer cells may be effective against a wide range of cancer types. CPI-613 is a novel, lipoic acid derivative that purportedly functions by leading to the inhibition of a mitochondrial enzyme (pyruvate dehydrogenase) that is essential for conversion of pyruvate to acetyl coenzyme A (acetyl-CoA). Cancer cells may be particularly sensitive to this disruption because the metabolic state of cancer cells downregulates both pyruvate dehydrogenase activity and other metabolic pathways that could provide a source of acetyl-CoA (e.g., fatty acid metabolism). In clinical trials, CPI-613 is an intravenous medication given at a dose of 3,000mg/m2m on days 1 and 4 of the first 3 weeks of each 4-week cycle. Cornerstone Pharmaceuticals, Inc., Cranbury, NJ Phase I/II trials ongoing in hematologic malignancies; phase I/II trial ongoing in pancreatic cancer; FDA granted orphan drug status for AML and pancreatic cancer	Various chemotherapy regimens	Increased overall survival Increased progression-free survival Improved quality of life
MRI-guided focused ultrasound therapy (ExAblate) for the treatment of pain from bone metastases	Patients experiencing pain from bone metastases	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. Pain is a common symptom of bone metastases and significantly hinders quality of life. Nonnarcotic treatments for the pain from bone metastases are needed, particularly in those ineligible to receive radiation therapy. ExAblate is a non-invasive, MRI-guided focused ultrasound device that provides targeted treatment to sites of bone metastases. High-intensity ultrasound waves are used to try to ablate the pain-causing nerves with the intention of providing rapid, extended relief. InSightec Ltd., Tirat Carmel, Israel FDA approved Oct 2012; post-approval registry trial ongoing	Opiates and other analgesics Palliative radiation therapy Radiopharmaceuticals	Decreased pain Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
MUC1 therapeutic vaccine (CVac) for ovarian cancer	Patients with ovarian cancer who are in 1st or 2nd remission after cytoreduction and chemotherapy	No maintenance therapies are 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.CVac is administered via intradermal injection, every 4 weeks for the 3 cycles, then every 12 weeks for 3 cycles Prima BioMed, Ltd., Melbourne, Australia Phase II/III trial ongoing	Other ovarian cancer vaccines (in development)	Decreased recurrence rates Increased overall survival Increased progression-free survival Improved quality of life
MUC1 therapeutic vaccine (TG4010) for nonsmall cell lung cancer	Patients with metastatic, chemotherapy-naïve nonsmall cell lung cancer (NSCLC) who are mucin-1 (MUC-1)-positive	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. About 60% of NSCLC tumors express MUC-1, and this protein is a potential therapeutic target for treating NSCLC. TG4010 is a therapeutic cancer vaccine that comprises a viral vector encoding both a tumor antigen (MUC-1) and an immune stimulant (interleukin-2). Patients' tumors must be MUC-1-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 in the 1st-line setting. The vaccine is given by subcutaneous injection on a weekly basis for the first 6 weeks of chemotherapy, and once every 3 weeks thereafter. Transgene SA, Cedex, France Phase IIb/III trial ongoing, phase IIb data expected 2H 2013; FDA granted fast-track status	Immunotherapies (in development, i.e., melanoma antigenic epitope-A3 therapeutic vaccine) 1st-line (standard of care): Combination chemotherapy (e.g., pemetrexed plus cisplatin) Targeted therapy (e.g., bevacizumab, cetuximab, 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
Nabiximols oromucosal spray (Sativex) for persistent chronic cancer pain	Patients with cancer who have persistent chronic pain	Effective pain management for chronic cancer pain is challenging because of side effects of available narcotic therapies and some patients' reluctance to avail themselves of narcotic therapy. For patients with advanced cancers, narcotic therapies may provide inadequate pain relief. Sativex, which is sprayed under the tongue, is a whole plant medicinal cannabis extract that contains tetrahydrocannabinol (THC) and cannabidiol as its main component. It is administered orally as a spray at a 100-µL dose, which contains 2.5 mg cannabidiol and 2.7 mg THC. GW Pharmaceuticals, plc, Salisbury, UK, and Otsuka Holdings Co., Ltd., Tokyo, Japan Phase III U.S. trials ongoing; approved in Europe and Canada for pain and symptom relief for patients with multiple sclerosis and neuropathic-related cancer pain	Oral and transdermal opioids	Avoidance of side effects from narcotic pain medications Reduced pain Improved quality of life
Nab-paclitaxel (Abraxane) for the treatment of pancreatic cancer	Patients in whom advanced/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. Nab-paclitaxel (Abraxane®) is an albumin-bound nanoparticle form of the microtubule stabilizing agent paclitaxel. In clinical trials for patients with pancreatic cancer nab-paclitaxel (125 mg/m2) is being administered in combination with gemcitabine. Besides the direct antitumor activity of paclitaxel, preliminary studies have indicated that it may lead to increased intratumoral concentrations of gemcitabine. Celgene Corp., Summit, NJ Phase III trial complete; supplemental new drug application submitted to FDA; FDA granted priority review status; approval decision date set for Sept 21, 2013	Various chemotherapies including 1 or more of the following: 5-Fluorouracil Capecitabine Erlotinib Gemcitabine Leucovorin Oxaliplatin	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
Necitumumab for treatment of advanced nonsmall cell lung cancer	Patients in whom advanced squamous nonsmall cell lung cancer (NSCLC) has been diagnosed	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. Necitumumab is a monoclonal antibody antagonist directed against the epidermal growth factor (EGF) receptor 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. The drug is in a similar class as cetuximab, which is used for treating many cancers but is not labeled for treating NSCLC. In clinical trials, this agent was administered at a dose of 800-mg, intravenously, on days 1 and 8 of every 3-week cycle; it has been tested in the 1st-line setting in combination with cisplatin and gemcitabine or pemetrexed. Eli Lilly and Co., Indianapolis, IN; formerly in partnership with Bristol-Myers Squibb, New York, NY Phase III trials ongoing	Combination chemotherapy (e.g., pemetrexed plus cisplatin) Targeted immunotherapy (e.g., bevacizumab, cetuximab, erlotinib)	Increased overall survival Increased progression-free survival Improved quality of life
Nelipepimut (NeuVax) for prevention of breast cancer recurrence	Patients with HER2-positive early stage breast cancer who are positive for human leukocyte antigen (HLA)-A2 and/or HLA-A3.	Although many patients with early-stage breast cancer achieve remission after 1st-line chemotherapy, a significant proportion eventually have disease recurrence. Although some patients undergo maintenance therapy with trastuzumab, only patients whose tumors express high levels of HER2 are eligible for this therapy. NeuVax™ is a therapeutic cancer vaccine that combines an HER2-derived peptide (E75) with the immune stimulant granulocyte macrophage colony-stimulating factor. The vaccine is designed to induce a cytotoxic T-cell response against cells expressing HER2. NeuVax is under study as maintenance therapy for disease-free patients whose tumors expressed low levels of the HER2 protein. It is administered by intradermal injection, monthly for 6 months, then once every 6 months as maintenance therapy. RXi Pharmaceuticals Corp. subsidiary of Galena Biopharma, Lake Oswego, OR Phase III ongoing under FDA special protocol assessment; phase II trial ongoing for combination therapy with trastuzuamb	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
Nintedanib (Vargatef) for treatment of ovarian cancer	Patients in whom chemotherapy-naïve ovarian cancer has been diagnosed	A significant fraction of patients with ovarian cancer have disease that is resistant or refractory to current 1st-line treatments. Nintedanib (Vargatef™) is a tyrosine kinase inhibitor that has activity against vascular endothelial growth factor receptor, platelet-derived growth factor receptor, and fibroblast growth factor receptor tyrosine kinases, which regulate tumor growth and angiogenesis. In late-phase clinical trials, nintedanib is being tested as an adjunct to the conventional 1st-line therapy of intravenous carboplatin plus paclitaxel. Nintedanib is administered as an oral tablet, at a dose of 200 mg, twice daily. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trial ongoing, enrollment completed	Combination chemotherapy including one or more of the following: Carboplatin Docetaxel Gemcitabine Paclitaxel Pegylated liposomal doxorubicin Topotecan	Increased overall survival Increased progression-free survival Improved quality of life
Nintedanib (Vargatef) for treatment-resistant nonsmall cell lung cancer	Patients with nonsmall cell lung cancer (NSCLC) whose disease has progressed during or after 1st-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 1st-line chemotherapy have few treatment options. Nintedanib is a tyrosine kinase inhibitor that has activity against vascular endothelial growth factor receptor, platelet-derived growth factor receptor, and fibroblast growth factor receptor tyrosine kinases, which regulate tumor growth and angiogenesis. In late-phase clinical trials, nintedanib is being tested as an adjunct to conventional 2nd-line therapies (i.e., pemetrexed monotherapy, docetaxel monotherapy). Nintedanib is administered as an oral tablet, twice daily. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trial ongoing	Various combination therapies including: Bevacizumab Carboplatin Crizotinib Docetaxel Erlotinib 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
Nivolumab (anti-PD-1 monoclonal antibody) for treatment of advanced melanoma	Patients in whom advanced melanoma has been diagnosed	Clinical trials with the immune checkpoint inhibitor ipilimumab (Yervoy) have demonstrated the potential of immune therapies in melanoma. However, the utility of ipilimumab is limited by its relatively low response rate, and the prognosis for patients with advanced melanoma remains poor. Nivolumab (BMS-936558) is a fully human monoclonal antibody that targets an immune-checkpoint pathway distinct from that of ipilimumab. Nivolumab purportedly blocks the programmed death-1 (PD-1) co-inhibitory receptor expressed by activated T cells. The activity of this pathway has been shown to limit T cell activation; therefore, blocking its activity may enhance the body's immune response, potentially overcoming immune tolerance to melanoma. This agent is being tested in patients with nonresectable advanced melanomas and in patients whose disease progressed following prior anti-CTLA-4 therapy. In clinical trials, nivolumab is administered intravenously at a dose of 3 mg/kg, once every 2 weeks. Bristol-Myers Squibb, New York, NY Phase III trials ongoing in several treatment settings as monotherapy and combination therapy with ipilimumab; FDA granted fast-track status	Dacarbazine Dabrafenib (if *BRAF*+) Ipilimumab Trametinib (if *BRAF*+) Vemurafenib (if *BRAF*+)	Increased overall survival Increased progression-free survival Improved quality of life
Nivolumab (anti-PD-1 monoclonal antibody) for treatment of advanced nonsmall cell lung cancer	Patients with platinum-resistant advanced or metastatic non-small cell lung cancer (NSCLC)	Patients with squamous or nonsquamous NSCLC whose disease has progressed after 1st-line platinum-based chemotherapy have few treatment options and a poor prognosis. One of the hallmarks of cancer is its ability to evade an immune response. Nivolumab is a novel therapeutic that is intended to prevent immune tolerance of tumor cells. The drug's target is the programmed death-1 (PD-1) pathway, which acts as an immune checkpoint that downregulates T-cell activity. Nivolumab is a monoclonal antibody specific for the PD-1 receptor that purportedly blocks activation of this pathway. In trials, nivolumab is administered as a 3 mg/kg of body weight intravenous infusion, once every 2 weeks. Bristol-Myers Squibb, New York, NY Phase III trials ongoing; FDA granted fast-track status	Docetaxel Erlotinib Pemetrexed Platinum doublet (plus or minus bevacizumab)	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
Nivolumab (anti-PD-1 monoclonal antibody) for treatment of advanced renal cell carcinoma	Patients in whom advanced or metastatic clear cell renal cell carcinoma (ccRCC) has been diagnosed and who have undergone prior treatment with at least 1 antiangiogenic kinase inhibitor	Patients in whom advanced renal cell carcinoma has been diagnosed and whose disease has progressed after 1st-line treatment with a tyrosine kinase inhibitor have few treatment options and a poor prognosis. One of the hallmarks of cancer is its ability to evade an immune response. Nivolumab is a novel therapeutic that is intended to prevent immune tolerance of tumor cells. The drug's target is the programmed death-1 (PD-1) pathway, which acts as an immune checkpoint that downregulates T-cell activity. Nivolumab is a monoclonal antibody specific for the PD-1 receptor that purportedly blocks activation of this pathway. Nivolumab is administered as a 3 mg/kg of body weight intravenous infusion, once every 2 weeks. Bristol-Myers Squibb, New York, NY Phase III trial ongoing; FDA granted fast-track status	Axitinib Bevacizumab Everolimus Interferon Interleukin-2 Pazopanib Sorafenib Sunitinib	Increased overall survival Increased progression-free survival Improved quality of life
Off-label maraviroc (Selzentry) for prevention of graft-versus-host disease	Patients at high risk for graft-versus-host disease (GVHD) after undergoing allogeneic stem cell transplantation	About 50% of patients undergoing allogeneic stem cell transplantation develop GVHD, a condition in which donor cells in an allogeneic hematopoietic stem cell transplant mount an immune response against recipient tissues. Patients with acute GVHD typically exhibit damage to the skin, liver, and gastrointestinal tract, and GVHD is lethal in up to 80% of patients with severe forms of the disease. Current prophylactic treatments for GVHD target donor immune cells in a way that may delay immune system reconstitution and/or limit graft-versus-tumor immune responses. A potential molecular target in GVHD is chemokine (C-C motif) receptor 5 (CCR5), which has been shown to play a role in the pathogenesis of GVHD by promoting lymphocyte recruitment to tissues involved in GVHD. Maraviroc is a CCR5 antagonist that may limit lymphocyte recruitment to target tissues, potentially limiting the extent of recipient tissue damage. In clinical trials, daily maraviroc is administered at a dose of 300 mg, orally, in combination with standard GVHD prophylaxis. University of Pennsylvania, Philadelphia Phase II trial ongoing; FDA approved in 2007 for treating HIV; marketed by Pfizer, Inc. (New York, NY), as Selzentry®, but the manufacturer does not appear to be seeking a labeled indication for this use	Methotrexate Tacrolimus	Reduced rate of acute GVHD 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
Off-label metformin for treatment of breast cancer	Patients in whom breast cancer has been diagnosed	Retrospective studies of patients with diabetes taking metformin, preclinical studies of in vitro cell lines, and in vivo cancer models have demonstrated that metformin may have antineoplastic properties. Metformin may exert its effects through activation of AMP-activated protein kinase, which functions to limit downstream components of the mTOR pathway. Additionally, metformin's actions in reducing circulating insulin levels may be antineoplastic because of 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. National Cancer Institute, Bethesda, MD, and multiple other academic institutions Phase II trials ongoing in neoadjuvant setting; phase III trial ongoing in adjuvant setting to prevent recurrence; phase I/II trials ongoing in metastatic disease	Various chemotherapy regimens Various hormone therapies	Increased overall survival Increased progression-free survival Improved quality of life
Off-label rosuvastatin (Crestor) 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 in the 1st 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 (Crestor) is believed to have potential as a chemopreventive agent for colon cancer. National Surgical Adjuvant Breast and Bowel Project, Pittsburgh, PA (investigator) National Cancer Institute, Bethesda, MD (investigator) Phase III trial ongoing	No commonly used chemopreventive agent exists for treating colorectal cancerCompounds under investigation include:AspirinCalcium supplementsCurcuminNonsteroidal anti-inflammatory drugsOmega-3 fatty acids	Reduced recurrence rate of adenomatous polyps Increased overall survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Omacetaxine mepesuccinate (Synribo) for treatment of tyrosine kinase inhibitor–resistant chronic myelogenous leukemia	Patients with tyrosine kinase inhibitor–resistant chronic myelogenous leukemia (CML)	CML often responds to treatment with tyrosine kinase inhibitors targeting the BCR-ABL fusion gene; however, patients whose disease progresses after 1st- and 2nd-line tyrosine kinase inhibitor treatment have few treatment options and a poor prognosis. Omacetaxine mepesuccinate (Synribo®) is a cytotoxic alkaloid derived from the evergreen tree *Cephalotaxus harringtonia*. Omacetaxine mepesuccinate purportedly acts as a reversible, transient inhibitor of protein elongation. This inhibition leads to cell death through multiple mechanisms of action, including inhibition of HSP90, which leads to destabilization of BCR-ABL and downregulation of the antiapoptotic protein MCL-1. In clinical trials, omacetaxine mepesuccinate was administered twice daily, by subcutaneous injection. Cephalon unit of Teva Pharmaceutical Industries, Ltd., Petach Tikva, Israel, (developed by ChemGenex Pharmaceuticals, Ltd., which was acquired by Cephalon) FDA approved Oct 2012 for treating adults with CML whose disease is resistant to or who cannot tolerate other FDA-approved drugs for CML	Allogeneic stem cell transplantation Ponatinib	Increased overall survival Increased progression-free survival Improved quality of life
Onartuzumab (MetMAb) for treatment of advanced nonsmall cell lung cancer	Patients with Met-positive advanced (stage IIIb/IV) nonsmall cell lung cancer (NSCLC) that has progressed after 1st-line systemic chemotherapy	Patients with advanced/metastatic NSCLC that has progressed after 1st-line therapy have a 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 epidermal growth factor receptor (EGFR) inhibition. Onartuzumab (MetMAb) is a 1-armed monoclonal antibody that blocks ligand-mediated activation of the MET receptor tyrosine kinase. In a late-stage trial, it is being studied in combination with the EGFR inhibitor erlotinib in the 2nd-line setting. Earlier stage trials are investigating this agent as part of combination therapy with bevacizumab and systemic chemotherapy. Ornatuzumab is administered at 15mg/kg, intravenously, on day 1 of each 3-week cycle. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trial ongoing in combination with erlotinib; earlier stage trials ongoing in combination with bevacizumab and/or systemic chemotherapy	Crizotinib Docetaxel Erlotinib monotherapy Pemetrexed Tivantinib (c-Met kinase inhibitor 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
Onartuzumab (MetMAb) for treatment of metastatic *HER2*-negative gastric cancer	Patients with locally advanced or metastatic gastric cancer that expresses high levels of MET and low levels of HER2	Patients with locally advanced or metastatic gastric cancer have a poor prognosis with current treatment options. MET is a receptor tyrosine kinase that can promote cell proliferation, survival, motility, and invasion. MET overexpression has been reported in gastric cancers and correlates with a poor prognosis. Onartuzumab is a monoclonal antibody that binds to the extracellular domain of MET. This binding may prevent receptor activation by the extracellular domain's cognate ligand (hepatocyte growth factor), potentially having an antineoplastic effect. Onartuzumab is administered intravenously (dosage not listed). In clinical trials it is being used to treat metastatic *HER2*-negative adenocarcinoma of the stomach or gastroesophageal junction in combination with a chemotherapy regimen consisting of oxaliplatin, folinic acid, and 5-fluorouracil (5-FU). F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trial ongoing	Various chemotherapy regimens, including 1 or more of the following: Capecitabine Carboplatin Cisplatin 5-Docetaxel Epirubicin Fluoropyrimidine 5-FU Irinotecan Oxaliplatin Paclitaxel	Increased overall survival Increased progression-free survival Improved quality of life
Oncolytic reovirus (Reolysin) for treatment of platinum-resistant head and neck cancer	Patients with recurrent or metastatic head and neck cancers	Advanced head and neck cancer has a poor prognosis and high recurrence rate, suggesting the need for novel treatment options. Reolysin® is an oncolytic reovirus being developed to treat various cancer and cell proliferative disorders. It replicates specifically in cells that have activated RAS, which may play a role in more than 2/3 of all cancers. In a phase III trial, Reolysin was administered to patients in the 2nd-line treatment setting following 1st-line treatment with a platinum-based chemotherapy. In this trial, Reolysin was administered in combination with paclitaxel and carboplatin. Oncolytics Biotech, Inc., Calgary, Alberta, Canada Phase III trial ongoing; top-line data reported in Dec 2012	Various combination or monotherapy regimens including: 5-fluorouracil Bleomycin Cetuximab Cisplatin Docetaxel Gemcitabine Ifosfamide Methotrexate Paclitaxel Vinorelbine	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
Ovarian tissue cryopreservation for fertility preservation in women undergoing gonadotoxic cancer treatment	Females undergoing gonadotoxic cancer treatment who wish to preserve fertility	As cancer treatments have improved resulting in long-term survival, procedures for maintaining long-term quality of life are of increasing interest. Females (children or adults) who have undergone systemic chemotherapy or whole-body radiation therapy especially may wish to preserve their ability to have children. A new option involves ovarian tissue cryopreservation. Prior to undergoing treatment, ovarian tissue is collected from the patient via a laparoscopic procedure requiring general anesthesia. Collected tissue is prepared to withstand the freezing process, and is then cryopreserved until completion of cancer treatment, when it is transplanted back into the patient. Various research institutions Case reports of successful pregnancies and births	Oocyte cryopreservation Ovarian suppression with gonadotropin releasing hormone analogs or antagonists	Successful pregnancy Live births
Palbociclib (cyclin-dependent kinase 4/6 inhibitor) for treatment of breast cancer	Patients in whom estrogen receptor-positive breast cancer has been diagnosed	Although endocrine therapies (e.g., estrogen receptor antagonists, aromatase inhibitors) are often effective in treating patients with estrogen receptor–positive breast cancer, the response duration is typically limited to about 1 year. Palbociclib is a dual inhibitor of cyclin-dependent kinase (CDK) 4 and CDK 6, 2 kinases involved in controlling cell cycle progression. CDK 4 and CDK 6 regulate a cell-cycle checkpoint controlling initiation of DNA synthesis. Therefore, their inhibition may limit tumor growth mediated by cell proliferation. Preclinical studies have demonstrated that estrogen receptor–positive breast cancer may be highly sensitive to CDK 4/6 inhibition and that this inhibition may be synergistic with endocrine therapies. The drug is being studied for use in combination with the aromatase inhibitor letrozole in the 1st-line setting for locally advanced or metastatic disease. In clinical trials, palbociclib has been administered in a once daily, oral dose of 2.5 mg. Pfizer, Inc., New York, NY Phase II/III trial ongoing; FDA granted breakthrough status	Anastrozole Fluoxymesterone Fulvestrant High-dose estrogen Letrozole Progestin Tamoxifen Toremifene	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
Pazopanib (Votrient) for preventing recurrence of ovarian cancer	Patients with stage II–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 1st-line treatment of cytoreduction and chemotherapy; however, a large number of these patients will experience disease recurrence. Therapies intended to prolong remission are needed. Pazopanib (Votrient™) is a tyrosine kinase inhibitor with activity against multiple kinases including vascular endothelial growth factor (VEGF) receptor 1 (VEGFR1), VEGFR2, VEGFR3, platelet-derived growth factor receptor-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 dosage of 800 mg, daily, for 24 months. GlaxoSmithKline, London, UK Phase III trial ongoing; topline data announced Jun 2013; survival data collection ongoing; FDA approved for renal cell carcinoma and soft tissue sarcoma	Bevacizumab as maintenance therapy after bevacizumab-containing treatment regimens Paclitaxel Watchful waiting	Increased overall survival Increased progression-free survival Improved quality of life
Pazopanib (Votrient) for treatment of soft tissue sarcomas	Patients with advanced soft tissue sarcoma (excluding gastrointestinal stromal tumors [GIST] and liposarcomas) who have undergone prior systemic chemotherapy	Until recently, doxorubicin was the only FDA-approved treatment option 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 (vascular endothelial growth factor receptor 1 [VEGFR1], VEGFR2, VEGFR3, platelet-derived growth factor receptor, 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. Pazopanib is administered at a dose of 800 mg, once daily; its indicated for treating patients who have received prior chemotherapy. GlaxoSmithKline, Middlesex, UK FDA approved Apr 2012 for treating soft tissue sarcoma in the 2nd-line setting	2nd-line treatments: Sorafenib (off label) Sunitinib (off label)	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 arginine deiminase (ADI-PEG 20) for treatment of hepatocellular carcinoma	Patients with advanced hepatocellular carcinoma (HCC) whose disease has failed to respond to 1 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. This agent is intended for use in the 2nd-line setting. It is administered at 18 mg/m2, by intramuscular injection, weekly. Polaris Pharmaceuticals, Inc., San Diego, CA Phase III trial initiated under FDA special protocol assessment; FDA granted orphan drug status	Locoregional therapy Sorafenib (if not used in 1st-line setting)	Increased overall survival Increased progression-free survival Improved quality of life
Peptide-cytokine complex (NGR-hTNF) for treatment of malignant pleural mesothelioma	Patients with malignant pleural mesothelioma who have undergone treatment with pemetrexed and cisplatin	NGR-hTNF (human tumor necrosis factor) is a peptide-cytokine complex; NGR peptide binds preferentially to tumor vasculature and TNF may induce an immune cell reaction/apoptosis, thereby destroying tumors. In clinical trials, this agent is administered at 0.8 mcg/m², intravenously, every 3 weeks until confirmed evidence of disease progression or unacceptable toxicity occurs. MolMed, S.p.A., Milan, Italy Phase III trial ongoing in 2nd-line setting; phase II trial ongoing in 1st-line setting; received patent from European Patent Office in Jun 2012	1st-line: Pemetrexed plus cisplatin 2nd-line: Single-agent chemotherapy (e.g., doxorubicin, gemcitabine, vinorelbine)	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
Pertuzumab (Perjeta) for treatment of metastatic breast cancer	Patients with metastatic HER2-positive breast cancer who are receiving 1st-line trastuzumab and docetaxel	No curative treatment for patients with metastatic breast cancer 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 purportedly functions 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 (Perjeta®) is a novel HER2-specific monoclonal antibody that binds to a different site on the HER2 extracellular domain; pertuzumab purportedly functions 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 approved for use in combination with trastuzumab for more comprehensive inhibition of HER2 activity. Pertuzumab is administered in an initial 840 mg dose, intravenously, then at a dose of 420 mg, intravenously, once every 3 weeks. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland FDA approved Jun 2012 for use in combination with trastuzumab and docetaxel for HER2-positive metastatic breast cancer; supplemental BLA submitted for neoadjuvant treatment, FDA granted priority review	Trastuzumab plus capecitabine, docetaxel, or vinorelbine Trastuzumab plus paclitaxel with or without carboplatin	Increased overall survival Increased progression-free survival Improved quality of life
Photodynamic therapy with Tookad photosensitive agent for treatment of 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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
PI3 kinase delta isoform inhibitor (idelalisib) for treatment of chronic or small lymphocytic leukemia	Patients in whom chronic lymphocytic leukemia or small lymphocytic leukemia has been diagnosed	Idelalisib inhibits a novel target: phosphoinositide 3-kinase (PI3K) delta, which is a kinase that promotes cell survival, division, and growth. The delta isoform of Class I PI3K is expressed only in blood cells, and targeted inhibition could treat blood-based cancers without side effects on nonblood tissues. The drug is under study in combination with rituximab or rituximab plus bendamustine for previously treated chronic or small lymphocytic leukemia. In ongoing trials, the drug is administered orally 150 mg twice daily. Gilead Sciences, Inc., Foster City, CA Phase III trials ongoing	Various combination chemotherapies including 1 or more of the following: Cyclophosphamide Doxorubicin Fludarabine Prednisolone Rituximab Vincristine	Increased overall survival Increased progression-free survival Improved quality of life
Plitidepsin (marine depsipeptide) for treatment of recurrent or treatment-refractory multiple myeloma	Patients with multiple myeloma who have undergone at least 3 treatments, including bortezomib- and lenalidomide-based regimens	Although treatments for multiple myeloma have improved, the median life expectancy for patients in whom multiple myeloma is diagnosed is only 5–7 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 mitogen-activated protein kinase. In a late-stage clinical trial for treating multiple myeloma, plitidepsin is being administered by infusion at a dose of 5 mg/m2 of body surface area in combination with orally administered dexamethasone. PharmaMar subsidiary of Grupo Zeltia, Madrid, Spain Phase III trial ongoing; FDA granted orphan drug status	Combination chemotherapy including 1 or more of the following: Bendamustine Bortezomib Cisplatin Cyclophosphamide (including high dose) Dexamethasone Etoposide Lenalidomide 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
Olaparib (poly ADP-ribose polymerase inhibitor) for treatment of ovarian cancer	Patients in whom BRCA-mutated 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 2nd 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 the 2nd-line setting for BRCA-mutated patients following treatment with a platinum-based chemotherapy. In clinical trials, olaparib is administered at a dosage of 300 mg, orally, twice daily. AstraZeneca, London, UK Phase III trial ongoing	Bevacizumab Monotherapy or combination therapy with one of the following: Docetaxel Etoposide Gemcitabine Paclitaxel Topotecan	Increased progression-free survival Increased overall survival Improved quality of life
Polydisperse oligonucleotide (defibrotide) for treatment of chemotherapy-induced severe veno-occlusive disease	Patients receiving chemotherapy in whom severe veno-occlusive disease has been diagnosed	Veno-occlusive disease is a side effect of the high-dose chemotherapy that is used as part of hematopoietic stem cell transplantation procedures. Severe veno-occlusive disease has a mortality rate approaching 100% with current treatments. Defibrotide is an orally administered, polydisperse oligonucleotide with local antithrombotic, anti-ischemic, and anti-inflammatory activities. Study investigators have suggested that the drug may increase survival of endothelial cells and preserve the function of microvasculature. In a phase III trial, the drug was administered at 25 mg/kg, intravenously, 4 times per day. Gentium S.p.A., Villa Guardia, Italy Phase III trial ongoing; FDA granted orphan drug and fast-track statuses; Gentium previously submitted new drug application in Jul 2011; FDA issued a refuse to file response and the company withdrew the application in Aug 2011, stating that it would work to address the issues and resubmit; several regulatory agencies abroad have also denied approval	Analgesia Diuresis Renal replacement therapy Transfusion	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
Pomalidomide (Pomalyst) for treatment-refractory multiple myeloma	Patients with treatment-resistant (i.e., lenalidomide and bortezomib) multiple myeloma	Treatments for multiple myeloma have improved, but the median life expectancy for patients in whom it is diagnosed is only 5–7 years. Additionally, as several newer treatments for multiple myeloma have moved to the 1st -line setting as combination therapies, additional salvage treatments are needed in cases in which the disease no longer responds to treatment. Pomalidomide (Pomalyst) is a novel thalidomide derivative that has modulatory effects on angiogenesis, inflammation, and immune cell costimulation. In clinical trials for treating multiple myeloma, pomalidomide is administered orally, at a daily dose of 4 mg, in combination with low-dose dexamethasone. Celgene Corp., Summit, NJ Phase III trial ongoing; in Feb 2013, pomalidomide received accelerated approval from FDA, which based its opinion on phase II data. Pomalidomide carries a boxed warning and Risk Evaluation and Mitigation Strategies certification will be required for prescribers.	Combination chemotherapy including 1 or more of the following: Bendamustine Bortezomib Cisplatin Cyclophosphamide (including high dose) Dexamethasone Doxorubicin Etoposide Thalidomide	Increased overall survival Increased progression-free survival Improved quality of life
Ponatinib (Iclusig) for treatment of chronic myelogenous leukemia or Philadelphia chromosome–positive acute lymphoblastic leukemia	Patients in whom chronic myelogenous leukemia (CML) or Philadelphia chromosome–positive negative acute lymphoblastic leukemia (ALL) has been diagnosed	Patients with treatment-refractory CML or ALL generally have a poor prognosis, rapidly progressing disease, and few treatment options. 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 disease is harder to treat). Ponatinib (Iclusig™) 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 orally, 45 mg, once daily. Ariad Pharmaceuticals, Inc., Cambridge, MA FDA granted accelerated approval in Dec 2012 for patients with CML or Philadelphia chromosome–positive ALL that is resistant or intolerant to available tyrosine kinase inhibitors; phase III trial in 1st-line treatment of CML ongoing	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
Primary care physician-administered colonoscopy (Endoscopy Training in Primary Care) for prevention of colorectal cancer	Patients eligible to receive colonoscopy	Research suggests that disparities exist in colorectal cancer (CRC) incidence and mortality for individuals who live in rural areas or otherwise medically underserved areas. This disparity may be attributable to the limited access that rural residents have to CRC prevention tools. To address this unmet need, researchers have begun investigating the feasibility and efficacy of training primary care physicians to perform colonoscopies in rural areas. According to its developers, the Endoscopy Training in Primary Care (ETPC) program involves the following: (1) an online didactic seminar, (2) an endoscopy simulator to provide the opportunity for basic and advanced skill acquisition, and (3) proctored endoscopy with an endoscopist. Colorado Area Health Education Center, Department of Family Medicine, University of Colorado, Denver Trials completed	Colonoscopy performed by gastrointestinal specialists	Earlier diagnosis of CRCIncreased screening rates
Prophage G-series therapeutic vaccines (HSPPC-96) for treatment of gliomas	Patients diagnosed with primary or recurrent gliomas, including glioblastoma multiforme (GBM)	Gliomas, which include GBM, can be very difficult to treat and are often associated with a poor patient prognosis. Prophage (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. Vaccination with these antigens are given to stimulate an immune response against residual cancer cells. Two version of the vaccine are in clinical trial testing; Prophage G-100 is under investigation in newly-diagnosed gliomas and Prophage G-200 is being studied for progressive or recurrent glioma. In clinical trials, the vaccines are delivered as weekly or biweekly intradermal injections as part of combination therapy with temozolomide or bevacizumab. Agenus, Inc., Lexington, MA, in collaboration with UCSF, San Francisco, CA and the National Cancer Institute, Bethesda, MD Phase I/II trials (in collaboration with UCSF) ongoing, no longer recruiting, in adults for newly-diagnosed and recurrent gliomas; ongoing phase II trial of combination therapy with bevacizumab for GBM (in collaboration with NCI); FDA granted orphan drug status	Adjuvant: Radiation therapy Temozolomide Recurrence: Bevacizumab Bevacizumab plus chemotherapy Combination PVC Cyclophosphamide Nitrosourea Platinum-based regimens 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
Prostate cancer antigen 3 (Progensa PCA3) assay to determine need for repeat prostate biopsy	Patients undergoing digital rectal examinations for prostate cancer screening	The assay is a urine test that is performed after a digital rectal examination; it detects a nonprotein coding messenger RNA, prostate cancer antigen 3, that is highly overexpressed in the "vast majority" of prostate cancers. Assay was developed as a test kit. The FDA indication approved in Feb 2012 is "for use in conjunction with other patient information to aid in the decision for repeat biopsy in men 50 years of age or older who have had 1 or more previous negative prostate biopsies and for whom a repeat biopsy would be recommended by a urologist based on the current standard of care, before consideration of the assay results. A negative Progensa PCA3 assay result is associated with a decreased likelihood of a positive biopsy. A prostate biopsy is required to diagnose cancer." Gen-Probe subsidiary of Hologic, Inc., Bedford, MA FDA approved Feb 2012; Conformité Européene (CE) marked in 2006	Digital rectal examination alone Prostate-specific antigen blood test screening	Increased sensitivity and specificity Improved predictive values Avoided unnecessary followup (i.e., biopsy)
ProstVac immune therapy for castration-resistant prostate cancer	Patients in whom asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer (CRPC) has been diagnosed	Men with progressive metastatic, CRPC often have a poor prognosis and few treatment options. No viral vector vaccine is approved. ProstVac® is a prime-boost immune therapy strategy using fowlpox and vaccinia viral vectors encoding prostate specific antigen and 3 immune costimulatory molecules; the patient's immune system is primed using the vaccinia virus followed by multiple fowlpox vector boosts. Given in 1 prime step and then weekly injections to generate an immune response. BN ImmunoTherapeutics unit of Bavarian Nordic A/S, Kvistgård, Denmark Phase III trial ongoing	Abiraterone Enzalutamide 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
Quizartinib (FLT3 kinase inhibitor) for treatment of acute myeloid leukemia bearing FLT3 mutations	Patients with treatment-refractory acute myeloid leukemia (AML) bearing an internal tandem duplication in the FLT3 gene (ITD-FLT3)	No FLT3 inhibitors are available for treating AML, and patients with recurrent or treatment-refractory AML have no effective options. About 30% of AML cases bear an activating mutation in the gene encoding the receptor tyrosine kinase FLT3, which causes constitutive activation of various cell proliferative and anti-apoptotic pathways. Patients whose disease harbors an activating FLT3 mutation have a worse prognosis than patients whose disease does not harbor a FLT3 mutation. Quizartinib is an orally administered selective inhibitor of FLT3 kinase activity that is currently under study as a treatment for AML. Ambit Biosciences, San Diego, CA Phase II trial ongoing; FDA granted orphan drug status in 2009 and fast-track status in 2010	Cladribine, cytarabine, and granulocyte colony stimulating factor (G-CSF) plus or minus mitoxantrone or idarubicin High dose cytarabine and anthracycline Fludarabine, cytarabine, and G-CSF plus or minus idarubicin Mitoxantrone, etoposide, and cytarabine	Increased progression-free survival Increased overall survival Improved quality of life
Radiofrequency ablation of liposomal-encapsulated doxorubicin (ThermoDox) for treatment of hepatocellular carcinoma	Patients in whom hepatocellular carcinoma (HCC) has been diagnosed	Patients with HCC that cannot be surgically resected have few treatment options and a poor prognosis. ThermoDox™ is a heat-labile liposomal encapsulation of the chemotherapeutic agent doxorubicin. When radiofrequency (RF) energy is applied to the target tissue following administration of ThermoDox, it induces local hyperthermia (39.5 to 42 oC) and targeted release of the cytotoxic agent. ThermoDox is being testing in patients with treatment-naïve HCC who are not eligible for surgical resection. Celsion Corp., New York, NY Phase III trial failed to meet primary endpoint of progression-free survival in Jan 2013; secondary survival analysis ongoing. Jun 2013, manufacturer reported potential benefit for large subgroup of patients with optimized RF ablation procedure time	RF tumor ablation Systemic chemotherapy Targeted immunotherapy (e.g., sorafenib) Transcatheter arterial chemoembolization	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 dichloride (Xofigo) 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. Radium-223 dichloride is a preparation of radium-223, an alpha particle–emitting isotope that has a natural affinity for bone. It 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. Radium-223 dichloride is administered at 50 kBq (1.35 microcurie)/kg body weight, at 4 week intervals for 6 total injections. Algeta ASA, Oslo, Norway, in collaboration with Bayer AG, Leverkusen, Germany In May 2013, FDA granted approval (after priority review) for treating bone metastases associated with advanced hormone-refractory metastatic prostate cancer; investigation in osteosarcoma and breast cancer with bone metastases ongoing	Standard therapy plus denosumab or cabozantinib (Cometriq™) Standard therapy with and without Radium-223 dichloride	Increased overall survival Increased progression-free survival Increased rate of alkaline phosphatase normalization Reduced pain from bone metastases Improved quality of life
Ramucirumab for the treatment of gastric cancer	Patients in whom metastatic gastric cancer has been diagnosed	Patients with gastric cancer that has progressed after 1st-line chemotherapy have a poor prognosis with median survival times of less than 1 year. Ramucirumab is a novel monoclonal antibody that binds to the extracellular domain of vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2), which is a receptor tyrosine kinase that acts as a central mediator of tumor angiogenesis. Available inhibitors of the VEGF pathway include a monoclonal antibody specific for VEGF and small-molecule inhibitors of the kinase activity of VEGFR2 (and other receptor tyrosine kinases). Therefore, ramucirumab represents a novel mechanism of action for inhibiting VEGF-pathway signaling. Treatment is intended for disease that has progressed after standard 1st-line platinum-based or fluoropyrimidine-based regimens. In clinical trials for gastric cancer, ramucirumab is intravenously administered at a dose of 8 mg/kg of body weight, once every 2 weeks. ImClone Systems subsidiary of Eli Lilly and Co., Indianapolis, IN Phase III trials ongoing; REGARD trial met primary endpoints; FDA granted fast-track status; in Q1 2013, Lilly announced a rolling submission for ramucirumab as monotherapy treatment in 2nd-line gastric cancer	Taxane (e.g., docetaxel, paclitaxel) monotherapy Various irinotecan-based single and 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
Ramucirumab for treatment of hepatocellular carcinoma	Patients with advanced stage hepatocellular carcinoma (HCC) whose disease is not amenable to locoregional therapy and has been previously treated with sorafenib	No consensus exists on treatment for HCC that has progressed after treatment with sorafenib, and these patients have a poor prognosis. Ramucirumab is a novel monoclonal antibody that binds to the extracellular domain of vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2), which is a receptor tyrosine kinase that acts as a central mediator of tumor angiogenesis. Available inhibitors of the VEGF pathway include a monoclonal antibody specific for VEGF and small-molecule inhibitors of the kinase activity of VEGFR2 (and other receptor tyrosine kinases). Therefore, ramucirumab represents a novel mechanism of action for inhibiting VEGF-pathway signaling. This agent is intended for 2nd-line treatment following 1st-line sorafenib therapy. In clinical trials for HCC, ramucirumab is administered intravenously, 8 mg/kg of body weight, once every 2 weeks. ImClone Systems subsidiary of Eli Lilly and Co., Indianapolis, IN Phase III trials ongoing	No consensus exists on treatment for this patient population	Increased overall survival Increased progression-free survival Improved quality of life
Ramucirumab for treatment of metastatic breast cancer	Patients with metastatic or nonresectable locally advanced HER2-negative breast cancer who have received no prior chemotherapy for metastatic disease	Patients with metastatic or nonresectable locally advanced HER2-negative breast cancer have a poor prognosis with current treatment options. Ramucirumab is a novel monoclonal antibody that binds to the extracellular domain of vascular endothelial growth factor (VEGF) receptor 2 (VEFGR2), which is a receptor tyrosine kinase that acts as a central mediator of tumor angiogenesis. Available inhibitors of the VEGF pathway include a monoclonal antibody specific for VEGF and small-molecule inhibitors of the kinase activity of VEGFR2 (and other receptor tyrosine kinases). Therefore, ramucirumab represents a novel mechanism of action for inhibiting VEGF-pathway signaling. Treatment is intended to be used in the 1st-line setting for metastatic or nonresectable disease in combination with docetaxel. In clinical trials for breast cancer, ramucirumab is administered intravenously, 10 mg/kg of body weight, once every 3 weeks. ImClone Systems subsidiary of Eli Lilly and Co., Indianapolis, IN Phase III trial ongoing, enrollment complete	Taxane-based (e.g., docetaxel, paclitaxel) therapy with or without capecitabine or gemcitabine or bevacizumab or anthracycline-based therapy	Increased overall survival Increased progression-free surviva Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ramucirumab for treatment of metastatic colorectal cancer	Patients in whom metastatic colorectal cancer (CRC) has been diagnosed	Current 2nd-line treatments for metastatic CRC are of limited efficacy, and the median overall survival of these patients is less than 1 year. Ramucirumab is a novel monoclonal antibody that binds to the extracellular domain of vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2), which is a receptor tyrosine kinase that acts as a central mediator of tumor angiogenesis. Available inhibitors of the VEGF pathway include a monoclonal antibody specific for VEGF and small-molecule inhibitors of the kinase activity of VEGFR2 (and other receptor tyrosine kinases). Therefore, ramucirumab represents a novel mechanism of action for inhibiting VEGF-pathway signaling. Treatment is intended for patients whose disease has progressed after standard 1st-line chemotherapy with bevacizumab, oxaliplatin, and a fluoropyrimidine. In clinical trials for gastric cancer, ramucirumab is intravenously administered at a dose of 8 mg/kg of body weight once every 2 weeks as an adjunct to the standard 2nd-line FOLFIRI (folinic acid [leucovorin], 5-fluorouracil, and irinotecan) regimen. ImClone Systems subsidiary of Eli Lilly and Co., Indianapolis, IN Phase III trial ongoing	Various FOLFIRI-based therapies with or without cetuximab or panitumumab	Increased overall survival Increased progression-free survival Improved quality of life
Ramucirumab for treatment of metastatic nonsmall cell lung cancer	Patients in whom metastatic nonsmall cell lung cancer (NSCLC) has been diagnosed	Patients with metastatic NSCLC whose disease has progressed after 1st-line chemotherapy have few treatment options and a median overall survival of less than 1 year. Ramucirumab is a novel monoclonal antibody that binds to the extracellular domain of vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2), which is a receptor tyrosine kinase that acts as a central mediator of tumor angiogenesis. Available inhibitors of the VEGF pathway include a monoclonal antibody specific for VEGF and small-molecule inhibitors of the kinase activity of VEGFR2 (and other receptor tyrosine kinases). Therefore, ramucirumab represents a novel mechanism of action for inhibiting VEGF-pathway signaling. Treatment is intended for patients whose disease has progressed after 1 round of platinum-based chemotherapy. In clinical trials for NSCLC, ramucirumab is intravenously administered at a dose of 10 mg/kg of body weight, once every 3 weeks as an adjunct to standard 2nd-line chemotherapy with docetaxel. ImClone Systems subsidiary of Eli Lilly and Co., Indianapolis, IN Phase III trials ongoing, primary completion Jan 2014	Crizotinib (if ALK+) Erlotinib Single agent chemotherapy (e.g., docetaxel, 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
Reconstructive laryngeal surgery after treatment of malignancies in the cricoid area	Patients undergoing reconstructive surgery after surgery for cancer in the cricoid cartilage area	Often, malignancies of the cricoid area (i.e., chondrosarcoma) require complete laryngectomy, forcing patients to communicate with voice prostheses or alternative electronic devices. A University of Michigan surgeon has created a surgical procedure that involves resecting the tumor and surrounding cricoid cartilage, harvesting the tip of the patient's shoulder blade (selected for its curvature and blood supply from surrounding muscle), reshaping the bone piece to match the shape of resected cartilage, and transplanting the portion of bone and muscle into the voice box. Dr. Douglas Chepeha, University of Michigan, Ann Arbor 1 case report	Laryngectomy	Preserved larynx and reconstructed cricoid Improved quality of life
Regorafenib (Stivarga) for treatment of gastrointestinal stromal tumors	Patients with advanced gastrointestinal stromal tumors (GIST) that has progressed after treatment with imatinib and sunitinib	Patients with GIST whose disease progresses after imatinib and sunitinib therapy have few treatment options and a poor prognosis with approximate progression-free survival of 100 days and overall survival of 300 days. Regorafenib (Stivarga®) is an inhibitor of multiple tyrosine kinases, including the pro-angiogenic kinases vascular endothelial growth factor receptor 2 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). For treating GIST, regorafenib is administered at a dose of 160 mg, orally, once daily for 3 weeks of each 4-week cycle. Bayer AG, Leverkusen, Germany Phase III trials ongoing; received FDA approval in Feb 2013	Sorafenib	Increased overall survival Increased progression-free survival Improved quality of life
Regorafenib (Stivarga) for treatment of hepatocellular carcinoma	Patients with unresectable hepatocellular carcinoma that has progressed after treatment with sorafenib	Patients with HCC that cannot be surgically resected have few treatment options and a poor prognosis; no 2nd-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). Regorafenib is administered at a daily dose of 160 mg, orally, for 3 weeks of every 4-week cycle. Bayer AG, Leverkusen, Germany Phase III trial ongoing; FDA approved for treating GIST and mCRC	Locoregional treatment	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 (Stivarga) for treatment of metastatic colorectal cancer	Patients in whom metastatic colorectal cancer (mCRC) has been diagnosed	Many treatment options are available for 1st-line treatment of mCRC, but 5-year survival rates are only about 25%. No multikinase inhibitors have been approved for use in metastatic CRC. Regorafenib (Stivarga®) inhibits multiple tyrosine kinases, including the pro-angiogenic kinases vascular endothelial growth factor receptor 2 and TIE-2 (as well as RAF, RET, and KIT); inhibiting both primary angiogenic kinase pathways is a novel combination in multikinase inhibitor drugs (e.g., sunitinib). Regorafenib is indicated for patients who were previously treated with fluoropyrimidine, oxaliplatin, and irinotecan. It is administered at a dose of 160 mg, orally, once daily for 3 weeks of each 4-week cycle. Bayer AG, Leverkusen, Germany FDA approved for treatment of mCRC in Sept 2012	1st-line therapy comparators include: FOLFOX (folinic acid [leucovorin], 5-fluorouracil [5-FU], oxaliplatin) alone or with targeted therapy (e.g., bevacizumab, cetuximab, panitumumab) Other cytotoxic chemotherapy regimens plus or minus targeted therapy (e.g., CapeOX, FOLFIRI, [leucovorin, 5-FU, and irinotecan], 5-FU/leucovorin, capecitabine, FOLFOXIRI [FOLFIRI plus oxaliplatin])	Increased overall survival Increased progression-free survival Improved quality of life
Remestemcel-L (Prochymal) for treatment of acute graft-versus-host disease	Pediatric patients with treatment-refractory, acute graft-versus-host disease (GVHD)	GVHD is a relatively rare condition that most often occurs when donor cells in an allogeneic hematopoietic stem cell transplant mount an immune response against recipient tissues. Patients with acute GVHD typically exhibit damage to the skin, liver, and gastrointestinal tract, and GVHD is lethal in up to 80% of patients with severe forms of the disease. Remestemcel-L (Prochymal®) is an off-the-shelf preparation of mesenchymal stem cells expanded from allogeneic donors. Mesenchymal stem cells are purported to have immunomodulatory effects that may downregulate the antirecipient immune response that underlies GVHD. In clinical trials, remestemcel-L was administered by intravenous injection, twice weekly, for 4 weeks. Osiris Therapeutics, Inc., Columbia, MD Phase III trials complete; FDA granted orphan drug and fast-track status; available under expanded access program since 2008; Health Canada approved 2012	Anti-thymocyte globulin Corticosteroids Methotrexate and cyclosporine Mycophenolate mofetil Other immunosuppressants Photopheresis	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
Rigosertib (Estybon) for treatment of myelodysplastic syndrome	Patients with azacitidine- or decitabine-refractory myelodysplastic syndrome with excess blasts	Patients with myelodysplastic syndrome with excess blasts that has not responded to azacitidine or decitabine treatment have a poor prognosis and no standard treatment options. Rigosertib (Estybon®) is a small-molecule, multikinase inhibitor with activity against both the alpha and beta isoforms of the phosphoinositide 3 kinase (PI3K) and pololike kinase 1 (PLK1). Inhibition of PI3K may disrupt cell signaling that promotes cell growth and survival, and inhibition of PLK1 may disrupt mitosis, leading to cell-cycle arrest. In clinical trials, rigosertib is being administered as a monotherapy in a 72-hour continuous intravenous infusion. Onconova Therapeutics®, Inc., Newtown, PA Phase III trial ongoing	Hematopoietic stem cell transplant Immunosuppressive therapy (e.g., antithymocyte globulin plus or minus cyclosporine)	Increased overall survival Increased progression-free survival Improved quality of life
Rilotumumab (anti-hepatocyte growth factor) for treatment of gastric cancer	Patients with locally advanced or metastatic gastric cancer that expresses high levels of MET and low levels of HER2	Patients with locally advanced or metastatic gastric cancer have a poor prognosis with current treatment options. MET is a receptor tyrosine kinase that can promote cell proliferation, survival, motility, and invasion. MET overexpression has been reported in gastric cancers and correlates with a poor prognosis. Rilotumumab is a monoclonal antibody that binds to the MET ligand hepatocyte growth factor (HGF). By neutralizing HGF, rilotumumab may inhibit MET activity, potentially having an antineoplastic effect. Rilotumumab is administered intravenously. In clinical trials it is being used in combination with a chemotherapy regimen consisting of epirubicin, cisplatin, and capecitabine. Amgen, Inc., Thousand Oaks, CA Phase III trial ongoing	Various chemotherapy regimens, including 1 or more of the following: Capecitabine Carboplatin Cisplatin Docetaxel Epirubicin Fluoropyrimidine 5-Flurouracil Irinotecan Oxaliplatin 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
Rindopepimut for treatment of glioblastoma multiforme	Patients with newly diagnosed glioblastoma multiforme (GBM) who have undergone primary surgical resection	GBM is difficult to treat and associated with a very poor patient prognosis. New therapies that improve survival and slow disease progression are needed. EGFRvIII is an oncogenic splice variant of the EGFR. This variant represents a potential target antigen for anticancer therapy. Rindopepimut is a peptide-based vaccine designed to stimulate an immune response to cells expressing the EGFRvIII variant. In clinical trials, rindopepimut is being administered in combination with the immune stimulant granulocyte macrophage colony-stimulating factor and standard maintenance chemotherapy (temozolomide). It is being tested in newly-diagnosed (phase III) and recurrent (phase II) GBM and is administered at a dose of 500 mcg rindopepimut/150 mcg of GM-CSF, via intradermal injection, biweekly during month 1, then monthly thereafter. Celldex Therapeutics, Inc., Needham, MA Phase III trial ongoing in 1st-line setting; phase II trial ongoing in recurrent GBM	Bevacizumab (under investigation) Temozolomide monotherapy	Increased overall survival Increased progression-free survival Improved quality of life
Rose Bengal (PV-10) for treatment of advanced melanoma	Patients in whom advanced or metastatic melanoma has been diagnosed	Patients with advanced melanoma have few treatment options and a poor prognosis. PV-10 is a solution of the fluorescein derivative Rose Bengal, which is administered by intralesion injection. Rose Bengal preferentially accumulates in cancer cells because of the increased lipid content of its cell membranes, which allows the drug to cross. Within the cells, Rose Bengal accumulates in lysosomes, triggering lysosomal release and cellular toxicity. Besides causing local tumor cell lysis, Rose Bengal has been associated with a bystander effect in which untreated lesions exhibit a response to treatment. This effect is thought to be because of uptake of tumor antigens by cells of the immune system after tumor lysis, leading to a systemic immune response. Provectus Pharmaceuticals, Knoxville, TN Phase II completed; Phase III trial special protocol assessment is being discussed with FDA; FDA granted orphan drug designation	Dacarbazine Granulocyte colony stimulating factor Interleukin-2 Ipilimumab Temozolomide 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
Ruxolitinib (Jakafi) for treatment of myelofibrosis	Patients who have myelofibrosis (primary myelofibrosis, post-polycythemia vera myelofibrosis, or post essential thrombocythemia myelofibrosis)	Ruxolitinib (Jakafi®) is a Janus kinase (JAK) inhibitor that inhibits the activity of both JAK 2 and JAK 1. Half of myelofibrosis cases bear an activating mutation in JAK 2; therefore, its inhibition is thought to be a key target. Ruxolitinib labeling indicates that the drug should be given as follows: At a starting dosage of 20 mg, twice daily, for patients with a platelet count greater than 200 × 10^9/L; at a dosage of 15 mg, twice daily, for patients with a platelet count between 100 × 10^9/L and 200 × 10^9/L; At a dosage of 5 mg, twice daily, for patients with a platelet count between 50 × 10^9/L and 100 × 10^9/L. As platelet counts allow, the dose may be increased up to 25 mg, twice daily, for patients with initial platelet counts greater than 100 × 10^9/L and up to 10 mg, twice daily, for patients with initial platelet counts between 50 × 10^9/L and 100 × 10^9/L. Incyte Corp., Wilmington, DE, in collaboration with Novartis International 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
Small-molecule drug conjugate (vintafolide) for treatment of platinum-resistant ovarian cancer	Patients with platinum-resistant ovarian cancer who have undergone 1 or 2 rounds of platinum-based chemotherapy	Patients in whom platinum-resistant ovarian cancer has been diagnosed have a poor prognosis and few treatment options. Vintafolide (EC145) is a novel, small-molecule drug conjugate that uses a peptide linker to couple a targeting ligand to a cytotoxic agent. In vintafolide, 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. In clinical trials, this agent is administered in combination with pegylated liposomal doxorubicin. Vintafolide is administered at a dose of 1 mg, intravenously, 5 days/week for the first 3 of each 4-week cycle, then at a maintenance dose of 2.5 mg, 3 days/week, during weeks 1 and 3 of each 4-week cycle. Endoctye, Inc., West Lafayette, IN, in collaboration with Merck & Co., Inc., Whitehouse Station, NJ Phase III trial ongoing	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
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 by targeting eukaryotic translation initiation factor 5A1; eIF5A1 functions as a shuttle protein, selectively translocating mRNAs from the nucleus to cytosolic ribosomes for translation. eIF5A1 exists in 2 forms: a pro-apoptotic form and an antiapoptotic form, which is generated by posttranslational modification. SNS01-T consists of 2 nucleic acid-based molecules: (1) a plasmid that drives expression of a pro-apoptotic form of eIF5A1 that has been modified to prevent its post-translational modification to the antiapoptotic form, and (2) an antisense molecule that inhibits expression of endogenous eIF5A1, which normally serves as the precursor to antiapoptotic eIF5A1. By altering the balance of pro-apoptotic and antiapoptotic eIF5A1, SNS01-T purportedly promotes cell death over cell growth and survival. In clinical trials, SNS01-T is administered by intravenous infusion, twice weekly. Senesco Technologies, Inc., Bridgewater, NJ Phase I/II trial ongoing; FDA granted orphan drug status	Various chemotherapeutic regimens, including 1 or more of the following: Bendamustine Bortezomib Cisplatin Cyclophosphamide Dexamethasone Etoposide Lenalidomide Liposomal doxorubicin Thalidomide	Increased overall survival Increased progression-free survival Improved quality of life
Sorafenib (Nexavar) for the treatment of differentiated thyroid cancer	Patients with radioactive iodine-refractory differentiated thyroid cancer	Radioactive iodine (RAI)-refractory thyroid cancer is difficult to treat and associated with poor prognoses, and affected patients have limited treatment options. Sorafenib is a multiple kinase inhibitor (tyrosine and Raf kinases) that targets the MAP kinase pathway to inhibit tumor cell proliferation and angiogenesis. Sorafenib is an oral medication approved for treating kidney and liver cancer; it is typically administered at a dosage of 400 mg, twice daily. Bayer AG, Leverkusen, Germany, and Onyx Pharmaceuticals, Inc., South San Francisco, CA Phase III trial ongoing; supplemental NDA submitted to FDA in Jul 2013	Ablation Chemotherapy Off-label sunitinib (trials ongoing) Radiation therapy Surgical intervention	Increased overall survival Increased progressi on-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
Specialized care model for adolescents and young adults with cancer	Adolescents and young adults with cancer	Adolescents and young adults undergoing treatment for cancer have unique care needs that often go unmet in traditional pediatric or adult cancer units. The Teenage Cancer Trust and Teen Cancer America work with hospitals to develop specialized cancer units and care programs that address the specific needs of this patient population. Program features include redesigned inpatient and outpatient facilities, provider training, clinical trial counseling/enrollment, and psychosocial support. Teen Cancer America and Ronald Reagan UCLA Medical Center, Los Angeles, CA 25 specialized teen cancer units are open in the United Kingdom; one U.S. center established with future sites in development	Adult cancer units Pediatric cancer units	Improved physical and emotional health outcomes Improved treatment adherence Improved quality of life
Spicamycin-derived, non-opioid-non-narcotic (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 bleeding associated with nonsteroidal anti-inflammatory 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. Although KRN5500 did not exhibit efficacy against leukemia, 1 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 IIa trial completed; FDA granted fast-track status in 2011; manufacturer submitted application for orphan drug status in Nov 2012	NSAIDs Opioid analgesics	Reduced pain Improved quality of life
Stool DNA molecular test (Cologuard) for colorectal cancer screening	All patients undergoing routine colorectal cancer (CRC) screening	A test that obviates the need for the bowel preparation required by current screening methods could improve adherence to recommended CRC screening guidelines. This genetic test (Cologuard™) screens DNA for genetic mutations and epigenetic modifications commonly found in CRCs; 4-gene plus 1 biomarker test performed on stool samples. This test kit is the next generation of the ColoSure™ test, which looked for epigenetic modification in only a single genetic locus. Exact Sciences Corp., Madison, WI 10,000-patient DeeP-C trial complete; company submitted premarket approval application to FDA Jun 2013	Colonoscopy Computed tomographic colonography Fecal occult blood testing Sigmoidoscopy	Increased 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
Tabalumab (anti-BAFF monoclonal antibody) for treatment of multiple myeloma	Patients in whom recurrent or refractory multiple myeloma has been diagnosed	Although treatments for multiple myeloma have improved, the median life expectancy for these patients is only 5–7 years. Tabalumab is a monoclonal antibody specific for the cytokine B-cell activating factor (BAFF). Researchers have observed elevated serum levels of BAFF in patients with MM, and BAFF is thought to stimulate multiple myeloma cell growth and promote multiple myeloma cell survival. Tabalumab is administered intravenously. In clinical trials, it is being administered 100 mg once intravenously over 30 minutes on day 1 every 21 days for 8 cycles in combination with dexamethasone and bortezomib. Eli Lilly and Co., Indianapolis, IN Phase II trial ongoing; FDA granted orphan drug status	Carfilzomib Pomalidomide	Increased overall survival Increased progression-free survival Improved quality of life
Talimogene laherparepvec 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. Talimogene laherparepvec (TVEC) granulocyte macrophage colony-stimulating factor (GM-CSF) is an oncolytic virus; the virus purportedly replicates only in tumor cells. OncoVex is engineered to lyse tumor cells and express tumor-specific antigens and GM-CSF, which help generate tumor-specific immune responses for additional benefit. In trials, it is administered up to 4 mL of 10^8 pfu/mL/per intratumoral injection. Amgen, Inc., Thousand Oaks, CA Phase III trial ongoing; manufacturer reported positive topline data in Mar 2013	Dacarbazine Dabrafenib (if BRAF-positive) Interleukin-2Ipilimumab Temozolomide Trametinib (if BRAF-positive) Vemurafenib (if BRAF-positive)	Increased overall survival Increased progression-free survival Improved quality of life
Tasquinimod for treatment of castration-resistant prostate cancer	Patients in whom asymptomatic or mildly symptomatic castration-resistant prostate cancer (CRPC) has been diagnosed	Median overall survival for patients with CRPC is only about 18 months. Advanced prostate tumors can become resistant to androgen-deprivation therapy; new treatments with novel mechanisms of action are needed. 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 at doses of 0.25, 0.5, or 1.0 mg/day. Active Biotech, AB, Lund, Sweden Phase III trial ongoing	Abiraterone Enzalutamide 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
Telotristat etiprate 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. In clinical trials, it is administered at a dose of 250 mg, orally, 3 times per day. Lexicon Pharmaceuticals, Inc., The Woodlands, TX Phase III trial ongoing; FDA granted orphan drug and fast-track statuses	Chemotherapy (e.g., capecitabine, dacarbazine, 5-fluorouracil, temozolomide) Interferon alpha Octreotide	Decreased rate of bowel movements Decreased 5-HIAA levels Decreased rate of flushing episodes Improved quality of life (e.g., less pain, discomfort)
Therapeutic melanoma antigen vaccine (POL-103A) to prevent melanoma recurrence	Patients at high risk of recurrence after surgical resection of stage IIB, IIC, or III melanoma	After surgical resection of a primary melanotic tumor, disease recurs in many patients, and few adjuvant treatments to prevent recurrence are available. POL-103A is a polyvalent vaccine that is generated by isolating peptides secreted by 3 human melanoma cell lines grown in culture. The vaccine is administered by intradermal injection as adjuvant therapy following surgical resection and radiation. Polynoma LLC subsidiary of CK Life Sciences Int'l (Holdings), Inc., Hong Kong Phase III trial ongoing	High-dose interferon	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 (GSK1572932A) for MAGE-A3-positive nonsmall cell lung cancer	Patients with nonsmall cell lung cancer (NSCLC) that expresses the melanoma antigenic epitope (MAGE)-A3 biomarker	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. 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. In a phase III trial, this immunotherapy was administered as an intramuscular injection in 13 doses. GlaxoSmithKline, Middlesex, UK Phase III trial ongoing in treatment-naïve patients, earlier phase trial ongoing in multiple treatment settings	Radiation therapy Surgery Various chemotherapies: 1st-line: Combination chemotherapy (e.g., pemetrexed plus cisplatin) Targeted immunotherapy (e.g., bevacizumab, cetuximab, erlotinib) 2nd-line: Erlotinib Single agent chemotherapy (e.g., docetaxel, pemetrexed)	Increased overall survival Increased progression-free survival Improved quality of life
Therapeutic vaccine (IMA901) for renal cell carcinoma	Patients in whom renal metastatic and/or locally advanced renal cell carcinoma (RCC) has been diagnosed	RCC is typically highly resistant to conventional chemotherapy/radiation therapy, and few treatment options exist for patients with RCC. IMA901 is a 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, and IMA901 purportedly has a stable, off-the-shelf formulation. This agent is intended for the 1st-line setting in advanced disease. The vaccine is administered intradermally, over the course of 4 months, with granulocyte macrophage colony-stimulating factor and sunitinib. Immatics Biotechnologies GmbH, Tübingen, Germany Phase III trial ongoing, enrollment completed Nov 2012; FDA granted orphan drug status	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
Tivantinib for treatment of hepatocellular carcinoma	Patients with unresectable hepatocellular carcinoma that has failed to respond to 1 prior sorafenib-containing therapy	Patients with HCC that cannot be surgically resected have few treatment options and a poor prognosis; no effective 2nd-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. In clinical trials, tivantinib is given at a dose of 240 mg, orally, twice daily. ArQule, Inc., Woburn, MA, in partnership with Daiichi Sankyo Co., Ltd., Tokyo, Japan Phase III trial ongoing	Locoregional therapy	Increased overall survival Increased progression-free survival Improved quality of life
Toll-like receptor 9 agonist (MGN1703) maintenance therapy after 1st-line therapy for metastatic colorectal cancer	Patients with metastatic colorectal cancer (CRC) whose disease has responded to 1st-line chemotherapy	Although many patients with metastatic CRC respond to 1st-line chemotherapy, disease ultimately progresses in the vast majority of patients. MGN1703 is under study as a maintenance therapy intended to prevent or delay disease recurrence. MGN1703 is a DNA molecule that is intended to function as an agonist of toll-like receptor 9 (TLR9). TLR9 signalling is a component of the innate immune system, and agonists of TLR9 purportedly promote immune system activation, possibly through dendritic cell maturation and/or differentiation of B cells into antibody-secreting plasma cells. Immune-response activation by MGN1703 could overcome immune tolerance to tumor-associated antigens, potentially leading to an anticancer immune response. MOLOGEN AG, Berlin, Germany Phase II trial completed; phase III trial in planning	Bevacizumab Chemotherapy-free interval Leucovorin plus 5-fluorouracil	Increased overall survival Increased progression-free survival mproved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Trametinib (Mekinist) for treatment of advanced melanoma with activating *BRAF* mutation	Patients with unresectable or metastatic melanoma that harbors an activating *BRAF* 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 *BRAF* mutations are driven in part by activation of the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (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. Trametinib is administered as an oral dose of 2mg, once daily. GlaxoSmithKline, Middlesex, UK Trametinib monotherapy FDA approved May 2013 in conjunction with a companion diagnostic test to detect *BRAF* ^{V600}E/K mutations (THxID BRAF, bioMerieux); phase III trial ongoing for combination therapy with the *BRAF* inhibitor dabrafenib; company announced Jun 2013 filing a supplemental NDA for dabrafenib plus trametinib combination therapy on the basis of phase I/II trial data	High dose interleukin-2 Dacarbazine Dabrafenib Ipilimumab Temozolomide Vemurafenib	Increased overall survival Increased progression-free survival Improved quality of life
Trebananib for treatment of ovarian, peritoneal, and fallopian tube cancers	Patients with epithelial ovarian, primary peritoneal, or fallopian tube cancer	Patients with treatment-resistant ovarian, peritoneal, or fallopian tube cancer have a poor prognosis, and more effective treatments are needed. Trebananib 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. It is intended to block activation of the TIE2 receptor by angiopoietin 1/2; the angiopoietin/TIE2 pathway acts in parallel with the vascular endothelial growth factor (VEGF)/VEGF receptor pathway to promote angiogenesis. The drug represents a novel 1st-in-class neutralizing inhibitor of angiopoietin 1/2. It is being tested in the 2nd-line setting following a platinum-based chemotherapy regimen and in the 1st-line setting as part of a combination therapy regimen to include with pegylated liposomal doxorubicin or paclitaxel and carboplatin. In clinical trials, trebananib is administered at a dose of 15 mg/kg, intravenously, once weekly. Amgen, Inc., Thousand Oaks, CA Phase III trials ongoing in 1st- and 2nd-line treatment settings; Jun 2013, manufacturer announced positive top-line data for TRINOVA-1 (2nd-line setting)	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
Tumor-treating fields therapy (NovoTTF-100L device) for nonsmall cell lung cancer	Patients in whom stage IIIb–IV nonsmall cell lung cancer has been diagnosed	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. The NovoTTF-100L system delivers tumor-treating fields (local alternating electrical fields) to the target tumor site. Electrical fields purportedly interfere with charged molecules that are involved cellular mitotic processes. In clinical trials, this therapy is delivered in conjunction with pemetrexed chemotherapy in the 2nd-line treatment setting. NovoCure Ltd., Haifa, Israel Phase I/II trial complete for treating primary lung tumors; phase II trial for treating brain metastases from NSCLC ongoing; company states it is preparing a phase III trial program to obtain FDA approval for investigational device exemption status to conduct the trial	2nd-line therapy: Erlotinib Radiation therapy Single agent chemotherapy (e.g., docetaxel, pemetrexed)	Increased overall survival Increased progression-free survival 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	Treatments that can provide better outcomes and reduced rates of recurrence are needed for patients with baldder cancer. Urocidin™ is a mycobacterial cell wall/DNA preparation proposed to create a localized immune response. The mechanism of action is unclear. In clinical trials, urocidin in administered to patients who did not respond to previous bacillus Calmette-Guérin (BCG)treatment. Urocidin is administered by transurethral catheter directly into the bladder at a dose of 8 mg, weekly. Bioniche Life Sciences, Inc., Belleville, Ontario, Canada; rights returned to Bioniche from Endo Pharmaceuticals in Apr 2013; Bioniche reached a licensing agreement with Paladin Labs, Inc., Montreal, Canada, to market and distribute the drug in Canada, South Africa, and Mexico Phase III trial completed; regulatory submission pending	Bacillus Calmette-Guérin treatment Cystectomy Intravesicular Chemotherapy Radiation therapy	Increased overall survival Increased progression-free survival Avoidance of cystectomy Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vemurafenib (Zelboraf) for treatment of metastatic melanoma	Patients who have metastatic melanoma with activated *BRAF* mutations	Patients with metastatic melanoma have a poor prognosis with current treatments yielding a 5-year survival rate of 15-20%. Roughly half of all melanomas are caused by the V600E mutation in the gene that encodes *BRAF*, a protein kinase that activates the extracellular signal-regulated kinase (ERK) signaling pathway. Vemurafenib (Zelboraf®) is a small-molecule, *BRAF* serine/threonine kinase inhibitor. The V600E mutation causes dysregulation of *BRAF* activity and overstimulation of ERK. This results in spontaneous generation of melanoma and the proliferation of malignant tissue. Vemurafenib is a potent inhibitor of *BRAF*; it shuts down the ERK signaling pathway and blocks proliferation of malignant cells carrying the $BRAF^{V600E}$ mutation but has no effect on tumor cells that lack the V600E mutation. It is administered orally. F. Hoffmann-La Roche, Ltd., Basel, SwitzerlandRoche Molecular Systems, Inc., Pleasanton, CA FDA-approved Aug 2011 as first *BRAF* inhibitor; approved in conjunction with companion diagnostic (cobas® 4800 $BRAF^{V600}$ Mutation Test, Roche)	Dacarbazine Dabrafenib High-dose interleukin-2 Ipilimumab Temozolomide Trametinib	Increased overall survival Increased progression-free survival Improved quality of life
Vismodegib (Erivedge) for treatment of basal cell carcinoma	Patients in whom advanced/metastatic basal cell carcinoma has been diagnosed	No systemic treatment was approved for treating basal cell carcinoma before the approval of vismodegib, and patients with advanced/metastatic disease not amenable to surgical resection had few treatment options. Vismodegib (Erivedge) inhibits the protein Smoothened, which is essential for transducing hedgehog signaling. Activation of the hedgehog signaling pathway, which is normally silenced after early development, has been implicated in the development and survival of a large percentage of basal cell carcinomas. It is an oral capsule administered once daily at 150 mg. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase II trials ongoing; FDA approved Jan 2012 based on phase II results for locally advanced and metastatic cancer; approval includes black box warning of potential risk of death or severe birth defects to unborn fetus	No other approved systemic treatment option available	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
Volasertib (polo-like kinase inhibitor) for treatment of acute myeloid leukemia	Elderly patients in whom acute myeloid leukemia (AML) has been diagnosed	Many patients with AML who are aged 65 years or older are unable to tolerate high-intensity induction chemotherapies; therefore, the disease remission rate in this patient population is relatively low. Volasertib inhibits pololike kinase (PLK), which plays a key role in cell cycle progression. Inhibition of PLK purportedly leads to cell cycle arrest and cell death in rapidly dividing cells. Volasertib is administered intravenously. In clinical trials, volasertib is being used in combination with low-dose cytarabine. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trial ongoing	5-azacytadine Decitabine Low-dose cytarabine	Increased overall survival Increased progression-free survival Improved quality of life
Vosaroxin (topoisomerase II inhibitor) for treatment of relapsed or refractory acute myeloid leukemia	Patients in whom acute myeloid leukemia (AML) 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 1st-in-class, anticancer quinolone derivative. During normal topoisomerase activity, the enzyme cleaves and then re-ligates double-strand breaks to maintain DNA topology during replication; vosaroxin purportedly intercalates into DNA and inhibits topoisomerase II activity, which 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. It is given as an intravenous infusion, 90 mg/m2 of body surface area for days 1 and 4 for induction and 70 mg/m2 for all other cycles. Sunesis Pharmaceuticals, Inc., South San Francisco, CA Phase III trial ongoing	Cladribine, cytarabine, and granulocyte colony-stimulating factor (GM-CSF) plus or minus mitoxantrone or idarubicin Clofarabine, cytarabine, and GM-CSF Etoposide and cytarabine plus or minus mitoxantrone Fludarabine, cytarabine, and GM-CSF plus or minus idarubicin High-dose cytarabine and GM-CSF plus or minus anthracycline	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
Zoptarelin doxorubicin 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. Zoptarelin doxorubicin (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, Zoptarelin doxorubicin 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/m2, every 3 weeks, up to six treatment cycles. AEterna Zentaris, Inc., Quebec, Quebec, Canada, in partnership with Ergomed Ltd., Frankfurt, Germany Phase III trial ongoing	Doxorubicin	Increased overall survival Increased progression-free survival Improved quality of life

Table 3. AHRQ Priority Condition: 03 Cardiovascular Disease: 45 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Abdominal stent graft system (Ovation) for treatment of abdominal aortic aneurysms with small vessel anatomy	Patients with abdominal aortic aneurysms (AAAs) who have small vessel anatomy	Endovascular repair of AAAs is a minimally invasive way to repair an aneurysm with lower perioperative risks and quicker recovery time. Patients with small vessel anatomy have not been eligible for endovascular repair of AAAs because of the relatively large size of available stent systems for endovascular repair. The Ovation abdominal stent graft system is intended to provide a minimally invasive alternative to open surgery for patients with AAAs and small vessel anatomy. TriVascular, Inc., Santa Rosa, CA FDA granted humanitarian device exemption in Nov 2011; FDA granted premarket approval Oct 2012	Open surgical Repair	Decreased perioperative risks Decreased mortality Faster recovery
Anacetrapib for lipid management in coronary artery disease	Patients in whom coronary artery disease has been diagnosed or who are at risk of developing the disease	Anacetrapib is a cholesterol ester transfer protein inhibitor intended to raise high-density lipoprotein by 100% and reduce low-density lipoprotein, improving lipid profile. Its precursor was torcetrapib; its development was stopped because of a 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	Lifestyle changes Pharmacotherapy (e.g., statins)	Reduced risk of heart attack Improved cardiovascular outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Angiogenic gene therapy (Ad5FGF-4, Generx) for treatment of chronic angina pectoris	Patients in whom coronary artery disease and stable angina has been diagnosed	Angina pectoris is a debilitating manifestation of coronary artery disease. According to 2007 American Heart Association statistics, more than 8.9 million people in the U.S. live with chronic angina pectoris, and angina is diagnosed in an estimated additional 400,000 Americans each year. Treatment strategies include surgical revascularization or pharmacologic agents. Many patients who are not suitable candidates for revascularization procedures experience chronic angina despite pharmacologic treatment. Ad5FGF-4 is a DNA-based angiogenic growth factor that purportedly increases myocardial blood flow through the development of collateral blood vessels around the heart to try to relieve angina symptoms. Ad5FGF-4 is administered through intracoronary infusion with percutaneous angioplasty and a novel adenovector delivery method that uses transient ischemia to enhance delivery of vector to the heart. Cardium Therapeutics, Inc., San Diego, CA Phase III trial using a new transient ischemia method for delivery is ongoing	Angioplasty Beta blockers Calcium channel blockers Coronary bypass surgery Coronary stents Long-acting nitrates Ranolazine	Decreased angina Fewer cardiovascular events Improved quality of life
Autologous bone marrow–derived 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 II trial completed	Percutaneous angioplasty and stenting Pharmacotherapy (e.g., cilostazol and pentoxifylline) Surgery	Tissue regeneration Improved circulation Reduced need for amputation Reduced morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Cardiac contractility modulation (Optimizer III Implantable Pulse Generator system) for treatment of heart failure	Patients in whom heart failure (HF) has been diagnosed	Optimizer III™ system is a device implant intended to treat patients who have chronic HF, are unable to achieve desired goals with optimal medical therapy, and are not candidates for cardiac resynchronization therapy. According to the manufacturer, "it is typically implanted in the right pectoral region and is connected to 3 standard pacemaker leads that are threaded through veins into the right side of the heart. One lead is used to sense atrial activity, and the other two are used to sense ventricular activity…." It purportedly delivers nonexcitatory electrical signals during the absolute refractory period (between beats) to purportedly produce more forceful contraction during the heartbeat. It is intended as an adjunct to optimal medical therapy. The system also uses the OMNI Programmer System, a portable programmer intended to enable medical personnel to tailor Optimizer signal parameters to individual patient needs. It uses a battery that can be charged in the patient's home. Impulse Dynamics, NV, Willemstad, Netherlands Antilles Phase II/III trial ongoing; Conformité Européene (CE) marked	Implanted pacemakers and/or defibrillators Pharmacotherapy (e.g., angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, digoxin, diuretics)	Symptom relief Improved 6-minute walk test Fewer hospitalizations Delayed progression of HF Delayed need for ventricular assist devices Improved quality of life
Cardiac resynchronization therapy for treatment of heart failure with atrioventricular block	Patients with atrioventricular block and heart failure	Atrioventricular block is typically treated with right ventricular pacing; however, ventricular dyssynchrony caused by right ventricular pacing is thought to adversely affect left ventricular function and geometry; therefore, it may present problems in patients with existing cardiac dysfunction. Cardiac resynchronization therapy (CRT) is an approved therapy for patients with heart failure who have a diminished ejection fraction and a prolonged QRS duration. Patients with atrioventricular block and heart failure often do not have the QRS indication for treatment with CRT, and thus CRT therapy is now being investigated as a new therapy for patients with atrioventricular block and heart failure. Medtronic, Inc., Minneapolis MN Clinical trial ongoing	Right ventricular pacing	Decreased heart failure-related hospitalizations Decreased mortality Improved functional status Improved quality of life

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 affects 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 radiofrequency 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	Pharmacotherapy (e.g., angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers) Renal artery stents	Controlled hypertension without medications Reduced rates of blindness, heart attacks, kidney failure, and stroke
Catheter-based ventricular restoration implant (Parachute) for treatment of heart failure	Patients in whom ischemic heart failure (HF) has been diagnosed	Left ventricular remodeling (enlargement) occurs in many patients who experience a myocardial infarction, resulting in decreased cardiac output, fatigue, and shortness of breath. The unaffected portion of the heart compensates for this output loss and becomes overloaded. Treatment options include medical management and surgical revision. This intervention has the potential to be the 1st minimally invasive, catheter-based treatment for ischemic HF. According to its manufacturer, the Parachute™ Ventricular Partitioning Device is an implant that is deployed in the left ventricle to partition the damaged portion of the heart from the functional heart segment, potentially decreasing the left ventricle's volume and restoring its geometry and function. CardioKinetix, Inc., Menlo Park, CA Phase III clinical trial ongoing	Heart transplant Pharmacotherapy (e.g., beta blockers) Surgical ventricular revision	Improved HF symptoms Increased cardiac output Increased survival Reduced left ventricular volume Reduced morbidity

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Early warning system (Health Recovery Solutions) to reduce hospital re-admission for heart failure	Patients in whom heart failure has been diagnosed	Approximately 1/3 of all patients hospitalized for heart failure are readmitted within 30 days of discharge. Although recommended practices exist for preventing hospital readmission in heart failure patients, implementation varies widely among hospitals, and fewer than 3% of all hospitals implement all the recommended practices. Health Recovery Solutions is a system that uses readmission risk algorithms integrated into electronic medical records, taking into account patient wellness and activity. The system uses a research-based platform that guides patients' behavior using software loaded on tablets given to them (PatientConnect). Additionally, the system makes patient clinical data instantly accessible for care providers through electronic medical record integration, Web monitoring portal, and smartphone applications (i.e., ClinicianConnect, CaregiverConnect), allowing care providers to take action when necessary to reinforce healthy lifestyles. Health Recovery Solutions, Inc., New York, NY Health Recovery Solutions is conducting pilot programs with providers	Current hospital discharge practices	Decreased hospital readmission 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
Electrical stimulation of carotid baroreceptors (Barostim neo System) for treatment of drug-resistant hypertension	Patients in whom severe, drug-resistant hypertension has been diagnosed	Baroreceptors in the aortic arch and the carotid sinuses are fibers that act as natural blood pressure sensors and control nervous system activity that affects the heart, kidneys, and peripheral blood vessels. When baroreceptors are stimulated by an increase in the body's blood pressure, sympathetic efferent nerves are inhibited. Signaling by sympathetic efferent nerves typically increases blood pressure through its effects on cardiac, renal, and vasomotor targets. Therefore, blocking sympathetic nervous system activity in response to elevated blood pressure, combined with a simultaneous increase in parasympathetic activity, can act as a negative-feedback loop to stabilize blood pressure by reducing heart rate and fluid volume, and dilating arteries. Researchers are investigating baroreceptor stimulation for treatment of hypertension that has not responded to medical therapy. The Neo-System uses a pacemaker-like implantable pulse generator (IPG), inserted subcutaneously near the clavicle, to continuously deliver electrical signals to baroreceptors in both the left and right carotid arteries in the neck, via two carotid sinus leads. Device voltage can be titrated by physicians, via an external programmer, until the patient reaches a predetermined hemodynamic endpoint or the maximum dose is reached. The Neo System has one carotid sinus lead and implantation requires only a unilateral incision. The company purports that this and the smaller lead design leads to a shorter procedure time and a greater patient safety profile than its first-generation Rheos system. CVRx, Inc., Minneapolis, MN Pivotal trials ongoing	Optimal medical management	Reduced hypertension Reduced stoke incidence Reduced cardiovascular events Improved quality of life
Evacetrapib (cholesteryl ester transfer protein inhibitor) for prevention of cardiovascular events	Patients in whom cardiovascular disease (CVD) has been diagnosed	Despite available treatments, CVD remains the leading cause of mortality worldwide. Evacetrapib is a cholesteryl ester transfer protein (CETP) inhibitor that is intended to raise functional high-density lipoprotein (HDL) by modulating CETP activity through a mechanism that purportedly differs from other CETP inhibitors in development. CETP, also known as LY2484595, is a plasma protein responsible for lipid transport. Eli Lilly and Co., Indianapolis, IN Phase III trial ongoing	Pharmacotherapy Sclerotherapy	Improved HDL profile Reduced cardiovascular morbidity and mortality Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Extra-aortic balloon counter-pulsation heart assist device (C-Pulse) for treatment of heart failure	Patients with New York Heart Association Class III or ambulatory Class IV heart failure (HF)	Available implanted devices for HF (e.g., intra-aortic balloon pump, left ventricular assist device) come into contact with the patient's blood, leading to a risk of stroke and blood clots, and are intended for use in patients with more advanced HF. The C-Pulse® heart-assist system consists of a mechanical balloon cuff that is wrapped around the outside of the aorta during a minimally invasive or full sternotomy procedure and is intended to reduce the workload of the left ventricle. The system's driver sits outside the body. According to the manufacturer, when the balloon is inflated, blood flow to the coronary arteries is increased, potentially providing additional oxygen to the heart. The company claims that during deflation, the workload required by the left ventricle is reduced. The company also states that the balloon counter-pulsation inflation and deflation is synchronized to the patient's electrocardiogram (similar to a pacemaker). Sunshine Heart, Inc., Eden Prairie, MN Feasibility trials completed; pivotal phase III trial initiated Nov 2012	Intra-aortic balloon pumps Left ventricular assist devices	Decreased morbidity Increased cardiac output Increased survival Reduced cardiac workload Reduced risk of stroke or thrombi
Fibrin-specific plasminogen activator (desmoteplase) for treatment of ischemic stroke	Patients in whom acute stroke has been diagnosed	Although stroke is a leading cause of death in the U.S., only a single drug, tissue plasminogen activator (tPA), is approved for neuroprotection. It is effective only when administered within a narrow window of symptom onset, and only a very small percentage of patients experiencing an acute stroke receive tPA because most do not present for treatment within the necessary time frame. Desmoteplase is a chemical derived from the saliva of vampire bats that catalyzes the conversion of plasminogen to plasmin, the enzyme responsible for breaking down fibrin blood clots. Structurally, the chemical is similar to tPA, but has much higher fibrin selectivity and, therefore, does not cause systemic plasminogen activation and fibrinogen depletion. H. Lundbeck a/s, Valby, Denmark One phase III trial complete; other phase III trials ongoing	tPA therapy	Increased blood flow to the brain Reversed damage Improved stroke-related outcomes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Freedom driver system for Total Artificial Heart as bridge to heart transplantation	Patients with nonreversible biventricular failure who are candidates for heart transplantation	The temporary Total Artificial Heart (TAH) functions in place of ventricles/valves by pumping blood to both the pulmonary and systemic circulations. 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, rather than remaining hospitalized. SynCardia Systems, Inc., Tucson, AZ TAH was FDA approved in 2004; Conformité Européene (CE) mark approval in Mar 2010 for Freedom portable driver; clinical trial (phase not indicated) ongoing for Freedom portable driver	TAH used with in-hospital driver	Restored mobility Possible recovery at home (reduction in hospitalization costs) Extended survival for patients awaiting heart transplantation
Human mononclonal antibody anti-PCSK9 (AMG 145) for treatment of hypercholesterolemia	Patients in whom hypercholesterolemia has been diagnosed.	Reductions in low-density lipoprotein cholesterol (LDL-C) levels are associated with decreased cardiovascular events. Statins are typically used to decrease cardiovascular risk in patients with high LDL-C levels; however, many patients are intolerant to statins or do not achieve a sufficient response. AMG 145 is a monoclonal antibody against proprotein convertase subtilisin/kexin type 9 (PCSK9), and purportedly decreases LDL-C levels by increasing the number of LDL receptors at the hepatocellular surface. In clinical trials AMG 145 has been given as subcutaneous injections in doses of 70, 105, or 140 mg every 2 weeks, or doses of 280, 350, or 420 mg every 4 weeks. Amgen, Inc., Thousand Oaks, CA Phase III clinical trial ongoing	Mipomersen (in development) MTP-I inhibitors (in development) Statins	Decreased cardiovascular events
Imatinib (Gleevec) for treatment of pulmonary artery hypertension	Patients in whom pulmonary artery 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 purportedly inhibits cellular processes that are responsible for uncontrolled growth of arterial smooth muscle cells. In clinical trials, imatinib has been administered orally, 200–400 mg, once daily. Novartis International AG, Basel, Switzerland 1 phase III trial completed; other phase III trials ongoing	Calcium channel blockers Endothelin receptor antagonists Phosphodiesterase type 5 inhibitors Prostanoids	Improved exercise capacity Reduced mortality Reduced hospitalization PAH

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Implantable cardiac monitor (AngelMed Guardian System) for detecting myocardial infarction	Patients at high risk of myocardial infarction (MI)	Patients who have had 1 MI are often at high risk of another MI. The AngelMed Guardian® system is an implantable cardiac device intended to detect rapid ST segment changes that might signal a major cardiac event. When it detects an ST segment change, the system is intended to alert patients so they can seek immediate medical care. The system alerts the patient through a series of vibrations, sounds, and visual warnings. Angel Medical Systems, Shrewsbury, NJ Phase II pivotal trial ongoing; Conformité Européene (CE) marked in Europe Sept 2010	Conventional, external MI detection technologies Patient report Routine physician follow up	Earlier detection of impending heart attack Prevention of heart damage Increased overall survival
Injectable biopolymer (Algisyl-LVR) for prevention or treatment of heart failure	Patients with an enlarged left ventricle (from mitral valve regurgitation, ischemia, dilated cardiomyopathy or other disorders)	No treatments are available to reverse the progression of heart failure (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. It is intended to thicken heart muscle wall, reduce chamber size, decrease local muscle wall stress, and allow for reshaping of dilated ventricle. The 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/III trial ongoing	Drug therapy to prevent HF	Increased left ejection fraction Reduced progression of HF Reduced regression of HF Improved cardiovascular outcomes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Lomitapide (Juxtapid) for treatment of homozygous familial hypercholesterolemia	Patients in whom homozygous familial hyper-cholesterolemia (HoFH) has been diagnosed	Outcomes with current medications 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) that, in turn, lowers plasma lipids. Lomitapide is intended to replace statins. It is given orally. Aegerion Pharmaceuticals, Inc., Cambridge, MA FDA approved Dec 2012 as “an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH)”	Extracorporeal apheresis Liver transplant Pharmacotherapy (e.g., statins)	Reduced low-density lipoprotein levels Improved cardiovascular outcomes Improved quality of life Improved long-term health outcomes
Noninvasive fractional flow reserve estimation using coronary computed tomographic angiography for diagnosis of coronary artery stenosis and virtual treatment planning	Patients in whom coronary artery stenosis is suspected.	Fractional flow reserve (FFR) measurement during invasive coronary angiography is used to identify coronary lesions that cause ischemia and aids in clinical decision making for coronary revascularization. No noninvasive methods exist that can determine the clinical significance of both a coronary lesion and stent placement at that lesion. FFR estimation using coronary computed tomography (CT) angiography is a noninvasive method that purportedly improves accuracy of diagnosing coronary lesions. Computer modeling associated with the FFR estimation technology aids in clinical decisionmaking for revascularization by predicting changes in FFR if a stent is placed across the diagnosed obstruction. HeartFlow, Inc., Redwood City, CA Phase IV trial ongoing; DISCOVER-FLOW study complete	FFR-guided coronary angiography	Improved coronary revascularization Decreased morbidity associated with invasive angiography

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label methotrexate for treatment of cardiovascular disease	Patients with type 2 diabetes or metabolic syndrome who have had a heart attack.	Inflammation is thought to play an important role in cardiovascular disease; however, it is not known if treating the inflammation will decrease the risk of cardiovascular disease. Conditions such as type 2 diabetes and metabolic syndrome are associated with an enhanced proinflammatory response, and patients with these conditions are at increased risk of experiencing myocardial infarctions and stroke. The anti-inflammatory agent methotrexate is being investigated as a drug to prevent stroke, myocardial infarction recurrence, and cardiovascular death in patients with type 2 diabetes or metabolic syndrome who have a history of myocardial infarction. In a new clinical trial, methotrexate will be administered orally at a dosage of 15–20 mg weekly. This study is funded by the National Heart Lung, and Blood Institute Phase III clinical trial registered with an estimated start date of Mar 2013	Anticoagulants Antidiabetes agents Antihypertensives Antiplatelets Cholesterol-lowering agents Lifestyle changes	Decreased risk of stroke Decreased risk of myocardial infarction recurrence Decreased risk of cardiovascular death Improved quality of life
Off-label minocycline as a neuroprotectant for ischemic or hemorrhagic stroke	Patients in whom ischemic or hemorrhagic stroke has been diagnosed	Thrombolysis using tPA during ischemic stroke has been associated with hemorrhage about 7% of the time, and continued bleeding is believed to contribute to poor outcomes in up to 40% of cases. Plasma levels of matrix metalloproteinase (MMP)-9 are known to be amplified by tissue plasminogen activator (tPA) and elevated MMP-9 levels are associated with neurological severity. MMP-9 also is known to predict the risk of tPA-related hemorrhage. Minocycline is known to be a potent MMP inhibitor; thus researchers are investigating whether concomitant administration of minocycline for treatment of stroke is neuroprotective. It is being researched for use in both ischemic and hemorrhagic stroke. Various research institutions Several trials completed and others ongoing	Standard of care	Reduced bleeding in stroke Improved neurologic outcomes after treatment for acute ischemic stroke

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label rituximab for treatment of systemic sclerosis-associated pulmonary artery hypertension	Patients in whom systemic sclerosis-associated pulmonary artery hypertension (SSc-PAH) has been diagnosed	1-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 treating 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 2 infusions, 1,000 mg each, 14 days apart. National Institute of Allergy and Infectious Diseases, Bethesda, MD (trial sponsor) Phase II trial ongoing	Calcium channel blockers Endothelin receptor antagonists Phosphodiesterase type 5 inhibitors Prostanoids	Improved exercise capacity Reduced mortality Reduced hospitalization
Oral sustained-release prostacyclin (treprostinil UT-15C) for treatment of pulmonary artery hypertension	Patients in whom pulmonary artery hypertension (PAH) has been diagnosed	PAH has no cure and can result in heart failure 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 1st 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. It is intended as an add-on therapy to current oral therapies. United Therapeutics Corp., Silver Spring, MD Phase III trials ongoing; Complete Response Letters declining United Therapeutics' new drug application were sent by FDA in Oct 2012 and Mar 2013. United Therapeutics plans to continue to pursue FDA approval	Calcium channel blockers Endothelin receptor antagonists Phosphodiesterase type 5 inhibitors Prostanoids	Improved exercise capacity Reduced mortality Reduced hospitalization
PCSK9 inhibitor (REGN727/SAR236553) for treatment of hypercholesterolemia	Patients in whom hypercholesterol-emia has been diagnosed	REGN727/SAR236553 represents a new mechanism of action for hypercholesterolemia treatment. The drug is a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor. PCSK9 is a protein involved in regulating circulating low-density lipoprotein (LDL) levels through degradation of the LDL receptor; therefore, pharmacologic inhibition of PCSK9 might decrease circulating LDL levels. REGN727/SAR236553 is administered subcutaneously. Sanofi, Paris, France Regeneron Pharmaceuticals, Inc., Tarrytown, NY Phase III trials ongoing	Pharmacotherapy (e.g., statins)	Improved lipid levels Reduced morbidity Reduced mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pediatric ventricular assist device (Excor) for pediatric end-stage heart failure	Pediatric patients in whom heart failure (HF) has been diagnosed who are in need of mechanical support as a bridge to cardiac transplantation	Adult heart-assist devices are too large to be used in children with end-stage HF. While awaiting transplant, the standard of care in this population is extracorporeal membrane oxygenation (ECMO), in which a pump circulates blood through an artificial lung back into the bloodstream. This technique is not approved and is associated with many limitations, including high incidence of complications when used for long-term support, high risk of stroke, and need for anticoagulation therapy. ECMO also requires immobilization of the patient, limiting rehabilitation. The Excor® Pediatric Ventricular Assist Device (VAD) is designed to support pediatric patients (newborns to teenagers) and to bridge patients awaiting heart transplantation for days to several months, until a donor heart becomes available. The device is a paracorporeal, pulsatile VAD, with blood pumps located outside the body and connected to the heart and blood vessels via cannulas. The device can be used for single- or double-ventricle assistance. Berlin Heart GmbH, Berlin, Germany FDA approved Dec 2011 under Humanitarian Device Exemption process	ECMO	Increased recovery of native heart (when used as destination therapy) Increased overall survival Reduced adverse events compared with ECMO
Percutaneous annuloplasty (Carillon Mitral Contour System) to treat functional mitral regurgitation	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 European clinical trials ongoing, but not FDA registered; Conformité Européene (CE) marked 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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Percutaneous left atrial appendage ligation using the Lariat Suture Delivery Device for prevention of atrial fibrillation-associated stroke	Patients in whom atrial fibrillation has been diagnosed	Atrial fibrillation has a prevalence of more than 2.7 million people in the U.S. and is associated with 15% to 25% of all strokes. Long-term anticoagulant therapy is the most effective stroke-prevention strategy in patients with atrial fibrillation; however, contraindications, bleeding complications, and patient adherence to therapy make this strategy difficult. Surgical ligation of the left atrial appendage (LAA) is performed in patients intolerant to anticoagulant therapy, but because of its invasive nature, many risks are associated with this procedure. The new percutaneous approach to ligating the LAA using the Lariat Suture Delivery Device may provide a minimally invasive option for stroke prevention in patients with atrial fibrillation. SentreHEART, Inc., Redwood City, CA FDA approved in 2009 for soft tissue ligation; an ongoing clinical trial is comparing the Lariat and Watchman devices	Amplatzer Cardiac Plug (in development)Anticoagulantsatriclip Left Atrial Appendage Exclusion SystemWatchman device (in development)	Decreased atrial fibrillation-associated stroke occurrence Decreased morbidity
Percutaneous left atrial appendage occlusion (Watchman) for prevention of atrial fibrillation-associated stroke	Patients with atrial fibrillation who are not good surgical candidates	Intended to block left atrial appendage opening and prevent clots from entering general circulation. Boston Scientific Corp., Natick, MA Phase III trial ongoing; Conformité Européene (CE) marked 2005; Commercialized outside the United States in 2009; CE mark indications expanded in 2012, to include patients in whom warfarin therapy is contraindicated	Long-term anticoagulation therapy	Reduction in stroke risk
Phospholipase A2 inhibitor (darapladib) for treatment of atherosclerosis	Patients with atherosclerosis who are at high risk of myocardial infarction	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 treating atherosclerosis. Darapladib is a lipoprotein-associated phospholipase A2 (LP-PLA2) inhibitor being investigated for treating 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	Pharmacotherapy (e.g., 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
Pneumatic abdominal aortic tourniquet (AAT) for treatment of inguinal hemorrhage on the battlefield	Soldiers on the battlefield with inguinal hemorrhage	For soldiers on the battlefield with inguinal bleeding, no products are available that can effectively stop the blood flow but also remain stable and in place during patient transport. The Institute of Surgical Research has identified this unmet need (uncompressible hemorrhage that is not treatable by a tourniquet in the leg, groin and inguinal region) as its priority for battlefield care because of the extremely high morbidity and mortality of this condition. The Abdominal Aortic Tourniquet (AAT™) is a pneumatic circumferential tourniquet that is placed around the body at the navel level, tightened, and inflated into the abdomen until it occludes the aorta and stops the bleeding. The product differs from available options (conventional tourniquets, knee pressing, clamps) because they aren't designed to tighten around a person's midsection, and the aortic artery is located under several inches of flesh, next to the spine. Compression Works, LLC., Birmingham, AL (manufacturer) Speer Operational Technologies, LLC, Greenville, SC (distributor) FDA granted 510(k) clearance Oct 2011, after expedited review	Clamps Conventional tourniquet Knee pressing	Improved bleeding control Reduced morbidity Reduced mortality
Point-of-care genetic testing to determine antiplatelet regimen after percutaneous coronary intervention	Patients undergoing percutaneous coronary intervention (PCI) who will be placed on dual antiplatelet (DAP) therapy	DAP therapy is the standard of care for patients who undergo PCI. The standard regimen consists of aspirin plus the P2Y12 inhibitor clopidogrel. However, a subset of patients who carry a loss-of-function allele of CYP2C19 (CYP2C19*2) are at increased risk of major adverse cardiovascular events when treated with this regimen. Investigators think the increase is caused by the failure of CYP2C19*2 to convert clopidogrel (Plavix®) to its active metabolite, lowering the therapeutic concentration of the drug. Prasugrel (Effient®) is an alternative P2Y12 inhibitor that is unaffected by the CYP2C19*2 polymorphism; however, its routine use is precluded by its association with an increased rate of bleeding. Therefore, prasugrel is typically reserved for patients who have been shown to harbor the CYP2C19*2 polymorphism. Because many of the adverse cardiovascular events after PCI occur within the 1st few hours of treatment, a need exists for highly accessible, rapid, genetic tests for the CYP2C19 genotype. The Spartan RX CYP2C19 test is a genetic test that could potentially be performed rapidly (about 1 hour), at the bedside, by clinical staff who lack formal clinical laboratory training. Spartan Bioscience, Inc., Ottawa, Ontario, Canada Phase IV trial registered Dec 2012; Conformité Européene (CE) marked; 510(k) premarket notification application submitted to the FDA in Jan 2013	No genetic testing Genetic testing performed in a clinical laboratory	Decreased cardiovascular death Decreased stent thrombosis Decreased nonfatal myocardial infarction Decreased high reactivity on DAP

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Recombinant human relaxin-2 (serelaxin) for treatment of acute heart failure	Patients in whom acute heart failure has been diagnosed.	About 80% of patients admitted to the hospital with acute heart failure experience dyspnea as a major symptom. In these patients, 50% do not experience relief 24 hours after treatment, and 25% still experience dyspnea at the time of discharge. New therapies for acute heart failure are needed for faster and more complete symptom resolution. Serelaxin is recombinant human relaxin-2, a naturally occurring vasoactive peptide hormone that regulates hemodynamic adaptations to pregnancy and is being investigated in the treatment of acute heart failure. In clinical trials, serelaxin (30 mcg/kg of body weight) was administered intravenously for 48 hours after acute heart failure diagnosis. Novartis International AG, Basel, Switzerland Phase II/III trial completed; received FDA breakthrough designation	Diuretics Vasodilators	Relief of dyspnea Decreased mortality
Renal denervation (Symplicity System) for treatment of heart failure	Patients in whom treatment-resistant heart failure (HF) and renal impairment have been diagnosed	Increased sympathetic nervous system (SNS) activity, especially in the heart and kidneys, is associated with reduced cardiac output and renal function. HF is primarily managed with pharmacotherapy, such as beta blockers, which address a patient's SNS. However, outcomes are still suboptimal, possibly because of beta blockers' incomplete blockage of the SNS. The Symplicity™ Renal Denervation System consists of a catheter and generator. A physician uses the system to endovascularly deliver low-power radiofrequency energy to the renal nerves, deactivating them. According to the manufacturer, this, in turn, reduces the activity of the SNS, potentially providing benefit to patients. Medtronic, Inc., Minneapolis, MN Phase IV trial (SYMPLICITY-HF) recruiting; the system is also in later-phase development for treatment-resistant hypertension	Pharmacotherapy (e.g., beta blockers)	Decreased HF-related morbidity Improved quality of life Increased survival Reduced SNS activity
Riociguat (BAY63-2521) for treatment of pulmonary artery hypertension	Patients in whom pulmonary artery hypertension (PAH) has been diagnosed	PAH has no cure and can result in heart failure and death. Riociguat purportedly stimulates the soluble guanylate cyclase pathway that is involved in nitric oxide signaling and vasodilation, which may relieve symptoms of PAH. In ongoing trials, riociguat is administered orally, 1.0, 1.5, 2.0, or 2.5 mg, 3 times daily. Bayer AG, Leverkusen, Germany 2 phase III trials completed; Feb 2013, manufacturer submitted for regulatory approval in the U.S. and EU	Calcium channel blockers Endothelin receptor antagonists Phosphodiesterase type 5 inhibitors Prostanoids	Improved exercise capacity Reduced mortality Reduced hospitalizations

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 artery hypertension	Patients in whom pulmonary artery hypertension (PAH) has been diagnosed	PAH has no cure and can result in heart failure and death. Selexipag (ACT-293987) is a 1st-in-class, selective prostacyclin (PGI2) receptor agonist; prostacyclin counteracts the vasoconstrictor and prothrombotic activity of endothelin. Selexipag is an orally available, long-acting, nonprostanoid prostacyclin receptor agonist that mimics the actions of endogenous prostacyclin and exerts vasodilating effects. Selexipag is administered as an oral tablet twice daily. Actelion Pharmaceuticals, Ltd., Allschwil, Switzerland Phase III trials ongoing	Calcium channel blockers Endothelin receptor antagonists Phosphodiesterase type 5 inhibitors Prostanoids	Improved exercise capacity Reduced mortality Reduced hospitalization
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 of symptom onset, and primary percutaneous coronary intervention (PCI) within 90 minutes, yet fewer than half of patients receive this care within the recommended time frame. Additionally, only 4% of patients who are transferred to a 2nd (PCI-capable) hospital are treated within the 90-minute time frame. Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments (RACE) Project is a 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). The goal is to improve both the rate and speed of STEMI care through 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 the following: educational symposia (on topics such as electrocardiogram [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 the following: leaving the patient on the original stretcher, creating system-compatible intravenous tubing and pumps, and eliminating the need for IV pumps (e.g., by administering intravenous bolus of unfractionated heparin). Sponsored by North Carolina Chapter of the American College of Cardiology Initial RACE project completed with data available; current phase of this project is called RACE CARS (Cardiac Arrest Resuscitation System) focusing on out-of-hospital cardiac arrest. The RACE project is being used as a national model for STEMI care, and a RACE Operations Manual is available on the program's Web site	Current STEMI practices (vary between hospitals)	Reduced door-in-to-door-out 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
Stem cell mobilization by granulocyte-colony stimulating factor for treatment of peripheral artery disease	Patients in whom peripheral artery disease with critical limb ischemia has been diagnosed.	Patients with critical limb ischemia are at high risk of amputation, and are limited in their ability to ambulate because of ulceration and pain. Small-vessel disease and other coexisting morbidities preclude many patients from surgical treatment, and noninvasive treatment options are needed. The use of granulocyte-colony stimulating factor (G-CSF) to mobilize angiogenic stem cells blood and promote angiogenesis in areas of ischemia is a new, noninvasive treatment option to improve blood flow in patients with critical limb ischemia. In an ongoing clinical trial, G-CSF is being injected subcutaneously at a dosage of 5 mcg/kg/day for 10 days. Sponsored by Washington University School of Medicine, St. Louis, MO Phase III clinical trial completed	Angioplasty with stent placement Bypass surgery Percutaneous transluminal angioplasty	Improved blood flow Improved ambulation Decreased ulceration Decreased pain Improved quality of life
Subcutaneous implantable cardioverter defibrillator (S-ICD System) for treatment of cardiomyopathy	Patients with cardiomyopathy who are at risk of sudden cardiac arrest	This subcutaneous implantable cardioverter defibrillator's (S-ICD®) wires do not connect to the heart and reduces risk of wires bending and causing unnecessary shocks; no imaging equipment required for placement. Boston Scientific Corp., Natick, MA (acquired developer Cameron Health Jun 2012) FDA approved Sept 2012 to provide defibrillation therapy for treating life-threatening ventricular tachyarrhythmias in patients who have no symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that can be terminated with antitachycardia pacing. Conformité Européene (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

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 (AS) has been diagnosed	AS occurs in about 4% to 5% of people aged 75 years or older, and an estimated 300,000 people have the condition worldwide. Causes of severe AS include buildup of calcium deposits on the aortic valve, prior radiation therapy, certain medications, and a history of rheumatic fever. An estimated 30% of all patients with symptomatic severe AS are not suitable candidates for valve implantation performed as an open-heart surgery procedure. The transcatheter aortic valve (CoreValve®) implantation 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 Phase III trials ongoing; Conformité Européene (CE) marked in 2007; available outside U.S. in 34 countries	Open surgery Optimal medical management Other transcatheter aortic valves	Improved cardiac function Increased survival Improved quality of life
Transcatheter aortic valve (Sapien) implantation for treatment of severe aortic stenosis	Patients with severe calcific aortic stenosis (AS) who are considered to be high-risk or nonoperable for conventional open-heart valve replacement surgery	AS occurs in about 4% to 5% of people aged 75 years or older, and an estimated 300,000 people have the condition worldwide. Causes of severe AS include buildup of calcium deposits on the aortic valve, prior radiation therapy, certain medications, and a history of rheumatic fever. An estimated 30% of all patients with symptomatic severe AS are not suitable candidates for valve implantation performed as an open-heart surgery procedure. 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 a severely stenotic aortic valve. Edwards Lifesciences Corp., Irvine, CA FDA approved Nov 2011 for “transfemoral delivery in patients with severe symptomatic native aortic valve stenosis who have been determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis. In Oct 2012, approval expanded to include patients with symptomatic severe aortic stenosis who are at high operative risk. A next-generation transcatheter aortic valve, Sapient XT, is in phase III clinical trials for patients who are determined to be inoperable or who are at high risk of operative mortality.	Open surgery Optimal medical management Other transcatheter aortic valves	Accurate valve replacemen tAvoided open surgery Decreased rehospitalization for heart failure Decreased mortality Improved quality of life

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 with degenerative mitral valve disease with prolapse who are not good candidates for open surgical repair	Mitral regurgitation can require invasive surgery when it is severe. Some patients are not candidates for open surgery and could benefit from a minimally invasive option. The MitraClip® purportedly provides a minimally invasive transcatheter approach that requires a transseptal puncture to access the left heart chambers. In lieu of sutures, a flexible metal clip covered in polyester fabric (MitraClip) is used. The device is intended for patients whose valve disease originates mainly from the center of the valve. Abbott Laboratories, Abbott Park, IL Phase III trial ongoing; Conformité Européene (CE) marked in 2008; FDA advisory committee voted Mar 2013 to recommend approval.	Open surgical mitral valve repair Pharmacotherapy	Decreased cost of HF complications Improved quality of life for patients who are not good surgical candidates Reduced mitral regurgitation Slowed disease progression
Terguride (serotonin receptor antagonist) 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. Terguride is an oral antagonist of the 5-HT2B and 5-HT2A (serotonin) receptors. Serotonin purportedly stimulates proliferation of smooth muscle cells in the pulmonary artery, and can induce fibrosis in pulmonary arteries, which can lead narrowing. By inhibiting the activity of serotonin on pulmonary arteries, terguride could improve the signs and symptoms of PAH. Administered orally. Pfizer, Inc., New York, NY Phase II trial completed. FDA granted orphan drug status for treatment of PAH	Calcium channel blockers Endothelin receptor antagonists Phosphodiesterase type 5 inhibitors Prostanoids	Improved exercise capacity Reduced mortality Reduced hospitalization

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ultrasound (ClotBust-ER) for treatment of acute ischemic stroke	Patients in whom acute ischemic stroke has been diagnosed	Transcranial ultrasound is a new treatment for ischemic stroke. However, technical challenges are associated with administration of transcranial ultrasound, and sonographers capable of detecting occluded cerebral artery segments are available only in specialized stroke centers or emergency departments (EDs). An unmet need exists to extend this therapy to smaller EDs. ClotBust™-ER is an ultrasound device that employs multiple transducers operating at 2 MHz, and it is intended to deliver therapeutic ultrasound energy to the vessel occlusion in the brain to treat ischemic stroke in patients eligible for intravenous thrombolytic therapy. The system includes multiple ultrasound transducers mounted on an adjustable head frame to administer therapeutic ultrasound in the principal regions in which the majority of vessel occlusions in the brain occur. Because the transducers self-align based on anthropometric landmarks, they do not need to be aimed by a trained sonographer. Cerevast Therapeutics, Inc., Redmond, WA Phase I/II trial completed; phase III trial registered, but not yet recruiting	Sonographer-administered ultrasound Tissue plasminogen activator therapy	Improved clot lysis Reduced stroke-related morbidity and mortality
Vagus nerve stimulation (CardioFit) for treatment of heart failure	Patients in whom severe congestive heart failure (HF) has been diagnosed	CardioFit® vagus nerve stimulation is an implantable device intended to improve heart-pumping capacity in patients with severe congestive HF. The system is intended to stimulate the vagus nerve, which purportedly controls parasympathetic innervation of the heart. The company purports that stimulation will stimulate the parasympathetic nervous system, potentially lowering the heart rate, lessening the heart's workload, and alleviating heart failure symptoms. The system consists of a stimulator that is implanted subcutaneously in the right subclavicular region (similar to a pacemaker); a sensing lead, which is passed through a vein into the right ventricle where it monitors heart activity and can halt stimulation as needed; and a stimulation lead, placed around the right vagus nerve about 2–3 cm below the carotid artery bifurcation. The company states that the stimulator is wirelessly programmed by the clinician The manufacturer states that the procedure can be conducted using either local or general anesthesia. BioControl Medical, Yehud, Israel Phase III trial ongoing	Heart transplantation Minimally invasive heart surgery Pharmacotherapy (e.g., angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta blockers, digoxin, diuretics) Ventricular assist devices	Improved left ventricular ejection fraction Improved 6-minute walk test Reduced need for medication Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Wireless monitoring system (Champion) for management of heart failure	Patients in whom moderately severe heart failure (HF) has been diagnosed	In hospitalized patients, catheters placed temporarily within the heart to monitor left atrial pressure are the gold standard for tracking blood movement (hemodynamics) and worsening HF; however, no devices are available for monitoring ambulatory patients. About 1/3 of patients with HF who have been discharged from the hospital are readmitted within 30 days, usually for worsening signs and symptoms of congestion. This congestion is caused by increases in intracardiac and pulmonary artery pressures, which are apparent several days to weeks before the onset of worsening signs, symptoms, and hospital admission. Thus, researchers suggest, monitoring these pressures might reduce the risk of readmission to hospital. The Champion device is a self-contained, paper clip–sized device placed in the pulmonary artery during a catheter-based procedure. A patient holds the external electronics module over the chest to wirelessly power the sensor and collect pressure data using radiofrequency energy. The handheld unit then transmits data to the CardioMEMS Champion Web site, which the physician monitors. This device may give clinicians more timely access to changes in symptoms and physiologic parameters, allowing them to quickly adjust medications and potentially reduce HF-related hospitalizations. This would be the 1st FDA-approved, permanent monitor implant for this indication. CardioMEMS, Inc., Atlanta, GA Premarket approval application submitted to FDA; Dec 2011 advisory panel voted 6-4 to not recommend approval because of potential bias in the trial design; company is deciding next steps.	Weight monitoring (for fluid retention) Symptom monitoring	Improved clinician access to changes in patient symptoms Earlier medical intervention Reduced HF-related hospitalizations Improved morbidity and mortality

Table 4. AHRQ Priority Condition: 04 Dementia (including Alzheimer's: 13 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Beta-amyloid precursor protein site cleaving enzyme inhibitor (MK-8931) for treatment of Alzheimer's disease	Patient in whom Alzheimer's disease (AD) has been diagnosed.	No approved disease-modifying agents are available for treating AD; available therapy options are limited to symptom management. MK-8931 is an oral beta-amyloid precursor protein site cleaving enzyme (BACE) inhibitor that is being investigated for the treatment of AD. The company states that the drug is intended to exert its effects by inhibiting BACE, an enzyme that is known to play a role in the initiation of synthesis of amyloid beta peptide. Because abnormal accumulation of amyloid beta peptide is thought to play a role in the progression of AD, the company states that this agent may have the potential to improve outcomes in this condition. Merck & Co., Inc., Whitehouse Station, NJ Phase II/III trial ongoing	Non-disease modifying pharmacotherapy (e.g., donepezil, galantamine, memantine, rivastigmine)	Reduced amyloid beta load in brain Regression or slowing of disease progression Reduced morbidity and mortality Improved quality of life
Deep brain stimulation for treatment of Alzheimer's disease	Patients in whom Alzheimer's disease (AD) has been diagnosed	The currently approved therapies for AD are unable to modify disease progression and have a minimal impact on symptoms. Therapeutic options are limited in efficacy. Deep brain stimulation (DBS) involves implanting a battery-operated neurostimulator in the brain to deliver electrical stimulation to targeted areas that moderate neural activity in the memory circuit, including the entorhinal and hippocampal areas. Researchers have suggested that continuous stimulation in these areas might reverse impaired glucose utilization in the temporal and parietal lobes, which some researchers think to be an issue in Alzheimer's disease. Johns Hopkins University School of Medicine, Baltimore, MD; University of Toronto, Canada; University of Pennsylvania, Philadelphia; University of Florida, Gainesville; and Banner Health System, Phoenix, AZ Pilot trial completed (Canada)	Behavior therapy Nutrition therapy Pharmacotherapy (i.e., Donepezil, memantine, rivastigmine)	Delayed progression to AD 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
FDDNP-positron emission tomography for diagnosis of chronic traumatic encephalopathy	Patients at risk of chronic traumatic encephalopathy (CTE)	An estimated 1.6 to 3.8 million repetitive, mild traumatic brain injuries occur in contact sports each year. CTE is a progressive neurodegenerative disease seen most often in athletes with a history of repetitive brain trauma. It can lead to dementia, memory loss, anger, confusion, and depression. At this time, the disease is diagnosed only after evaluation of brain tissue posthumously, with evidence of tissue degeneration and elevation of tau protein. Researchers recently studied positron emission tomography (PET) imaging with 2-(1-{6-[(2-[fluorine-18]fluoroethyl)(methyl)amino]-2-naphthyl}-ethylidene)malononitrile (FDDNP), a radiotracer that binds to tau protein and amyloid deposits for its usefulness in locating these tau protein deposits in the brain's subcortical region and in the amygdala. Compared with tau protein deposits in control patients, the imaging revealed tau protein deposits in these regions in all of the participating 5 retired National Football League players. University of California, Los Angeles Unphased trial completed	Posthumous diagnosis	Improved treatment protocol Reduced mild cognitive impairment and other CTE symptoms Improved quality of life
Florbetapir F18 positron emission tomography imaging agent (Amyvid) for detecting beta-amyloid plaques	Patients suspected of having beta amyloid–associated disease	No definitive method exists for diagnosing AD in a living person. Despite the lack of effective AD treatment, an unmet need exists for diagnostic/screening tools that can detect the condition before significant loss of memory, cognition, and activities of daily living occur. Diagnosis is made on the basis of clinical signs and symptoms, sometimes aided by positron emission tomography (PET) using a contrast agent. Florbetapir F18 (Amyvid™) is a radiopharmaceutical that binds specifically to beta amyloid and is visualized by PET imaging. Contrast agent would be indicated for visualization of beta-amyloid aggregates; a negative result could help to rule out presence of pathologically relevant levels of beta-amyloid plaques. Avid Radiopharmaceuticals subsidiary of Eli Lilly and Co., Indianapolis, IN FDA approved Apr 2012 for detecting beta-amyloid plaques	Blood tests for AD biomarkers Cerebrospinal fluid tests for AD biomarkers Neuropsychological test battery Positron emission tomography scans with beta amyloid–binding contrast agents	Increased sensitivity and specificity of beta-amyloid plaque detection

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Flutemetamol positron emission tomography imaging agent for detecting beta-amyloid plaques	Patients in whom Alzheimer's disease (AD) is suspected	No definitive method exists for diagnosing AD in a living person. Despite the lack of effective AD treatment, an unmet need exists for diagnostic/screening tools that can detect the condition before significant loss of memory, cognition, and activities of daily living occur. Diagnosis is made on the basis of clinical signs and symptoms, sometimes aided by positron emission tomography (PET) using a contrast agent. Flutemetamol is a PET imaging agent intended to detect normal or raised beta-amyloid plaques in the brain to confirm a diagnosis of AD. General Electric Co., Fairfield, CT Phase III trials completed and met primary endpoints; Jan 2013, FDA accepted new drug application submission	Blood tests for AD biomarkers Cerebrospinal fluid tests for AD biomarkers Neuropsychological test battery PET scans with beta amyloid–binding contrast agents	Sensitivity and specificity of PET for diagnosing AD Improved positive and negative predictive values Earlier diagnosis of AD Earlier intervention for managing early AD

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Gantenerumab (beta-amyloid monoclonal antibody) for treatment of prodromal Alzheimer's disease	Patients in whom prodromal Alzheimer's disease (AD) has been diagnosed	No approved disease-modifying agents are available for treating AD; available therapy options are limited to symptom management. Gantenerumab is a fully human anti-beta–amyloid antibody. It has been shown to pass the blood-brain barrier purportedly with a high capacity to bind to beta-amyloid plaques in the brain. This binding purportedly clears amyloid plaques by a process called phagocytosis. In clinical trials, gantenerumab is given as subcutaneous dose every 4 weeks, for 104 weeks. F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trial ongoing	Cholinergic agents (e.g., donepezil, galantamine, tacrine) NMDA inhibitor (e.g., memantine)	Slowed disease progression, or regression Reduced morbidity 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 Alzheimer's disease (AD) is suspected	No definitive method exists for diagnosing AD in a living person. Diagnosis is made on the basis of clinical signs and symptoms, sometimes aided by positron emission tomography (PET) using a contrast agent. Despite the lack of effective AD treatment, an unmet need exists 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 (ERPs); 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 in a 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)	Blood tests for AD biomarkers Cerebrospinal fluid tests for AD biomarkers Neuropsychological test battery PET scans with beta amyloid–binding contrast agents	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
MRI-based algorithm to screen for Alzheimer's disease or frontotemporal lobar degeneration	Patients in whom a diagnosis of Alzheimer's disease (AD) is suspected	No definitive method exists for screening or diagnosing AD in a living person. Despite the lack of effective AD treatment, an unmet need exists for less invasive diagnostic/screening tools that can detect the condition before significant loss of memory, cognition, and activities of daily living occur so that patients and families can plan for care. Screening and diagnosing AD currently rely on interpretation of clinical signs and symptoms, sometimes aided by positron emission tomography (PET) using a contrast agent. More invasive diagnostic measures include lumbar puncture to analyze cerebrospinal fluid (CSF) to detect total tau and beta-amyloid protein accumulation. The ability to better screen patients noninvasively is needed to determine those patients in whom lumbar puncture is indicated so that unnecessary lumbar punctures can be avoided. Magnetic resonance imaging using an algorithm to measure the ratio of two total tau and beta-amyloid protein present in a patient's brain is under study to do this. Researchers purport that this method could be useful to more accurately screen for early presence of disease and disease progression. Perelman School of Medicine, University of Pennsylvania, Philadelphia Clinical trial completed 2012	Blood tests for AD biomarkers Cerebrospinal fluid tests for AD biomarkers Neuropsychological test battery PET scans with beta amyloid–binding contrast agents	Improved ability to diagnose, rule out, and/or screen for AD or frontotemporal lobar degeneration Earlier intervention Improved outcomes Improved quality of life
Off-label atomoxetine (Strattera) for treatment of mild cognitive impairment	Patients in whom mild cognitive impairment (MCI) has been diagnosed	MCI may be a precursor to Alzheimer's disease (AD). No disease-modifying agents are available for treating AD; available therapy options are limited to symptom management. Atomoxetine (Strattera®) is a selective norepinephrine reuptake inhibitor (SNRI) that is approved for improving attention span and decreasing impulsiveness and hyperactivity in children and adults with attention-deficit hyperactivity disorder. SNRIs increase brain levels of norepinephrine, which controls behavior. Researchers hypothesize that these properties may have some use in treating MCI. This drug class has been studied in patients with dementia, but not yet in patients with MCI. It is given orally. Eli Lilly and Co., Indianapolis, IN (manufacturer) Emory University, Atlanta, GA, with the National Institute on Aging, Bethesda, MD (investigators) Phase II trial ongoing; manufacturer does not appear to be seeking a labeled indication change	Off-label AD pharmacotherapy; Pharmacotherapies in development	Improved cognitive performance Delayed progression to AD Reduced morbidity

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label carvedilol (Coreg) for the treatment of Alzheimer's disease	Patients in whom Alzheimer's disease (AD) has been diagnosed	The available therapies for Alzheimer's disease (AD) do not modify the disease or halt progression and are known to have minimal impact on symptoms. Carvedilol is a beta-adrenergic receptor antagonist indicated for hypertension and certain types of heart failure. Research suggests that inhibition of the beta adrenergic system might reduce amyloid beta load and slow cognitive decline from AD. Carvedilol is available in 3.125, 6.25, 12.5, and 25.0 mg tables, given at a maximum dose of 50 mg per day. A controlled-release formulation is also available at 10, 20, 40, and 80 mg oral doses, given daily. A daily, oral dose of 25mg is being tested in AD patients. GlaxoSmithKline, Middlesex, UK (manufacturer)Johns Hopkins University, Baltimore, MD, in collaboration with Icahn School of Medicine at Mount Sinai, New York, NY (study sponsors) Phase IV trial ongoing	Amyloid beta monoclonal antibodies (in development) Donepezil Galantamine Memantine Nutritional supplements (in development) Other off-label beta blockers Other pharmacotherapies (in development) Rivastigmine Tacrine	Decreased beta amyloid levels in cerebrospinal fluid Delayed disease progression Improved episodic memory Improved quality of life
Off-label intranasal insulin for treatment of Alzheimer’s disease	Patients in whom Alzheimer’s disease (AD) has been diagnosed	No approved disease-modifying agents are available for treating AD; available therapy options are limited to symptom management. This intervention represents a new mechanism of action for treating 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 beta amyloid, and providing neuroprotection for synapses against beta amyloid. Patients with AD have reduced levels of insulin and insulin activity. Insulin can be delivered directly to the central nervous system via the olfactory and trigeminal neural pathways at doses low enough to avoid significant systemic effects. Therefore, researchers have begun delivering insulin intranasally (branded insulin, delivered via a nasal drug delivery device), administered at 20 or 40 IU total dose, twice daily. HealthPartners Research Foundation, Minneapolis, MN University of Kansas, Lawrence University of Washington, Seattle Wake Forest University, Winston-Salem, NC, in collaboration with Alzheimer's Disease Cooperative Study, a service of the National Institute on Aging and University of California, San Diego Phase II and II/III trials ongoing; insulin manufacturers do not appear to be pursuing expanded labeling of insulin to treat AD	Cholinergic agents (e.g., donepezil, galantamine, tacrine) NMDA inhibitor (e.g., memantine)	Slowed disease progression, or regression Improved memory Improved long-term outcomes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Solanezumab (beta-amyloid monoclonal antibody) for treatment of Alzheimer's disease	Patients in whom mild Alzheimer's disease (AD) has been diagnosed	No approved disease-modifying agents are available for treating AD; available therapy options are limited to symptom management. Solanezumab is a fully humanized anti-beta-amyloid antibody that binds specifically to soluble beta amyloid and is intended to draw the peptide away from the brain through the blood to promote clearance of beta-amyloid protein from damaged sites in the brain. It is intended for mild-to-moderate AD and is administered 400 mg intravenously every 4 weeks for 80 weeks in clinical trials. Eli Lilly and Co., Indianapolis, IN Phase III trials completed (EXPEDITION 1 and 2 trials); EXPEDITION-EXT ongoing; Aug 2012 report of top-line results indicated drug failed to reach its goals in either of 2 phase III studies, but showed improvement in pooled results; phase II/III trial ongoing; new phase III trial in mild AD to start by Sept 2013	Cholinergic agents (e.g., donepezil, galantamine, tacrine) NMDA inhibitor (e.g., memantine)	Decreased brain beta-amyloid load Slowed or halted disease progression Improved memory and cognition Improved survival Improved quality of life
Tau aggregation inhibitor (LMTX) for treatment of Alzheimer's disease	Patients in whom Alzheimer's disease (AD) has been diagnosed	No disease-modifying agents are approved for treating AD; available therapy options attempt to mitigate some symptoms, but have minimal impact. LMTX™ (leuco-methylthioninium) is a tau aggregation inhibitor said to dissolve tau protein tangles and oligomers, which are believed to be precursors of tau tangles in the brain. Tau proteins, found mostly in neuronal cells, are believed to stabilize microtubules, but if they become defective, they no longer perform this function. Some researchers think this leads to AD and dementia. TauRx Pharmaceuticals Ltd., Singapore, Republic of Singapore Phase III trials ongoing	Cholinergic agents (e.g., donepezil, galantamine, tacrine) NMDA inhibitor (e.g., memantine)	Increased survival Slowed progression of AD Improved quality of life

Table 5. AHRQ Priority Condition: 05 Depression and Other Mental Health Disorders: 19 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Amitifadine (EB-1010) for treatment of depression	Patients with major depressive disorder whose disease does not respond adequately to selective serotonin reuptake inhibitors	Despite the many available therapeutic options for major depression, treatment side effects and low remission rates remain an issue. Amitifadine (EB-1010) is a novel, unbalanced, triple serotonin-norepinephrine-dopamine reuptake inhibitor antidepressant that acts simultaneously as a reuptake inhibitor for the 3 monoamines. It demonstrates greatest affinity for transporters that inhibit serotonin reuptake, 1/2 as much against norepinephrine reuptake, and 1/8 as much against dopamine reuptake. Euthymics Biosciences, Inc., Cambridge, MA Phase IIb/IIIa trial ongoing	Pharmacotherapy (e.g., serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants) Psychotherapy	Increased serotonin, norepinephrine, and dopamine neurotransmission Improvement in symptoms, as measured by standard depression rating scales Improved quality of life
Bright-light adjunctive therapy for nonseasonal major depressive disorder and bipolar major depression	Patients in whom nonseasonal major depressive disorder (MDD) has been diagnosed	Many pharmacologic and psychotherapeutic options are available for major depressive disorder and major depression in bipolar disorder, yet fewer than half of patients achieve remission, and many treatments have undesired side effects. 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. Studies have been completed and several are ongoing by various entities using bright light therapy as an adjunct to other treatments, including pharmacotherapy and behavior therapy. Douglas Mental Health University Institute, Montreal, Quebec, Canada National Institute of Mental Health, Bethesda, MD New York State Psychiatric Institute, New York, NY University of British Columbia, Vancouver, Canada University of Pittsburgh, PA Trials completed and ongoing	Cognitive behavior therapy Pharmacotherapy (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants) Psychotherapy	Improved depression rating scale scores Improved sleep patterns Improved quality of life Reduced rate of suicide attempts and completed suicides

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 Expanded phase III trial ongoing; FDA granted fast-track status for this indication; FDA approved for Cushing's syndrome in Feb 2012	Antipsychotics in combination with antidepressants Electroconvulsive therapy	Improvement in psychotic symptoms Reduced suicide rate Improved quality of life
Deep brain stimulation (Reclaim System) therapy for treatment-resistant major depressive disorder	Patients in whom treatment-resistant depression has been diagnosed	Despite the many available therapeutic options for major depression, treatment side effects and low remission rates remain an issue. Once multiple medications, psychotherapy, and electroconvulsive therapy have failed, no proven treatment options exist for major depressive disorder. The neurostimulator (Reclaim system) is implanted subcutaneously in chest and delivers controlled electrical stimulation to targeted parts of the brain via thin wire electrodes. Medtronic, Inc., Minneapolis, MN Phase III trial ongoing	Deep brain stimulation (with other systems, or in other brain areas) Electroconvulsive therapy Repetitive transcranial magnetic stimulation Vagus nerve stimulation	Improved depression rating scale scores Improved sleep patterns Improved quality of life Reduced rate of suicide attempts and completed suicides

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Deep brain stimulation for treatment-resistant Tourette's syndrome	Patients in whom Tourette's syndrome (TS) has been diagnosed	In some patients with TS, symptoms can become severe and unresponsive to being adequately managed with pharmacotherapy. Deep brain stimulation (DBS) involves implanting a battery-operated neurostimulator in the brain to deliver electrical stimulation to targeted areas, such as the globus pallidus internus, centromedian-parafascicular, or ventralis oralis complex of the thalamus. Studies are testing various stimulation delivery models, including unilateral and bilateral, continuous and intermittent, and various targets in the brain. The type of DBS device being used is not indicated in all ongoing studies, but Medtronic, Inc., is an example of a company that makes DBS devices that have been approved for other indications, such as Parkinson's disease and obsessive compulsive disorder. Johns Hopkins University, Baltimore, MD University Hospitals, Cleveland, OH University of Florida Center for Movement Disorders and Neurorestoration, Gainesville, FL Various universities worldwide Completed phase I and II trials; several ongoing phase II and III trials	Botulinum toxin type A injections Pharmacotherapy (antidepressants, 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-resistant major depressive disorder	Patients in whom treatment-resistant major depressive disorder (MDD) has been diagnosed	Despite many available therapeutic options for MDD, treatment side effects and low remission rates remain an issue. When multiple medications, psychotherapy, and electroconvulsive therapy have failed, no treatment options are available for MDD. The Libra™ Deep Brain Stimulation (DBS) System is an implant intended to send 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 typically 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 BROADEN pivotal investigational device exemption U.S.trial ongoing (BROdmann Area 25 DEep brain Neurostimulation)	DBS (with other systems, or in other brain areas) Electroconvulsive therapy Repetitive transcranial magnetic stimulation Vagus nerve stimulation	Improved depression rating scale scores Improved sleep patterns Improved quality of life Reduced rate of suicide attempts

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Glycine transporter type 1 inhibitor (bitopertin) for treatment of negative symptoms of schizophrenia	Patients in whom schizophrenia has been diagnosed	Existing pharmacotherapies for schizophrenia may have limited efficacy and are associated with unwanted side effects in many patients. Additionally, available treatment options inadequately address the negative and cognitive symptoms of schizophrenia. Bitopertin is a glycine transporter type 1 inhibitor. Elevation of extracellular synaptic glycine concentration by blockade of glycine transporter type 1 has been hypothesized to potentiate N-methyl-D-aspartate receptor function. Intended to mediate negative symptoms, which include blank stares, monotone and monosyllabic speech, lack of animation, seeming lack of interest in the world and other people, and inability to feel pleasure. Current treatment focuses on positive symptoms. In trials, the drug is being given orally once daily at several dose levels (unstated in trial description) for up to 3 years. F. Hoffmann-La Roche, Ltd., Basel, Switzerland Phase III trials ongoing	Pharmacotherapy (e.g., atypical antipsychotics)	Symptom improvement Improved quality of life
Lisdexamfetamine (Vyvanse) for treatment of binge-eating disorder	Patients in whom binge-eating disorder has been diagnosed	No pharmacotherapies are FDA approved for binge-eating disorder, and off-label pharmacotherapies are associated with limited efficacy, undesirable side effects, and low adherence. Lisdexamfetamine (Vyvanse®) is a prodrug of dextroamphetamine; it is FDA approved currently for treating attention-deficit hyperactivity disorder. The agent is thought to induce the release of dopamine and norepinephrine, which contribute to maintaining alertness, focus, thought, effort, and motivation; however, the company has not yet described the mechanism of action through which this agent is expected to exert its effects in this population. In trials, the drug is being administered orally, once daily at 50 or 70 mg for up to 52 weeks. Shire, plc, Dublin, Ireland Phase III trial completed; 3 other phase III trials ongoing	Off-label pharmacotherapies (e.g., antiepileptics, norepinephrine reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors)	Decreased morbidity Fewer binge-eating episodes Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mobile apps for psychotherapy	Patients in whom a mental health condition (e.g., major depressive disorder, anxiety) has been diagnosed	Psychotherapy traditionally involves in-person meetings between a therapist and patient or client. This method has limitations, including access by all those in need, lack of intervention at critical moments, and an inability to reach individuals who lack the means or willingness to enter a traditional therapeutic relationship. To address these unmet needs, some researchers have created mobile applications ("apps") that purport to provide some psychotherapeutic benefit to patients even if they don't attend traditional therapy. These apps range in their capabilities and intended benefits. For example, the Mobilyze app is designed to use data from sensors already embedded in the device (e.g., GPS, Bluetooth, Wi-Fi, accelerometers) to identify patient states, without requiring patient self-reporting. This automated system for detecting mood-related states is intended to address nonadherence and other treatment difficulties as they occur in real time. For example, if the app detects that an individual is becoming isolated, it will recommend that he or she calls a friend. Another app is intended to decrease social anxiety and excessive worrying by reducing the tendency of anxious people to focus on threatening items around them. The app purportedly trains people to divert attention away from negative stimuli that appear on the screen. Various research institutions, including Northwestern University, Evanston, IL McNally Laboratory at Harvard University, Cambridge, MA Clinical trials ongoing	In-person psychotherapy Internet-delivered (nonmobile device) psychotherapy	Improved performance on mental health rating scales Reduced morbidity Reduced mortality Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mobile phone 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 their chronic nature. New behavioral therapy approaches are needed that engage participants. Text-messaging has been used as an adjunct and follow up to treatment. In 1 program, participants sent a nightly text message to clinicians to report the number of binge-eating and purging episodes and rate their urges to binge and purge. They received automatic feedback messages tailored to their self-reported symptoms. This approach is being studied in conjunction with a cognitive behavior therapy program to keep patients engaged in therapy. In another program, text messaging was used to follow-up (step-down therapy) with patients after discharge from residential treatment. University of North Carolina at Chapel Hill Institute of Psychiatry, London, UK Center for Psychotherapy Research, University Hospital Heidelberg, Heidelberg, Germany Pilot studies completed	Antidepressants Nutritional counseling Psychological counseling	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 rates
Nicotinic alpha-7 agonist (EVP-6124) for treatment of cognitive symptoms of schizophrenia	Patients in whom schizophrenia has been diagnosed	Existing pharmacotherapies for schizophrenia have limited efficacy and are associated with unwanted side effects in many patients. Additionally, available treatment options inadequately address the negative and cognitive symptoms of schizophrenia. EVP-6124 is a selective, potent compound that is intended to enhance synaptic transmission in the brain and act as a co-agonist in combination with acetylcholine (ACh) to enhance cognition. According to the manufacturer, the agent sensitizes the alpha-7 receptor, thereby allowing smaller amounts of naturally occurring ACh to be effective in activating the alpha-7 receptor. The company purports that this mechanism could alleviate the undesirable side effects caused by other systemic compounds (e.g., acetylcholinesterase inhibitors), which are associated with toxic side effects at certain doses. 2 dose levels being tested as a once-daily oral drug. EnVivo Pharmaceuticals, Watertown, MA Phase III trials ongoing	Pharmacotherapy (e.g., atypical antipsychotics)	Improved cognitive 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
Off-label armodafinil (Nuvigil) 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 off-label pharmacotherapies are associated with limited efficacy, undesirable side effects, and low patient adherence to treatment recommendations. Armodafinil (Nuvigil®) is a wakefulness-promoting drug with an unknown mechanism of action; it was approved in 2007 for treating excessive sleepiness associated with narcolepsy, obstructive sleep apnea, and shift work disorder. Some investigators have suggested that binge-eating disorder may mediate a known relationship between narcolepsy and obesity, so researchers are investigating its off-label use in patients with binge-eating disorder. In a clinical trial, the drug is being given orally, at a variable dosage of 150–250 mg/day. Teva Pharmaceutical Industries, Ltd., Petach Tikva, Israel (manufacturer) Lindner Center of Hope, Mason, OH (investigator) Phase III trial ongoing	Off-label pharmacotherapies (e.g., antiepileptics, norepinephrine reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors)	Improved symptoms of binge eating Reduced morbidity Reduced mortality
Off-label botulinum toxin A (Botox) for treatment of depression	Patients in whom depression has been diagnosed	Fewer than half of patients with MDD achieve remission with currently approved antidepressant therapy, and available pharmacotherapies are often associated with undesirable side effects. The neurotoxin botulinum toxin A targets the neuromuscular junction, blocking neurotransmission for several months. Paralysis of the facial musculature responsible for frowning may regulate mood through a feedback mechanism and alleviate depression symptoms. Botulinum toxin injection to the glabellar region of the brow is under study as an adjunctive treatment for major depression. Allergan, Inc., Irvine, CA Several ongoing trials of botulinum toxin in depression (cumulative n=140), initial results published in May 2012	Antidepressants Combination therapy Deep brain stimulation Electroconvulsive stimulation Psychotherapy Transcranial magnetic stimulation Vagus nerve stimulation	Improved 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
Off-label intranasal oxytocin for treatment of schizophrenia	Patients in whom schizophrenia has been diagnosed	Existing pharmacotherapies for schizophrenia may have limited efficacy and are associated with unwanted side effects in many patients. Additionally, available treatment options inadequately address the negative and social cognitive symptoms of schizophrenia. Psychotherapeutic interventions are limited by suboptimal efficacy and availability. Release of oxytocin is associated with social bonding, empathy, and trust. Given oxytocin's importance in social behavior, researchers purport it may have utility in improving the negative symptoms of schizophrenia and their social cognition deficits. The drug is under study in varying doses (e.g., 0.60 ml) that are self administered intranasally at different intervals (e.g., twice daily). Several institutions, including University of California, Los Angeles, and University of North Carolina, Chapel Hill Clinical trials ongoing	Other medications for negative symptoms Behavioral therapy	Improved social cognition Improved quality of life
Off-label ketamine for treatment-resistant major depressive disorder	Patients in whom treatment-resistant major depressive disorder (MDD) or bipolar depression has been diagnosed	Despite the many available therapeutic options for MDD, treatment side effects and low remission rates remain an issue. Available options for treatment-resistant MDD (e.g., deep brain stimulation [DBS], vagus nerve stimulation [VNS], transcranial magnetic stimulation [TMS], or repetitive transcranial magnetic stimulation [rTMS]) are surgically invasive and must be performed in a hospital setting. N-methyl-D-aspartate (ketamine) is under study for rapid (within 40 minutes) relief of severe treatment-resistant depression and suicidal ideation. The drug is under study in 2 formulations: intravenous administration 0.50 mg/kg of body weight once or more weekly; intranasal administration up to 50 mg per single dose. Various institutions conducting trials sponsored by National Institutes of Health, Bethesda, MD Phase II-IV trials ongoing	DBS Electroconvulsive therapy Pharmacotherapy (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants) Psychotherapy TMS VNS	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
Off-label riluzole (Rilutek) for treatment of major depressive disorder	Patients in whom treatment-resistant major depressive disorder (MDD) has been diagnosed	Despite the many available therapeutic options for major depression, treatment side effects and low remission rates remain an issue. Available options for treatment-resistant MDD (e.g., deep brain stimulation [DBS], vagus nerve stimulation [VNS], transcranial magnetic stimulation [TMS], or repetitive TMS) are surgically invasive and must be performed in a hospital setting. The mechanism of action of riluzole (Rilutek®) would be novel for this disease state. Riluzole is a glutamatergic modulator FDA approved for treating amyotrophic lateral sclerosis; 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. Sanofi, Paris, France (manufacturer) National Institute of Mental Health, Bethesda, MD (investigator) Phase II trials ongoing; 1 phase II trial completed	DBS Electroconvulsive therapy Pharmacotherapy (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants) Psychotherapy TMS VNS	Glutamatergic modulation Improved MDD symptoms Improved quality of life
Off-label scopolamine (intravenous, transdermal, oral) for treatment of depression	Patients with major depressive disorder whose disease does not respond adequately to selective serotonin reuptake inhibitors	Despite the many available therapeutic options for major depression, treatment side effects and low remission rates remain an issue. Depression treatments also typically take 3–6 weeks before patients experience relief, warranting the need for better, faster-acting medications. Researchers have indicated that acetylcholine-mediated activity could play a role in depression. Scopolamine is a muscarinic antagonist that blocks the muscarinic acetylcholine receptors, thus blocking the actions of acetylcholine (anticholinergic effect), and pilot study results have suggested it might yield results quickly—within days. In ongoing studies, scopolamine is being administered alone and in conjunction with other medications. It is being tested as an intravenous drug given about 3–5 days apart at varying dosages (e.g., 2, 3, or 4 mcg/kg of body weight followed by 45 minutes of saline infusion), as a transdermal patch, and as oral medication (e.g., 0.5 mg twice daily). Massachusetts General Hospital, Boston National Institute of Health, Bethesda, MD Clinical trials ongoing	Deep brain stimulation Electroconvulsive therapy NMDA receptor antagonist (in development) Psychotherapy Serotonin-norepinephrine reuptake inhibitors Tricyclic antidepressants	Improvement in symptoms, as measured by standard depression rating scales Improved quality of life Reduced remission rates

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label venlafaxine (Effexor) for treatment of compulsive hoarding	Patients with compulsive hoarding habits who have no other identified psychiatric morbidity	Compulsive hoarding affects an estimated 2% to 5% of individuals in the U.S. The condition can be difficult to treat, and only a single study has been conducted to determine whether pharmacotherapy is an effective treatment. Selective serotonin reuptake inhibitors (SSRIs) have been used in this population, but they are associated with side effects and suboptimal efficacy, especially in older adults. Extended-release venlafaxine (Effexor XR®) is a selective norepinephrine reuptake inhibitor that is indicated in the U.S. for treating depression, generalized anxiety disorder, social anxiety disorder, and panic disorder. Because this agent is well tolerated and has shown efficacy in treating obsessive-compulsive disorder (often associated with hoarding), researchers hypothesize that it may have utility in patients in whom compulsive hoarding has been diagnosed. In trials, the drug was administered orally, once daily. Pfizer, Inc., New York, NY (manufacturer) University of California, San Diego (investigator) Clinical trial completed; manufacturer does not appear to be seeking a labeled indication change	Psychotherapy Selective serotonin reuptake inhibitors	Improved scores on hoarding rating scales Reduced morbidity Reduced mortality Improved quality of life
Vortioxetine (Brintellix) for treatment of major depressive disorder	Patients in whom major depressive disorder (MDD) has been diagnosed	Despite the many available therapeutic options for major depression, treatment side effects and low remission rates remain an issue. Vortioxetine (Brintellix®) 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 available products. Planned oral dosages include 10, 15, and 20 mg. Takeda Pharmaceutical Co., Ltd., Osaka, Japan, jointly with H. Lundbeck a/s, Valby, Denmark Phase III trials completed; FDA accepted manufacturers' new drug application; expected decision date Oct 2013	Pharmacotherapy (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants) Psychotherapy	Improved depression rating scale scores Improved sleep patterns Improved quality of life Reduced rate of suicide attempts and completed suicides

Table 6. AHRQ Priority Condition: 06 Developmental Delays, Attention-Deficit Hyperactivity Disorder, and Autism: 5 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mavoglurant (AFQ056) for treatment of fragile X syndrome	Patients in whom fragile X syndrome (FXS) has been diagnosed	No cure exists for FXS; medications and behavior interventions alleviate individual symptoms but do not address the syndrome's cause. Individuals with FXS have DNA mutations in the FMR1 gene that basically turn off the gene; it is the most common known heritable cause of cognitive and behavioral disability. 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), can potentially normalize the excessive protein synthesis and control symptoms associated with FXS. In trials, it is taken as an oral capsule at doses of 25, 50, or 150 mg, twice a day. Novartis International AG, Basel, Switzerland Phase II/III trials ongoing in adults and adolescents; drug also under study for treating Parkinson's disease, Huntington's disease, obsessive-compulsive disorder, and nicotine addiction	Physical and behavior interventions including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Pharmacotherapy (e.g., antipsychotics. central nervous system stimulants, clonidine [Catapres®], folic acid, selective serotonin reuptake inhibitors, melatonin)	Change from baseline in behavioral symptoms using the Aberrant Behavior Checklist

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label intranasal oxytocin (Syntocinon) for treatment of autism spectrum disorders	Patients in whom autistic spectrum disorder (ASD) or Asperger's syndrome has been diagnosed	Most individuals with an ASD are treated through highly structured behavioral programs to try to improve social cognition and functioning, Pharmacologic therapies address symptoms of hyperactivity and depression, but 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. In ongoing studies of children and adults with ASDs, this treatment is administered intranasally (e.g., 12-unit puff per nostril, twice daily, totaling 48 IU daily). Children's Hospital of Pennsylvania, PA Mount Sinai School of Medicine, New York, NY Montefiore Medical Center, Bronx, NY Stanford University School of Medicine, CA University of Illinois at Chicago, IL Phase II trials ongoing	Behavior and physical interventions including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Central nervous system pharmacology Melatonin Selective gamma aminobutyric acid type B receptor agonist (in development)	Improved Diagnostic Analysis of Nonverbal Accuracy results Improved Social Responsivity Scale scores Improved Clinical Global Impressions Scale - Improvement scores
Off-label N-acetylcysteine for treatment of autism spectrum disorders	Children in whom autism has been diagnosed	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 (NAC) is a glutamate modulator and antioxidant known to increase glutathione in children who have autism. For children with autism, NAC has been administered orally or intravenously at various doses and regimens (e.g., weekly intravenous administration of 20 mg/kg of body weight mixed with glutathione 600 mg IV and vitamin C 2000 mg; oral 60mg/kg/day thrice daily to a maximum dose of 4200 mg/day). Stanford University School of Medicine, Stanford, CA Indiana University School of Medicine, Indianapolis National Alliance for Autism Research, Princeton, NJ Phase II trials completed	Behavior and physical interventions including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Central nervous system pharmacology Melatonin Selective gamma aminobutyric acid type B receptor agonist (in development)	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
Video game software for treatment of attention-deficit hyperactivity disorder	Patients in whom attention-deficit hyperactivity disorder (ADHD) has been diagnosed	ADHD is the most-diagnosed behavioral disorder in children, affecting about 3% to 5% of children. ADHD can cause depression, sleeping problems, anxiety, learning disabilities, and other behavioral abnormalities. Available ADHD treatments have variable outcomes, warranting the development of more innovative treatment. Research has suggested that action video games can improve a person's cognitive abilities. Video game therapy is intended to improve concentration skills, reduce anxiety, and enforce correct and quick decisionmaking, skills lacking in patients with neurological conditions such as ADHD. Therapy is delivered online. Two companies have petitioned FDA asking to have their software to be regulated as devices delivering therapy. Akili Interactive Labs, Boston, MA Brain Plasticity, Inc., San Francisco, CA Posit Science Corporation, San Francisco, CA Pilot trials ongoing	Behavioral therapies Combination therapies Drug therapies	Improved attentiveness and academic performance Reduced behavioral abnormalities Improved quality of life
XBox 360 musical program (Kinect audio project) for improving social skills in childhood autism	Children in whom autism has been diagnosed	Experts indicate no single treatment is effective for all individuals with an autism spectrum disorder (ASD). Treatment options for ASD include behavior and communication therapies (including applied behavior analysis) and dietary, medical, and complementary interventions. Interactive therapy using XBox 360's Kinect system has been targeted by researchers attempting to improve social skills in patients with autism. The Kinect Audio Project is an XBox 360 program/system that uses the Kinect camera and motion sensor with PC software to allow children to participate in virtual music lessons by providing them with virtual gloves that allow "touching" of virtual music notes when they place the gloves over the symbol on the screen. This allows for inclusion of children with autism in student music activities that might have otherwise been difficult with normal instruments. This program is intended to increase mobility skills, improve understanding of movement and association, enhance unsolicited participation, and improve overall social interaction. South Downs Community Special School, Eastbourne, UK Clinical trial ongoing	Educational and behavior programs for autistic children	Improved social skills and human interaction Improved activities of daily living Improved quality of life

Table 7. AHRQ Priority Condition: 07 Diabetes Mellitus: 16 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Alpha-1 antitrypsin for treatment of type 1 diabetes	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 anti-inflammatory 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 4-week intervals. Kamada, Ltd., Ness Ziona, Israel National Institute of Allergy and Infectious Disease, Bethesda, MD University of Colorado, Denver, in collaboration with Omni Bio Pharmaceuticals, Inc., Greenwood Village, CO Phase II trials ongoing; FDA granted orphan drug status Aug 2011	Insulin modifications Islet cell transplantation Pancreas transplantation	Reduced daily insulin usage Improved glycosylated hemoglobin (HbA1c) levels Reduced complications of diabetes Improved quality of life
Artificial pancreas device system for treatment of diabetes	Patients with type 1 or type 2 diabetes mellitus who require insulin and are highly motivated to use a closed system and monitor its function	An artificial pancreas device system (APDS) 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 yet succeeded in creating a total closed-loop system. Several systems are in trials. Various manufacturers in collaboration with Juvenile Diabetes Research Foundation More than 25 early and mid-phase trials ongoing; FDA placed on innovation pathway and issued final regulatory guidance on the systems Nov 9, 2012; FDA is prioritizing review of research protocols, setting performance and safety standards, holding discussions between government and private researchers, sponsoring public forums, and finding ways to shorten study and review time.	Insulin modifications Islet cell transplantation Pancreas transplantation	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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Buccal insulin (Oral-lyn) for treatment of type 1 or type 2 diabetes	Individuals with type 1 diabetes mellitus (T1DM) or uncontrolled type 2 diabetes mellitus (T2DM) 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; it has a short duration of activity. It is intended for dosing before and after meals, for use adjunctively with long-acting, injectable or infused insulin, and as a substitute for injectable short-acting insulin. Buccal insulin is not intended to reach the lungs and may pose less risk of respiratory or pulmonary complications than inhaled insulin does. Generex Biotechnology Corp., Toronto, Ontario, Canada Phase III trial completed in India; positive results reported Jul 2013; Sept 2012 company announced it wil conduct several short studies to meet FDA requirments; FDA approved in 2009 under the Treatment Investigational New Drug program, which allows Generex to provide early access to people with serious or life-threatening T1DM or T2DM who have no satisfactory alternative treatments and who are not eligible for participation in the company's ongoing phase III clinical trial of the drug	Diet and lifestyle changes Exenatide Insulin Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Improved target glycosylated hemoglobin (HbA1c) levels Reduced glycemic excursions related to meals Prevented onset of T2DM in prediabetic individuals Delayed insulin dependence in T2DM Improved quality of life
Cogenzia gentamicin antimicrobial sponge for treatment of infected diabetic foot ulcers	Patients in whom a moderately infected diabetic foot ulcer has been diagnosed	Approximately 3 million patients a year develop diabetic foot ulcers, and an estimated 15% require amputation of an appendage. Although theoretically logical, little evidence exists to support the use of topical antimicrobials for treating diabetic foot ulcers, and no topical treatment is approved for this indication. Cogenzia is a gentamicin impregnated antimicrobial biodegradeable sponge that is intended to deliver high levels of gentamicin to the wound site while avoiding systemic side effects and being resorbed. Cogenzia is used in conjunction with standard wound care and administration of an oral antibiotic (levofloxacin). It is under study in two sizes, both of which deliver 50 mg of gentamicin sulfate. Innocoll, Inc., Ashburn, VA FDA agreed to special protocol assessment for company's phase III development program	Standard wound care and systemic antibiotics Levofloxacin monotherapy	Improved clinical cure rate Improved pathogen response Pathogen eradication Decreased wound surface area (healing rate)

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
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 under study for treatment of various secondary complications of diabetes, including neuropathy. In trials, it is given as an injection at high dose (2.4 mg) or low dose (0.8 mg), once weekly, for up to 52 weeks. Cebix, Inc., La Jolla, CA Phase II trial ongoing; FDA granted fast-track status for diabetic peripheral neuropathy	Analgesics Lidocaine patches Duloxetine (antidepressant), Pregabalin (anticonvulsant) Selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, antiepileptics	Reduced pain Improved quality of life
DiaPep277 (peptide immune modulator) for treatment of type 1 diabetes	Patients in whom type 1 diabetes mellitus (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 1 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. If approved, the therapy would be delivered as a vaccine in a physician's office rather than as a self-administered drug (or self-administered insulin) Andromeda Biotech, Ltd., Yavne, Israel Phase III trials ongoing	Insulin modifications Islet cell transplantation Pancreas transplantation	Improved beta-cell function (measured as change from baseline in stimulated C-peptide secretion during a mixed-meal tolerance test) Increased glycemic control

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Exenatide extended-release (Bydureon) for treatment of diabetes	Patients with type 2 diabetes mellitus (T2DM) 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 subsidiary of Bristol-Myers Squibb, New York, NYAlkermes, Inc., Waltham, MA FDA approved Jan 2012 with black box warning; FDA requested several studies to examine C-cell hyperplasia and compare glucagon-like peptide-1 receptor expression on human, rat, and mouse thyroid C-cells. The company must also maintain a 15-year case series registry to monitor the incidence of medullary thyroid carcinoma and its association, if any, to Bydureon. FDA also required company to conduct a double-blind, placebo-controlled trail to evaluate the effects of Bydureon on the incidence of major adverse cardiovascular events in patients with T2DM; medullary thyroid carcinoma biomarkers; and long-term effects on specific disorders of the thyroid and pancreas. The approval also required the company to create a Risk Evaluation and Mitigation Strategy plan.	Diet and lifestyle changes Insulin Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Improved target glycosylated hemoglobin (HbA1c) levels Reduced glycemic excursions related to meals Delayed insulin dependence in T2DM Improved quality of life
Fluocinolone acetonide implant (Iluvien) for treatment of diabetic macular edema	Patients in whom diabetic macular edema (DME) has been diagnosed	DME affects an estimated 560,000 patients in the United States. Only a single FDA-approved drug therapy (Ranibizumab) is available for treating DME. 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 anti-inflammatory and anti-VEGF (vascular endothelial growth factor) activity and has a history of effectiveness in treating ocular disorders. Alimera Sciences, Inc., Alpharetta, GA Phase III trials completed; new drug application (NDA) submitted Jun 2010; FDA issued complete response letter in Dec 2010 asking for additional safety data; NDA resubmitted May 2011. Nov 2011, FDA issued complete response letter not approving the drug. Company submitted response to the 2nd complete response letter from FDA. Iluvien received marketing approval in several European nations. Company announced that a Prescription Drug User Fee Act date of Oct 17, 2013 has been set.	Intravitreal triamcinolone acetonide with or without laser photocoagulation Laser photocoagulation Pharmacotherapy (e.g., VEGF antagonists)	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
Fasiglifam (G-protein coupled receptor 40 agonist) for treatment of type 2 diabetes mellitus	Patients in whom type 2 diabetes mellitus (T2DM) has been diagnosed	Many treatments for T2DM help control glucose levels but can be associated with significant side effects, including nausea, diarrhea, weight gain, hypoglycemia, and edema. Additionally, many patients have difficulty achieving blood-glucose control with current treatments. Fasiglifam (TAK-875) is a selective G-protein coupled receptor 40 (GPR40) agonist, a specific receptor located and expressed in pancreatic islet cells. GPR40 agonists purportedly mediate fatty acid potentiation, which could acutely increase insulin secretion and, therefore, improve glucose tolerance. The developer purports the selectivity of this G-protein-coupled receptor could potentially reduce hypoglycemia risk. In trials, the drug is administered orally as a tablet at 25- and 50-mg doses daily. Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trial completed; results reported May 2013	Diet and lifestyle changes Various approved drugs for treating T2DM Other GPR40 agonists in development Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Halted or delayed acute and secondary diabetes complications Improved glycated hemoglobin (HbA1c) levels
ITCA 650 (exenatide continuous subcutaneous delivery) for treatment of type 2 diabetes	Patients with type 2 diabetes mellitus who have not achieved desired blood glucose goals with metformin	ITCA 650 is a proprietary form of exenatide (a glucagon-like peptide-1 (GLP1) mimetic) delivered subcutaneously and continuously through a tiny implanted stick-shaped pump, is purported to remain stable at body temperature for as long as a year, according to the most recently presented data. The delivery system is a semipermeable, osmotic mini-pump that a physician or physician assistant implants into the patient's arm or abdomen during an outpatient procedure that takes about 5 minutes. The device is intended to deliver a steady dose for up to 12 months (after which it must be reimplanted), potentially providing a more convenient dosing option for patients.[37] The system is also designed to minimize the nausea associated with twice-daily dosing. Amylin Pharmaceuticals subsidiary of Bristol-Myers Squibb, New York, NY (drug) Intarcia Therapeutics, Inc., Hayward, CA (device) Phase III trials ongoing; ITCA 650 technology FDA approved for drug delivery; exenatide formulation for use with pump is under study; in Nov 2011, Eli Lily and Co. (Indianapolis, IN) returned all development rights of exenatide to Amylin	Diet and lifestyle changes Insulin Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Improved target glycosylated hemoglobin (HbA1c) levels Reduced glycemic excursions 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
Inhaled insulin (Afrezza) for treatment of diabetes	Patients with type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM) who require insulin injections	Inhaled insulin (Afrezza®) to control blood glucose levels. Afrezza is categorized as an ultra-rapid–acting insulin therapy to be taken at mealtime by individuals with T1DM or T2DM who require exogenous insulin. This combination drug-device product uses a proprietary inhalation powder that has been metered into single-use dose cartridges. The inhaler device is small and fits within the palm of the user's hand. MannKind Corp., Valencia, CA Phase III trials ongoing; in Mar 2010, FDA issued a complete response letter questioning whether the inhaler used in mid-phase trials was comparable to a new-generation inhaler that the company wants to market with the drug. In Jan 2011, company received a 2nd response letter outlining additional trials needed for approval; Aug 2011, 2 phase III trials were planned after manufacturer met with FDA. Jun 2013, company announced completion of 1 pivotal trial and anticipated completion of the other in 2013.	Diet and lifestyle changes Exenatide Insulin modifications Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Improved target glycosylated hemoglobin (HbA1c) levels Reduced glycemic excursions related to meals Delayed insulin dependence in T2DM Improved quality of life
Interactive text messaging program (Care4Life) to improve management of type 2 diabetes mellitus	Patients in whom type 2 diabetes mellitus (T2DM) has been diagnosed	Despite available treatments and blood glucose monitoring devices for T2DM, achieving adequate glycemic control remains a prominent issue for patients. Care4Life is an interactive text messaging program intended to help improve treatment adherence and achieve better glycemic control in patients with T2DM. The text messaging and online health record system is intended to deliver customized educational content based on the user's own medication plan and health goals. The system delivers messages intended to motivate a patient to keep track of blood glucose levels, his or her fitness and weight goals, and improve medication adherence. Patients can enter health data via text that will be captured on a Web portal that can be made accessible to the patient's health care team. Text messages can be delivered in both English and Spanish. This intervention could be especially useful for reaching underserved communities with limited access to health care providers. The company offered this service to health care providers and health insurance plans for free until the end of 2012. Vovixa, Inc., Washington, DC (manufacturer) HealthInsight, Salt Lake City, UT (investigator) Pilot trial ongoing; program launched Oct 2012	Diabetes behavior and lifestyle support groups Hardcopy patient education Internet-based patient education	Improved glycated hemoglobin (HbA1c) levels Reduced secondary complications Reduced health disparities and improved access to diabetes program Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Metabolic (bariatric) surgery for resolution of diabetes in obese and nonobese patients	Obese and nonobese patients in whom type 2 diabetes mellitus (T2DM) has been diagnosed	Metabolic surgery (i.e., gastric bypass, lap banding, sleeve gastrectomy) has been observed to restore metabolic imbalances in morbidly obese patients who have undergone bariatric surgery for weight loss. This led to interest in the surgery for patients with diabetes–who are overweight or obese as well as not obese–because researchers have observed that metabolic abnormalities have resolved independent of weight loss, and some think weight is not the only factor contributing to the metabolic abnormalities observed in patients with T2DM. Some researchers suggest that metabolic surgery could be used to possibly "cure" T2DM regardless of body mass index and independent of weight loss Multiple U.S. academic research centers Mid-to-late phase trials completed and ongoing	Behavior and lifestyle modifications Various approved drugs for treating T2DM Other GPR40 agonists in development Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Improved quality of life Reduced use of diabetes medications Reduced secondary complications Resolution of diabetes
Off-label salsalate for treatment of type 2 diabetes	Patients in whom type 2 diabetes mellitus (T2DM) has been diagnosed	Research has demonstrated a link between T2DM progression and inflammation. Salsalate is a widely available anti-inflammatory derivative of salicylic acid; although 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 anti-inflammatory activity Joslin Diabetes Center, Boston, MA; various academic research centers Phase II/III trial completed; other phase II/III trials ongoing	Diet and lifestyle changes Exenatide Insulin Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Improved target glycosylated hemoglobin (HbA1c) levels Reduced glycemic excursions related to meals Improved quality of life

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 in whom clinically significant diabetic macular edema (DME) has been diagnosed	DME affects an estimated 560,000 patients in the U.S. 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 antiangiogenic that has been FDA approved to treat the "wet" type of age-related macular degeneration, a common form of age-related vision loss. Ranibizumab has been studied for DME (a new indication) and was the first medication approved by FDA for DME. The approved dosage is 0.3 mg, once monthly, administered by injection into the eye. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, SwitzerlandNovartis International AG, Basel, Switzerland FDA approved Aug 2012 for treating DME Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, SwitzerlandNovartis International AG, Basel, Switzerland FDA approved Aug 2012 for treatment of DME	Intravitreal triamcinolone acetonide with or without laser photocoagulation Laser photocoagulation Pharmacotherapy (e.g., vascular endothelial growth factor antagonists)	Improved vision Stabilized vision Reduced side effects of existing treatment Improved quality of life
Ultra-long-acting insulin (Tresiba, degludec; Ryzodeg degludec plus aspart) for treatment of type 1 or 2 diabetes	Patients with type 1 or 2 diabetes mellitus who require insulin or insulin and oral medication	Degludec (Tresiba®) is an ultra-long–acting insulin that releases over several days—its action extends beyond 42 hours, according to the company. The flexible dosing regimen allows 8–40 hours between dosing, which could lead to thrice-weekly dosing, or dosing once in the evening. Novo Nordisk a/s, Bagsvaerd, Denmark Phase III trials completed for degludec and degludec plus aspart; Nov 2012, FDA advisory committee voted 8-4 to recommend approval of both formulations; FDA panel unanimously also recommended a cardiovascular outcomes trial be conducted; approved Sept 2012 in Japan; submitted for approval in Europe. The manufacturer is developing another formulation that combines degludec with insulin aspart (Ryzodeg®). Company received complete response letter from FDA in Feb 2013 for both drugs requesting additional cardiovascular data from a dedicated cardiovascular outcomes trial.	Diet and lifestyle changes Exenatide Insulin Insulin sensitizers (pioglitazone, rosiglitazone) Metformin Sitagliptin Sodium glucose co-transporter 1 and/or 2 inhibitors (in development) Sulfonylurea drugs (glimepiride)	Achieved target glycosylated hemoglobin (HbA1c) levels Reduced progression of complications Improved quality of life

Table 8. AHRQ Priority Condition: 08 Functional Limitations and Disability: 78 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Adenosine 2A antagonist (SYN115) 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 could improve quality of life and management of the disease. SYN115 is an oral, adenosine 2A (A2A) receptor antagonist intended to increase “on” time for patients 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 blocking of neurons associated with PD. Biotie Therapies Corp., Turku, Finland Phase II/III trial completed	Adenosine A2A receptor antagonist (in development) Dopamine agonists Glutamate receptor 5 modulators (in development) Levodopa/carbidopa Monoamine oxidase-B inhibitors Nicotinic receptor agonist (in development)	Improved motor skills Improved symptoms Reduced disease progression Reduced incidence/severity of levodopa-induced dyskinesia 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 (Lemtrada™) represents a new mechanism of action for RRMS. Alemtuzumab is a humanized monoclonal antibody 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 said to last for more than 1 year. The drug is given as a once-yearly treatment regimen (once a day for 5 days) via intravenous administration. Genzyme Corp., Cambridge, MA Phase III trial ongoing; FDA accepted the company’s new drug application filing in Jan 2013 (after having issued the company a refusal-to-file letter in Aug 2012 requesting data reorganization). The drug is FDA approved for treating refractory chronic lymphocytic leukemia.	Dimethyl fumarate (Tecfidera) Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b 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-tocopheryl 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 dosage, twice daily. Edison Pharmaceuticals, Inc., Mountain View, CA Phase IIa trail completed; FDA granted orphan drug and fast-track statuses	Drugs currently under investigation: Idebenone (Phase III) Deferiprone EGb761EPI-743OX1 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
Amitriptyline/ketamine analgesic cream (AmiKet) for the treatment of peripheral neuropathy	Patients in whom chemotherapy-induced peripheral neuropathy (PN) has been diagnosed	PN results from damage to the peripheral nerves caused by drug-related toxicity (e.g., chemotherapeutics) or mechanical trauma (e.g., surgery, injury) and can result in significant pain and reduce quality of life. This condition often responds poorly to standard pain treatment approaches. AmiKet (4% amitriptyline/2% ketamine topical cream) is a novel approach to the treatment of neuropathic pain, combining the tricyclic antidepressant amitriptyline and the NMDA receptor antagonist ketamine into a topical analgesic. In clinical trials, this topical agent is applied to the affected areas twice daily. Immune Pharmaceuticals (formerly EpiCept Corp.), Tarrytown, NY University of Rochester, Rochester, NY Phase II/III trials ongoing by separate developers/institutions; FDA granted fast-track status Apr 2012	Antiepileptic agents Interventions for treating the primary cause of nerve damage Opioid analgesics Oral tricyclic antidepressants Over-the-counter analgesics	Decreased pain frequency and intensity 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 after 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 diet, lifestyle, stress management, and self-awareness treatments. Stress tools and techniques are performed for a minimum of 30 minutes a day in a single sitting (meditation, "soften and flow," 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 completed (unphased); sold as a proprietary program; clinically implementable	Behavior and lifestyle changes Pharmacotherapy (e.g., antidepressants, sleeping aids) Psychotherapy	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 after 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 a single sitting (meditation, "soften and flow," 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, UKAnn Vincent, M.D., Mayo Clinic, Rochester, MN Trial completed (unphased); sold as a proprietary program; clinically implementable	Pharmacotherapy (e.g., duloxetine, fluoxetine, gabapentin, lorazepam, milnacipran, pregabalin, tricyclic antidepressants) Behavior and lifestyle modification	Improved ability to perform daily activities Reduced symptoms Improved quality of life
Asfotase alfa (ENB-0040) for treatment of hypophosphatasia in infants and children	Infants and children receiving a diagnosis of hypophospha-tasia	Hypophosphatasia is a rare metabolic disorder caused by deficiency of the tissue-nonspecific isoenzyme of alkaline phosphatase (TNSALP). No other pharmacologic therapy is available. 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 or osteomalacia or both. Incidence has been estimated at 1 per 100,000 births. Asfotase alfa 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 effects and at a half-life 30% longer in bone, compared with its half-life in serum. In trials, asfotase alfa is administered as daily subcutaneous injection of 0.3 or 0.5 mg/kg of body weight. Alexion Pharmaceuticals, Inc., Cheshire, CT Phase II/III trials ongoing; 2 phase II trials completed; FDA granted fast-track and orphan drug statuses	Pharmacotherapy (e.g., cortisone) Vitamin supplementation (e.g., magnesium, vitamin B6, zinc)	Restored 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
Autologous bone-marrow-derived mesenchymal stem cell therapy (NurOwn) for amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	Effective therapy for treatent of ALS is lacking and morbidity and mortality are high from the disorder. NurOwn™ is a differentiated autologous adult mesechymal stem cell (MSC) therapy intended to slow or halt ALS disease progression by regenerating damaged tissue and cells. The company terms the therapy MSC-NTF ("neuron-supporting cells") and collects MSCs from the patient's own bone marrow. The MSCs are processed in vitro using a proprietary process intended to differentiate the cells into astrocyte-like cells capable of releasing neurotrophic factors, including glial-derived neurotrophic factor, to repair and regenerate diseased tissue. The processed cells are reinfused through either a single intrathecal injection into the cerebrospinal fluid or multiple intramuscular injections into the patient's biceps or triceps. BrainStorm Cell Therapeutics, Inc., New York, NY Phase IIa trial ongoing in Israel; FDA granted orphan drug status Feb 2011; U.S.-based phase II multicenter trial planned to begin by end of 2013	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
Balloon angioplasty and/or stenting of azygos and internal jugular vein for treatment of multiple sclerosis	Patients with multiple sclerosis (MS) 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 veins, is hypothesized to play a role in the etiology, disease progression, and pathogenesis of MS. Image-guided interventional endovascular management is a procedure in which an interventional radiologist performs percutaneous transluminal angioplasty using 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 the U.S.; first reported by University of Ferrara, Italy University of British Columbia, Canada Phase I/II trials ongoing	Dimethyl fumarate (Tecfidera) Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b Mitoxantrone Natalizumab	Improved cognitive and motor function Reduced relapse Reduced lesions on imaging Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bioartificial liver system (ELAD System) 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 lost liver functions, such as synthesis of metabolic enzymes and key proteins. The cell-based liver support system adds a "bioreactor" filter to standard liver dialysis systems that temporarily removes blood from the body to remove circulating toxins. ELAD incorporates cultured human hepatocytes in bioreactor cartridges as part of a dialysis-like system. It functions as bridge while a transplant candidate awaits a donor liver. The device is regulated as a combination biologic by FDA's Division of Cellular, Tissue and Gene Therapy in the Center for Biologics Evaluation and Research. Vital Therapies, Inc., San Diego, CA Phase III trials recruiting	Pharmacotherapy (e.g., antibiotics and lactulose) Liver transplantation	Improved rate of 30-day transplant-free survival
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	For patients whose chronic pain is resistant to standard medications, more effective treatment options are needed. Buprenorphine is an opioid that is used in current formulations for treating opioid maintenance therapy 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 cheek for buccal delivery. In clinical trials, BEMA buprenorphine is applied to the buccal mucosa, twice daily. BioDelivery Sciences International, Raleigh, NC Phase III trial ongoing, enrollment completed and data read-out anticipated for late 2013/early 2014; technology was FDA approved for use with fentanyl and is under development for delivery of buprenorphine and buprenorphine/naloxone combinations	Standard pharmacotherapy (e.g., COX-2 inhibitors, Buprenex, nonsteroidal anti-inflammatory drugs, opioids)	Reduced pain Reduced risk of addiction

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
BreathID MBT test to monitor liver function in acute liver failure	Patients in acute liver failure	Breath test (BreathID® MBt) is intended to monitor liver function in patients with acute liver failure by working in conjunction with a marker targeted to challenge hepatic metabolism. The marker purportedly can be measured in the breath of the patient and thus inform clinical decision making regarding need for liver transplantation. The theory is that breath test could give additional liver function assessment information not available with blood tests. The company purports to provide a novel diagnostic option in patients with impaired liver function. The test requires a patient to breathe into a device and is administered in the physician's office. Exalenz Bioscience, Inc., Modi'in, Israel Phase II trial ongoing; FDA granted humanitarian use device exemption (HUD) for monitoring hepatic metabolism in acute liver failure patients. HUD is intended for technology used for a condition that affects fewer than 4,000 people in the United States each year.	Liver function blood tests	Improved patient comfort Increased adherence with liver function testing Earlier detection of liver function problems
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. Progressive keratoconus requires invasive interventions, such as corneal transplants and insertion of corneal rings, and it is the leading cause in corneal transplants in the U.S. 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 performed by removing the corneal epithelium and applying riboflavin drops to the eye; the eye is then exposed to ultraviolet light, which interacts 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 2 phase III trials ongoing; 1 phase III trial completed; FDA granted orphan drug status. Manufacturer submitted new drug application to FDA in Mar 2012. Conformité Européene (CE) marked	Corneal ring segment inserts Surgical therapy	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 multiple sclerosis (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-protecting myelin sheath. Administered by subcutaneous injection, 150 mg, once every 4 weeks. Biogen Idec International GmbH, Zug, Switzerland Abbott Laboratories, Abbott Park, IL Phase III trials ongoing; data were expected in late 2012; FDA granted fast-track status	Dimethyl fumarate (Tecfidera) Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b Mitoxantrone Natalizumab	Delayed disease progression Decreased demyelination Fewer relapses Improved quality of life
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 Parkinson's disease are used to control symptoms. Davunetide, also known as AL-108, is a 1st-in-class agent intended to target tau tangles—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. It also is intended to promote neurite growth and restore transmission between nerve cells. The drug is derived from a naturally occurring protein called activity-dependent neuroprotective protein. Administered intranasally, 30 mg, twice daily. Allon Therapeutics, Inc., Vancouver, British Columbia, Canada Phase II/III trial completed; FDA granted orphan drug status Jan 2010	Botulinum toxin type A (Botox®) injection Pharmacotherapy (e.g., anticholinergic medications, antidepressants)	Improved symptom control Delayed or halted disease progression 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 chronic kidney disease (CKD) is hydration and avoidance of nephrotoxic drugs. Deferiprone (Ferriprox®) is an orally active hydroxypyridin-4-one iron chelator that binds and removes excess iron from the body. If proven effective, deferiprone could become the 1st therapeutic drug to prevent CI-AKI in CKD. Deferiprone 900 mg is administered orally, 1 immediate release tablet and 2 extended-release tablets, 1–3 hours before angiography, and then every 12 hours for 8 days. CorMedix, Inc., Bridgewater, NJ Phase III trial ongoing under FDA special protocol assessment	Pharmacotherapy (e.g., 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
Deferiprone (Ferriprox) for treatment of pantothenate kinase-associated neurodegeneration	Patients in whom pantothenate kinase-associated neurodegeneration (PKAN) has been diagnosed	Investigators have not found a cure for PKAN, a life-threatening, progressive, and degenerative disease. Deferiprone (Ferriprox®) is purported to be an iron chelator that could reduce the accumulation of iron in patients' brains that is suspected of causing pathogenesis. In a clinical trial, deferiprone will be administered as oral solution, twice daily, for 18 months at a dosage of 5 mg/kg to 15 mg/kg. ApoPharma, Inc., Toronto, Ontario, Canada Phase III trial ongoing	Iron chelators	Improved motor skill functions and movement control Slowed disease progression Improved quality of life
Dimethyl fumarate (Tecfidera) for treatment of relapsing multiple sclerosis	Patients in whom relapsing forms of multiple sclerosis have been diagnosed	Available treatments provide unsatisfactory efficacy for many patients with MS. Dimethyl fumarate (BG-12, Tecfidera™) is a fumaric acid ester (FAE) which purportedly reduces peripheral CD4+ and CD8+ T lymphocytes because FAE can induce apoptosis. Dimethyl fumarate purportedly represents a novel mechanism of action through modulating the Nrf-2 pathway, mediating neuroprotective and anti-inflammatory effects, Safety profile may allow combination dosing. Administered orally, 120 mg twice daily for 7 days followed by a maintenance dosage of 240 mg, twice daily. Biogen Idec International GmbH, Zug, Switzerland FDA approved Mar 2013 for treating relapsing forms of MS	Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b Mitoxantrone Natalizumab	Reduced frequency of relapse Reduced symptom severity Slowed disease progression Improved quality of life
Drisapersen (GSK-2402968, PRO-051) for treatment of Duchenne muscular dystrophy	Ambulatory patients 5 years of age or older who have Duchenne muscular dystrophy (DMD) and a dystrophin gene mutation (deletions of exons 50, 52, 45–50, 48–50, and 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 orthotic devices. GSK2402968 is an antisense oligonucleotide that 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	Pharmacotherapy (e.g., corticosteroids, beta2 agonists) Physical therapy Orthopedics Respiratory support (respirator/ ventilators)	Decreased muscle degeneration Improved symptoms Decreased need for supportive devices 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
Droxidopa (Northera) for treatment of symptomatic neurogenic orthostatic hypotension	Patients with Parkinson's disease, multiple system atrophy, and/or pure autonomic failure who are at risk of neurogenic orthostatic hypotension	Current treatment options for symptomatic neurogenic orthostatic hypotension include pharmacotherapy but do not achieve an adequate response in many patients; more effective treatment options are needed to address the underlying cause. 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 3 times daily. Chelsea Therapeutics, Inc., Charlotte, NC Phase III trials completed; FDA granted orphan drug and fast-track statuses; Jul 2012, FDA issued a 2nd complete response letter requesting an additional trial; the company provided additional data in Dec 2012 and in Feb 2013, FDA responded with guidance on an NDA resubmission. The company plans to resubmit NDA in 2nd half of 2013.	Diet and lifestyle modifications Pharmacotherapy (e.g., midodrine hydrochloride)	Decreased orthostatic hypotension Decreased risk of falling Decreased confusion from reduced cerebral circulation
Eliglustat tartrate for treatment of Gaucher's disease	Patients in whom Gaucher's disease has been diagnosed	Gaucher's disease is caused by a hereditary deficiency of glucocerebrosidase, which leads to enlarged and malfunctioning organs, skeletal disorders, and painful neurologic complications. Eliglustat tartrate is an orally active glucocerebroside synthase inhibitor that purportedly decreases the amount of glucocerebroside in major organs such as the spleen and liver. If approved for marketing, eliglustat tartrate would be the first available oral treatment option for patients with Gaucher's disease. Compared with approved IV drug therapy in clinical trials, eliglustat tartrate proved to be as effective. In clinical trials to date, eliglustat tartrate has been administered twice daily. The manufacturer intends to ultimately market eliglustat as a once-daily treatment. Sanofi, Paris, France Phase III trial completed. In Feb 2013, manufacturer announced positive phase III data from 2 trials, ENGAGE and ENCORE.	Blood transfusions Bone marrow transplant Enzyme replacement therapy (e.g., imiglucerase, taliglucerase alfa) Joint replacement surgery Splenectomy	Decreased spleen volume Decreased liver volume 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 late-onset lysosomal acid lipase deficiency	Patients in whom late-onset lysosomal acid lipase (LAL) deficiency has been diagnosed	LAL deficiency is a rare genetic syndrome for which no treatment is FDA approved. The LAL enzyme breaks down cholesteryl esters and triglycerides; when it is lacking, these materials build up in the liver, the gut, other organs, and blood vessel walls. The deficiency occurs less often in infants than in children, adolescents, or adults. The early onset form is also known as Wolman disease, and is rapidly fatal, usually within the 1st year. Late-onset LAL is also known as cholesteryl ester storage disease (CESD), and can lead to liver fibrosis, cirrhosis, liver failure, cardiovascular events, and premature death.SBC-102 is a recombinant protein intended to be used as enzyme replacement therapy for this disease. If approved it would be the first treatment cleared for use in LAL deficiency. In ongoing trials, SBC-102 has been given in 4 once-weekly infusions (0.35, 1.0 or 3.0 mg/kg of body weight), followed by an infusion every other week (1 or 3 mg/kg) as part of a long-term open-label extension study. Synageva BioPharma, Lexington, MA Phase III trials ongoing; FDA granted orphan drug status	Palliative treatments	Improved cholesteryl ester and triglyceride levels Improved quality of life
Epratuzumab for treatment of systemic lupus erythrematosus	Patients in whom systemic lupus erythematosus (SLE) has been diagnosed	Investigators have not found a permanent cure for SLE and current treatments provide only partial relief of symptoms, so better treatments are needed. Epratuzumab is a fully humanized monoclonal antibody which purportedly binds and modulates 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. In clinical trials, the drug is administered as a subcutaneous injection, once monthly. UCB, S.A., Brussels, Belgium Phase III trials ongoing	Belimumab Rituximab Rontalizumab	Delayed disease progression Reduced symptoms Reduced flares Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Eprodisate disodium (Kiacta) for treatment of amyloid A amyloidosis	Patients at risk of amyloid A amyloidosis, especially those in whom rheumatoid arthritis or chronic infection is present	No curative treatment for AA amyloidosis is available. 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 trial ongoing; new drug application submitted to FDA in 2006, but FDA requested more data; company initiated phase III confirmatory trial in 2010 to address this concern	Biologics Immunosuppressants Supportive care 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
Exon-skipping agent (Eteplirsen, AVI-4658) for treatment of Duchenne muscular dystrophy	Patients in whom Duchenne muscular dystrophy (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 orthotic 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. Sarepta Therapeutics, Inc., Cambridge, MA (formerly AVI BioPharma, Inc., Bothell, WA) Phase IIb trial complete; phase III trial planned; in 2007, FDA granted orphan drug status	Corticosteroids Beta-2 agonists Orthotic devices Physical therapy Respiratory support devices	Delayed or halted muscle degeneration Reduced symptoms 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
Extended-release cysteamine bitartrate (Procysbi) for treatment of nephropathic cystinosis	Patients in whom nephropathic cystinosis has been diagnosed	Nephropathic cystinosis disease is characterized by the abnormal transport of cystine out of lysosomes, which leads to renal failure, growth failure, rickets and fractures, photophobia, and blindness. Poor patient adherence with conventional treatment because of dosing frequency (4 times a day) and side effects has led to complications for patients. Procysbi is an enteric-coated, delayed-release, microbead formulation of cysteamine bitartrate that is intended to reduce gastrointestinal adverse events associated with immediate-release cysteamine bitartrate. It requires 1/2 the number of daily doses as existing medical treatment. Cysteamine bitartrate converts cystine to cysteine and cysteamine-mixed disulfide, preventing resultant organ damage. The drug is is administered orally, 75 mg, twice daily. Raptor Pharmaceutical Corp., Novato, CA FDA approved Apr 2013 for management of nephropathic cystinosis in adults and children older than age 6	Growth hormone therapy Pharmacotherapy (e.g., Cystagon®, indomethacin) Renal transplantation Urinary loss supplementation	Improved glomerular function Reduced morbidity and mortality Improved quality of life
Glybera gene therapy for lipoprotein lipase deficiency	Patients in whom lipoprotein lipase deficiency (LPLD) has been diagnosed.	LPLD is a rare genetic disorder affecting approximately 1 in 1,000,000 individuals. Currently no treatments are available that address the underlying cause of the disease (loss of function of the lipoprotein lipase [LPL] gene). Glybera is an adeno-associated viral vector-based gene therapy product that encodes an LPL isoform intended to complement the genetic deficiency in patients with LPLD. Glybera is administered in a single series of intramuscular injections. Amsterdam Molecular Therapeutics, Amsterdam, the Netherlands Phase III trial completed. Glybera has been granted orphan drug status in the United States and Europe. In Nov 2012, it became the first approved gene therapy drug in EU.	Standard of care, including low fat diet	Improved plasma triglyceride levels Improved chylomicron (lipoprotein particle) levels

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Handheld intracranial scanner (Infrascanner, Model 1000) for detection of intracranial hematomas	Patients at risk of intracranial hematoma	About 1.7 million people sustain a traumatic brain injury (TBI) each year with direct costs and indirect costs such as lost productivity attributed to TBI reaching about $76.5 billion in the U.S. in 2000. An increase in improvised explosive device use in war has increased blast-induced TBI among U.S. soldiers, and intracranial hematomas can be particularly life threatening. These traumatic injuries can have occult signs, making them difficult to diagnose, particularly without the use of expensive, sophisticated equipment. The Infrascanner™ Model 1000 is a handheld spectroscopy device that directs near-infrared light into the skull, where it is absorbed by the blood from the intracranial hematoma. Because the blood from a hematoma absorbs light differently from vascular blood, the scanner can detect differences in optical density; it wirelessly transmits the results to a handheld computer. InfraScan Inc., Philadelphia, PA, in collaboration with the Office of Naval Research, Arlington, VA FDA approved Dec 2011. Updated model, Infrascanner Model 2000, received FDA approval Jan 2013.	Automated Neuropsychological Assessment Metrics (computerized cognitive test) Computed tomography scans MRI studies Onsite neurophysical exam	Reduced morbidity Reduced mortalityImproved quality of life
High-intensity focused ultrasound (EyeOP1 HIFU-system) for treatment of refractory glaucoma	Patients in whom refractory glaucoma has been diagnosed	Investigators have not found a cure for glaucoma, and if untreated or refractory to treatment, it leads to blindness. The EyeOP1 system is a device that uses high-intensity focused ultrasound (HIFU) and suction to deliver concentrated energy to the ciliary body of the eye. The goal of treatment is to reduce the production of aqueous humor, thus reducing intraocular pressure (IOP). EyeOP1 system contains a command center that works with a touch screen interface and a foot pedal for control. During the procedure, generators located in the command center power the ultrasound while the clinician controls a pressurized suction system. The pressure reduction system is designed to ensure fixation of the therapy device to the eye during the ultrasound treatment. This noninvasive procedure is performed in an outpatient setting while the patient is placed under general anesthesia. EyeTechCare, S.A., Rillieux la Pape, France Pilot trials completed in 2011. Multicenter unphased study ongoing in European Union.	Microbypass implant (I-stent) Pharmacotherapy (e.g., eye drops) Surgical therapy Trabectome (device)	Preserved vision Reduced IOP

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Idebenone (Catena) for treatment of Duchenne Muscular Dystrophy	Patients in whom Duchenne muscular dystrophy (DMD) has been diagnosed	Current treatments for DMD address symptoms only; additionally, patients who receive treatment still have reduced lifespans and require additional support from devices. Idebenone (Catena®/Raxone®) is a small molecule that purportedly facilitates electron transport within mitochondria. The developer asserts that maintaining correct electron balance is essential for normal energy metabolism, particularly in nerve and muscle cells, which demand more energy, making them more prone to rapid cell damage or death from mitochondrial dysfunction. Preserving mitochondrial function and protecting cells from oxidative stress might prevent cell damage and increase energy production within impaired nerve and muscle tissue in patients with DMD. Santhera Pharmaceuticals Holding AG, Liestal, Switzerland Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trial ongoing; FDA granted orphan drug status	Eteplirsen, AVI-4658 (in development) Symptom control using corticosteroids and beta-2 agonists Physical therapy Orthopedics Respiratory support (respirator/ventilators)	Delayed or halted muscle degeneration Improved quality of life Increased survival Reduced symptoms
Intranasal gel (Compleo TRT) for treatment of hypogonadism	Patients in whom hypogonadism has been diagnosed	About 13 million American men are affected by low testosterone levels, and as many as 90% go untreated. Treatment guidelines focus on restoring physiologic testosterone levels through exogenous testosterone preparations. Compleo TRT™ is a bioadhesive intranasal gel formulation of testosterone applied to the interior lateral wall of the nasal cavity, where absorption into the nasal mucosa occurs in 10–15 minutes. It is purported this targeted delivery area to the nasal mucosa will avoid skin-to-skin transference to others, an issue seen with existing topical testosterone gel preparations. Additionally, the drug-delivery system could mitigate adverse events from 1st-pass metabolism on the liver. Trimel Pharmaceuticals Corp., Mississauga, Ontario, Canada Phase III trial ongoing. Manufacturer submitted new drug application to FDA in Apr 2013	Various formulations of testosterone	Increased testosterone levels Reduced adverse events

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Intraoral Tongue-Drive Computerized System to Maneuver Electrically-Powered Wheelchairs	Patients with spinal cord paralysis, particularly from the neck down	The Tongue Drive System (TDS) is a computerized, tongue-operated, assistive neurotechnology. It consists of a lentil-sized, magnetic, tracer-stud that is embedded in a dental retainer worn in the mouth with the tracer affixed to the tongue, most commonly by piercing. The magnetic tracer-stud creates a magnetic field around the pierced glossal area, and magnetic sensors located on a wireless headset/headphones communicate with a wheelchair. In spinal cord injuries and neuromuscular diseases, the tongue is generally spared from injury because it is innervated by nerves from the brain and not the spinal cord. The tongue is also strong and does not fatigue easily, designating it the target of choice for the magnetic pierced-tongue mobility aid. The change in magnetic field (prompted by tongue movement) in the mouth is detected by the magnetic sensors on the headset, transmitting information wirelessly to a smartphone carried by the patient. The smartphone can then transmit information to a wheelchair or computer, commanding these devices to perform tasks such as wheelchair movement or daily computer tasks (e.g., email). This system can be recharged via a USB after 2 days of continuous use. A standby mechanism allows patients to perform daily tasks such as eating, sleeping, and conversing without unnecessary TDS use. According to the registered clinical trial protocol description, the TDS requires that the patient's teeth are brushed, the oral surface sterilized with chlorhexidine mouthwash, and local anesthetics applied on the tongue before clinicians pierce it with a titanium magnetic stud. Patients must undergo computer training with the TDS for the computer program to appropriately interpret and calibrate tongue movement, allowing proper control of the patient wheelchair and computer device. Georgia Institute of Technology, Atlanta Pilot trial and unphased trials 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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Laser ablation 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 about 1 million cases resistant to medical therapy. Pharmacologic therapies have helped treat epilepsy, but recurrence commonly occurs. Surgical procedures such as craniotomy may be performed, but they 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. Surgical technique being performed at additional institutions.	Pharmacotherapy (e.g., lamotrigine, levetiracetam, tiagabine, tricyclics, valproate)	Reduction or elimination of seizures
Macrophage regulator (NP001) for treatment of amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	Only a single agent (riluzole) is FDA approved for treating 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. 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. NP001 is intended to restore normal functioning of macrophages in central nervous system, reducing inflammation and normalizing the cellular environment. Administered intravenously. Neuraltus Pharmaceuticals, Inc., Palo Alto, CA Phase III trial planned; FDA granted fast-track and orphan drug statuses Aug 2011	Riluzole Supportive care	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
Masitinib (KIT tyrosine kinase inhibitor) for treatment of multiple sclerosis	Patients in whom multiple sclerosis (MS) has been diagnosed	Current treatments for MS may slow disease progression, but they are not effective in all patients, and the disease has no cure. Masitinib is a tyrosine kinase inhibitor purportedly targets the activity of mast cells, which are involved in triggering local inflammatory reactions in tissues. Masitinib purportedly selectively inhibits KIT, platelet-derived growth factor receptor, Lyn, and to a lesser extent, fibroblast growth factor receptor 3. In clinical trials, masitinib is being administered orally, 6 mg/kg of body weight, daily. AB Science S.A., Paris, France Phase IIb/III trial ongoing	Dimethyl fumarate (Tecfidera) Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b Mitoxantrone Natalizumab	Delayed disease progression Reduced symptoms Improved quality of life
Mecobalamin (E-0302) for treatment of amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	Only a single agent (riluzole) is FDA approved for treating 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. Mecobalamin (E-0302) is a methylated form of vitamin B12 proposed for parenteral therapy for ALS. Eisai Co., Ltd., Tokyo, Japan Phase II/III trials ongoing in Japan	Pharmacotherapy (e.g., riluzole) Supportive care	Increased survival rate Improved functional rating scale Increased safety Improved quality of life
Micro-bypass implant (iStent Trabecular Micro-Bypass Stent System) for treatment of glaucoma	Patients undergoing cataract surgery who are also at risk of developing glaucoma because of uncontrolled, elevated intraocular pressure (IOP)	iStent Trabecular Micro-Bypass Stent System is intended for implantation during cataract surgery in patients with or at risk of developing 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. Using this procedure avoids having to move the iris, conjunctiva, or sclera and preserves other surgical and medical options for treating glaucoma. Glaukos Corp., Laguna Hills, CA FDA approved Jul 2012 "for use in combination with cataract surgery to reduce pressure inside the eye (intraocular pressure) in adult patients with mild or moderate open-angle glaucoma and a cataract who are being treated with medication to reduce intraocular pressure." Conformité Européene (CE) marked in select nations in Europe; approved in Canada	Pharmacotherapy (e.g., eye drops) Surgical therapy Trabectome (device)	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
Mifepristone (Korlym) for treatment of endogenous Cushing's syndrome	Patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance and have failed or are not candidates for surgery	Cushing's syndrome is caused by chronic exposure to elevated levels of the hormone cortisol. Endogenous Cushing's syndrome is caused by the body's production of high levels of cortisol or a cortisol precursor (adrenocorticotrophic hormone) typically by pituitary, adrenal, or ectopic endocrine tumors. Although some tumors can be successfully treated by surgery and/or radiation therapy, patients who are ineligible for these treatments or who have persistant elevation of cortisol after treatment have no FDA-approved medical options for treatment. Mifepristone (Korlym) acts to block the cortisol receptor, potentially ameliorating the effects of elevated cortisol levels. Mifepristone is an oral medication that in clinical trials was taken once daily. Corcept Therapeutics, Inc., Menlo Park, CA Received FDA approval in Feb 2012	Ketoconazole (off label) Metyrapone (off label) Mitotane (off label)	Improved symptoms of Cushing's syndrome (e.g., diabetes, glucose intolerance, hypertension)
Migalastat hydrochloride (AT1001) for treatment of Fabry disease	Patients with Fabry disease who have either migalastat-responsive mutations in alpha-galactosidase A or are receiving enzyme replacement therapy	Current enzyme replacement therapies for Fabry disease are expensive and have been subject to recent shortages. AT1001 is a small-molecule drug that molegularly enhances the activity of alpha-galactosidase A, the enzyme that is deficient in Fabry disease. The drug 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, it is being tested as monotherapy and in combination with enzyme replacement therapy. Amicus Therapeutics, Inc., Cranbury, NJ Phase III trials ongoing. Mfr to meet with FDA to discuss approval pathway in 2nd half of 2014.	Enzyme replacement therapy Palliative treatment	Increased GL-3 levels (urine, kidney biopsy) Improved renal function (e.g., glomerular filtration rate) Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Mobile phone monitoring application (MyVision Track) for age-related macular degeneration	Patients in whom age-related macular degeneration (AMD) has been diagnosed	According to the National Eye Institute, an estimated 1.75 million people in the U.S. have received a diagnosis of AMD. The standard for monitoring AMD consists of a complete eye exam including the Amsler grid test. MyVisionTrack has the potential to fulfill an unmet need brought about by a lack of self-monitoring diagnostics for AMD. It is a mobile application provided via hand-held digital devices such as smartphones. The application purportedly enables patients with retinal eye diseases to self-monitor their vision status at home, helping them notice changes or a decline in vision that could indicate a need for medical attention. Test results are stored and automatically compared with earlier results. The results may be sent to a physician's office or a central monitoring service when a statistically significant change occurs. Vital Art and Science, Inc., Richardson, TX Pilot study completed	Complete eye exam with Amsler grid test Optical coherence tomography	Earlier intervention for vision decline Slowed vision decline Improved quality of life
Nabiximols oromucosal spray (Sativex) for treatment of multiple sclerosis spasticity and neuropathic pain	Patients in whom multiple sclerosis (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 components. 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 trial ongoing; approved in the UK, New Zealand and Canada for treating MS spasticity; approved in Canada for relief of MS-related neuropathic pain	Pharmacotherapy (e.g., nonsteroidal anti-inflammatory drugs, 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. The estimated U.S. prevalence is between 1,000 and 1,500 patients. No treatments exist to address the underlying cause of the disease; only palliative treatments are available. N-acetylgalactosamine 6-sulfatase (Vimizim) is an enzyme replacement therapy intended to treat the underlying disorder. In the pivotal phase III trial, the biologic is being administered at a dose of 2.0 mg/kg over a period of approximately 4 hours once a week or once every other week. BioMarin Pharmaceutical, Inc., Novato, CA Pivotal phase III trial preliminary data completed; Company announced FDA accepted biologics license application May 2013.	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
Neural reprogrammed autologous stem cells for treatment of amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	Only a single agent (riluzole) is 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. Neural reprogrammed stem cell therapy consists of autologous adipose–derived mesenchymal stem cells administered with the monoamine oxidase inhibitor selegeline, injected directly into the spine. Selegeline is purported to be a pre-inducer, which differentiates the stem cells into neuronal-like cells capable of regenerating neurons. Neural reprogrammed stem cell therapy purportedly not only halts disease progression but also improves motor function in patients with ALS. The therapy is administered via image-guided injection into the patient's spine. Precision StemCell (clinic), Gulf Shores, AL Procedure performed in 18 patients as of Dec 2012	Riluzole Supportive care	Increased survival Delayed disease progression Improved symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Noninvasive vagus nerve stimulation (gammaCore) for treatment-refractory migraine and cluster headaches	Patients who experience migraine or cluster headaches	Migraine and cluster headaches affect tens of millions of people each year. A variety of pharmacotherapies exists for treating headache, but many patients experience inadequate pain relief or unwanted side effects from treatments. Noninvasive neurostimulation presents a novel approach to headache prophylaxis and treatment. gammaCore is a small, portable, noninvasive vagus nerve stimulator for preventing and treating migraine and cluster headache. ElectroCore, LLC, Morris Plains, NJ Randomized controlled trials (unphased) ongoing; phase II ongoing comparing gammaCore to standard of care in cluster headache	Botox GABAergic modulators Opiates Triptans	Decreased headache pain Decreased headache symptoms Decreased headache frequency Improved quality of life
Ocrelizumab for treatment of relapsing-remitting multiple sclerosis	Patients in whom relapsing-remitting multiple sclerosis (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. It is a human monoclonal antibody intended to target CD20-positive B cells (believed to play a role in multiple sclerosis), then interact with immune system to eliminate these CD20-positive B cells. Administered via infusion, once every 6 months. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., San Francisco, CA Biogen Idec International GmbH, Zug, Switzerland Phase III trials ongoing	Dimethyl fumarate (Tecfidera) Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b Mitoxantrone Natalizumab	Decreased frequency of relapse Slowed disease progression Improved quality of life
Ocriplasmin (Jetrea) treatment for symptomatic vitreomacular adhesion including macular hole	Patients in whom focal vitreomacular 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 that join the vitreous gel to the macula; thus, intravitreal injection of ocriplasmin (Jetrea®) is a potential nonsurgical treatment for VMA. The recommended dose is 0.125 mg (0.1 mL) of the diluted solution, given by intravitreal injection to the affected eye once as a single injection. ThromboGenics NV, Heverlee, Belgium FDA approved Oct 2012 for treating symptomatic VMA	Pharmacotherapy (e.g., Macugen®) Surgical therapy	Preserved vision Reduced complications associated with surgical treatment 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 bevacizumab 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 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 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. Bevacizumab, used off label, is injected into the infant's vitreous to reduce incidence of blindness by suppressing VEGF. Genentech subsidiary of F. Hoffmann-La Roche, Ltd., Basel, Switzerland (manufacturer) BEAT-ROP cooperative (trial sponsor) Postmarket trial of off-label use completed; manufacturer is not pursuing a labeled indication	Peripheral retinal ablation with lasers (e.g., xenon, argon, diode)	Prevented recurrence of neovascularization arising from the retinal vessels Improved visual acuity
Off-label etanercept (Enbrel) 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. In many patients, the disease is refractory to current standard of care; new treatment options are needed for refractory disease. Etanercept (Enbrel®) is a soluble, dimeric form of the p75 tumor necrosis factor (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 of body weight per dose, 2 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	Corticosteroids High-dose aspirin IVIG	Improved survival Prevented increase in coronary artery diameter Prevented new coronary artery dilation/cardiac dysfunction Reduced fever

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Off-label etanercept for the treatment of chronic neurological dysfunction	Patients in whom chronic neurological dysfunction due to traumatic brain injury or stroke has been diagnosed	According to the Institute of Neurological Recovery, about 5 million people living in the U.S. today have experienced traumatic brain injury (TBI) and another 4.5 million have had a stroke. These individuals are treated with standard physical therapy and occupational therapy, but no option has been available to reduce brain swelling and inflammation. Off-label etanercept (Enbrel) has been studied for its effects on reducing brain inflammation stemming from TBI or stroke. Etanercept administered via injection purportedly neutralizes tumor necrosis factor, a chemical responsible for inflammation. Institute of Neurological Recovery, Los Angeles, CA Pilot trial completed	Anticonvulsants Antidepressants Corticosteroids Nonsteroidal anti-inflammatory drugs	Improved congnition Improved motor impairment Improved spasticity
Off-label fingolimod (Gilenya) for treatment of amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	Only a single agent (riluzole) is approved for treating ALS, and it is associated with limited efficacy in improving survival time and little to no efficacy in improving motor function. Novel therapies are urgently needed. Fingolimod (Gilenya®) is purportedly an agonist to sphingosine 1-phosphate receptors on the surface of thymocytes and lymphocytes. This mechanism of action is thought to reduce the number of circulating lymphocytes available to cause autoimmune reactions and destroy nerve tissue. Reduced inflammatory reactions against peripheral nerves could reduce ALS symptoms. Administered orally, 0.5 mg, daily. ALS Therapy Development Institute, Cambridge, MA Phase II trial registered; FDA approved for treating relapsing-remitting multiple sclerosis	Physical and speech therapy Medications for symptom management (muscle cramps, constipation, fatigue, excessive salivation, excessive phlegm, pain, depression) Riluzole (Rilutek®)	Reduced symptoms Slowed or halted disease progression 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
Off-label ketotifen for treatment of fibromyalgia	Patients in whom fibromyalgia (FM) has been diagnosed	Fibromyalgia is poorly understood and current treatment options are not effective for many patients. Increased numbers of mast cells have been observed in the skin biopsies of patients with FM. Mast cells are powerful inflammatory cells that can release chemokines and other chemical mediators, triggering inflammation and pain in the local area. Elevated levels of these mediators can be observed in the serum of patients with FM. Current FM treatments target only centrally acting pain pathways and neglect the potential for immunologic involvement on FM symptoms. Ketotifen is purportedly an antihistamine and mast cell stabilizer, which prevents mast cell degranulation (release of inflammatory meditators), which might mprove FM symptoms. Administered orally as a 1 mg tablet, once or twice daily. Indiana University-Perdue University, Indianapolis, IN Phase III trial ongoing; currently approved for preventing asthma attacks	Behavior and lifestyle modification Pharmacotherapy (e.g., duloxetine, fluoxetine, gabapentin, lorazepam, milnacipran, pregabalin, tricyclic antidepressants	Improved ability to perform daily activities Reduced pain symptoms Improved quality of life
Off-label mexiletine (Mexitil) for treatment of nondystrophic myotonia	Patients in whom nondystrophic myotonia (NDM) has been diagnosed	NDMs are rare diseases caused by mutations in skeletal muscle ion channels. NDM cause delayed muscle relaxation leading to limited functionally, stiffness, and pain. No effective treatments are available. Mexiletine (Mexitil®) is a class 1b antiarrhythmic medication purportedly has high affinity for muscle sodium channels. It purportedly reduces muscle fiber excitability caused by common NDM mutations in preclinical models. Mexiletine is administered orally, 200 mg 3 times daily. University of Kansas Medical Center, Kansas City, KS Phase II trial completed	Supportive care	Improved clinical myotonia assessment Improved handgrip Reduced stiffness, pain, weakness, and tiredness Improved quality of life
Off-label naltrexone for treatment of fibromyalgia	Patients in whom fibromyalgia has been diagnosed	Fibromyalgia is poorly understood and current treatment options are not effective for many patients. Naltrexone is an opiate antagonist purported to block the inflammatory effects of the toll-like receptor 4 (TLR-4) on glial cells. TLR-4 is purported by the investigators to be involved in pain felt by patients with fibromyalgia. Administered orally, 3.0–4.5 mg, once daily. Stanford University, CA Pilot study completed	Behavior and lifestyle modification Pharmacotherapy (e.g., duloxetine, fluoxetine, gabapentin, lorazepam, milnacipran, pregabalin, 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
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 purportedly reduces the aggregation of alpha-synuclein and the associated neurodegeneration in a preclinical model; it also disaggregates preformed alpha-synuclein fibrils. Mayo Clinic, Rochester, MN Phase III trial completed Jan 2013	Pharmacotherapy (e.g., anticholinergics, beta blockers, monoamine oxidase inhibitors, vasoconstrictors)	Improved symptoms based on Unified Multiple System Atrophy Rating Scale Reduced neurodegeneration Improved quality of life
Oral estriol (Trimesta) for treatment of multiple sclerosis	Female patients in whom relapsing-remitting multiple sclerosis (RRMS) has been diagnosed	Current treatments for RRMS can slow disease progression, but the disease has no cure and more effective treatments are needed. Estriol is an estrogen that is produced in the placenta during pregnancy and is thought to be involved in maintaining maternal immune tolerance for the fetus. Estriol purportedly induces spontaneous remission of helper T-cell, type-1-mediated autoimmune responses and may have other beneficial immunomodulatory effects in women with MS during pregnancy. Oral administration of exogenous estriol (Trimesta™) is postulated by the manufacturer to improve MS symptoms. Administered orally, 8 mg, daily. Synthetic Biologics, Inc., Ann Arbor, MI Phase II/III trial ongoing	Dimethyl fumarate (Tecfidera) Fingolimod Glatiramer acetate Interferon beta-1a Interferon beta-1b Mitoxantrone Natalizumab	Reduced frequency of relapse Slowed disease progression Improved quality of life
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. An increased prevalence of disease is seen in people of African and Mediterranean descent; about 1 in 500 African-American children born have sickle cell anemia. Despite advancements in managing complications of SCD (i.e., pain crises), the only drug 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. SCFAD 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; phase II trial ongoing; FDA granted orphan drug status	Allogeneic hematopoietic stem cell transplantation Antioxidant therapy Azacitidine Decitabine butyrate Gardos channel inhibition Gene therapy 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
Pasireotide (Signifor) for treatment of Cushing's disease	Patients who have Cushing's disease caused by an adreno-corticotropic hormone (ACTH)-secreting pituitary tumor	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 were available, and not all patients respond to surgical or radiotherapy treatment. Pasireotide (Signifor) is a subcutaneously administered somatostatin analog that activates a wide range of somatostatin receptors and has demonstrated the ability to inhibit ACTH secretion. Administered as a subcutaneous injection twice daily; available in 3 dosages: 0.3 mg/dL; 0.6 mg/dL; 0.9 mg/dL. Novartis International AG, Basel, Switzerland FDA granted priority review, fast-track, and orphan drug statuses; FDA approved Dec 2012 for patients who do not benefit from surgery; FDA required 3 postmarket studies. Postmarket studies ongoing.	Pharmacotherapy (e.g., ketoconazole, metyrapone, mitotane) Radiation therapy Surgical therapy	Reduced ACTH levels Reduced morbidity from excess cortisol Improved quality of life
Pasireotide (Signifor) for treatment of gastrointestinal injuries from acute radiation exposure	Patients with gastrointestinal (GI) injuries from acute radiation syndrome (ARS)	ARS is a disease caused by harmful exposure to high doses of ionizing radiation, resulting in bone marrow, cardiovascular, GI, respiratory, and skin complications. Few treatments exist for irradiated bone marrow, and none exist for irradiated GI organs. Additionally, no treatments are FDA approved for use as medical radiation countermeasures for preventing or treating ARS. Pasireotide is a cyclohexapeptide engineered to bind to multiple somatostatin receptor subtypes to mimic the actions of natural somatostatin. For ARS, pasireotide is intended to reduce pancreatic secretions known to invade the irradiated intestinal wall and induce an inflammatory response. Novartis International AG, Basel, Switzerland (manufacturer) University of Arkansas for Medical Sciences, Little Rock (investigator) Clinical trial phase not reported; in Sept 2011, the U.S. Department of Health and Human Services' Biomedical Advanced Research and Development Authority (BARDA) awarded $56.3 million in grants to 4 companies and the University of Arkansas to develop ARS treatments. Novartis is providing the drug to the university for this 2-year study; data generated are intended to form the basis for a new drug application that Novartis will submit to FDA	Pharmacotherapy (e.g., antibiotics, hematopoiesis-stimulating agents) Stem cell therapy	Prevented or reduced GI flora Decreased mortality

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	Phenylketonuria is an inherited disorder in which an enzyme that is needed to break down essential amino acid phenylalanine is missing. Pegylated recombinant phenylalanine ammonia lyase (PEG-PAL) might offer a new treatment; the drug is intended to reduce levels of phenylalanine in patients unresponsive to Kuvan®. Administered by injection, 1–3 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
Pimavanserin for treatment of Parkinson's disease psychosis	Patients in whom Parkinson's disease psychosis has been diagnosed	Parkinson's disease psychosis is a debilitating disorder associated with increased caregiver distress and burden, nursing home placement, and increased mortality.. No therapies have been FDA approved to treat Parkinson's disease psychosis. Antipsychotic drugs may be used off label to treat the psychosis; however, antipsychotic drugs block dopamine receptors, which can negate dopamine replacement therapy, leading to worsening of Parkinsonian motor symptoms. Additionally, antipsychotic drugs currently used are associated with a number of problematic adverse events in elderly patients with Parkinson's disease, especially elderly patients with dementia-related psychosis. Pimavanserin is a small molecule purported to selectively block the activity of the serotonin family 5-HT2A receptor, which is thought to play an important role in Parkinson's disease psychosis. Pimavanserin is intended to selectively target the 5-HT2A, receptor without compromising motor control or while maintaining acceptable tolerability. In a clinical trial, pimavanserin has been administered orally, 10–40 mg, once daily. ACADIA Pharmaceuticals, Inc., San Diego, CA Phase III trial completed; additional trials ongoing	Antipsychotics (off label)	Reduced symptoms Reduced side effects compared with other drugs Improved quality of life
Preladenant for treatment of moderate to severe Parkinson's disease	Patients in whom moderate to severe Parkinson’s disease (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; new interventions are needed. 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	Levodopa/carbidopa MOA-B inhibitors	Improved symptoms (motor function) Slowed disease progression Preserved independence Delayed need for assisted care

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pridopidine (Huntexil) for treatment of Huntington's disease	Patients in whom Huntington's disease (HD) has been diagnosed	No cure exists for HD, and current therapies only help to manage emotional and motor symptoms associated with the disease. Pridopidine (Huntexil®) is a small-molecule, dopamine stabilizer that purportedly increases or decreases dopamine to healthy levels in patients with HD. Pridopidine purportedly contrasts with neuroleptics that reduce dopamine activity regardless of baseline level. Administered orally, at doses of 45 or 67.5 mg, twice daily. Teva Pharmaceutical Ltd., Ballerup, Denmark Phase III trials completed; FDA granted orphan drug status	Pharmacotherapy (e.g., tetrabenazine, antidepressants, antipsychotics)	Improved clinical global impression of change, cognitive function, behavior, and symptoms of depression and anxiety Improved voluntary motor function
Prosthetic arm to restore natural arm functions	Patients with trauma-induced amputations of the upper limbs	This advanced prosthetic arm technology comprises 2 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). U.S. Defense Advanced Research Projects Agency, Arlington, VA (commissioned and funded research) 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 move innovative devices to market within 4 years of start of trials	Conventional prosthetic arms	Significant restoration of limb function compared with function of current prosthetic devices

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Rebiscan pediatric vision scanner for identifying children with possible strabismus or amblyopia	Pediatric patients who need screening for amblyopia ("lazy eye") or strabismus (misaligned eyes)	The leading causes of preventable monocular vision loss in children are amblyopia ("lazy eye") and strabismus (misaligned eyes). Currently, early detection of these conditions can be difficult because standard screening methods lack sufficient sensitivity and specificity, thereby missing cases of children who should be referred for further evaluation and possibly treatment. As many as half of affected children are not identified until school age. If found early, amblyopia and strabismus are fully treatable. The Rebiscan Pediatric Vision Scanner (PVS) purports to provide improved screening for these conditions through its portable device. It is intended as a screening tool for use in a pediatrician's office to identify children who should be referred to a specialist for further evaluation. The device uses proprietary technology called retinal birefringence scanning to screen for amblyopia and strabismus. Rebiscan, Inc., Cambridge, MA Unphased trials completed	Standard vision examination Photoscreening	Reduced vision loss Improved quality of life
Wearable artificial kidney (WAK) 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 Xcorporeal, Inc. (purchased by Fresenius Medical Care Holdings AG & Co. KGaA) FDA selected this technology in Apr 2012 as 1 of 3 technologies to be piloted for its new innovation pathway designation. Phase I study completed by developers Royal Free London NHS Foundation Trust (formerly Royal Free Hampstead NHS Trust) and Xcorporeal, Inc. in the United Kingdom; 5 randomized controlled trials planned, but none registered at National Clinical Trials database of Jul 2013	Conventional home dialysis systems Kidney transplantation	Adequate filtration of toxins from kidneys Improved mobility Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Wearable battery powered exoskeletons to enable walking after spinal cord injury (ReWalk and Ekso systems)	Patients with spinal cord injury resulting in paraplegia and need for wheelchair use	Conventional manual and powered wheelchairs are the primary assistive devices to restore some degree of mobility in people with paraplegia. However, these devices do not help users walk or climb stairs. Wearable powered exoskeletons in development, the ReWalk-I™ (institutional) and ReWalk-P™ (personal use), and Ekso systems could provide greater mobility and freedom to persons with paraplegia from spinal cord injury. The ReWalk system comprises a set of computer-controlled, motorized leg braces that restore the ability to walk with crutches to patients with paraplegia who are able to use their hands and shoulders to walk with crutches and who have good bone density and cardiovascular health. The Ekso system is a described by the manufacturer as a ready-to-wear, battery-powered exoskeleton worn over the user's clothing. The device weighs 45 lb, but purportedly transfers its load to the ground so the patient doesn't bear the weight. The system is adjustable to fit people weighing 220 pounds or less with a height between 5 feet, 2 inches, and 6 feet, 2 inches, and with partial upper body strength. The system has 3 walk modes. The patient provides the balance and proper body positioning. Argo Medical Technologies, Ltd., Yokneam Illit, Israel (ReWalk system) distributed in the U.S. by Bionics Research, Inc., Mt. Laurel, NJ Ekso Bionics, Richmond, CA (Ekso system) The ReWalk-I system is FDA-listed for institutional use only. The company registered the ReWalk-P system for personal use with FDA for routine use outside of institutions and it became available in late 2012. The Ekso system was available through 21 U.S. rehabilitation centers as of Jul 2013. It received the CE mark in May 2012	Wheelchairs	Improved mobility Improved independence Improved quality of life
Recombinant porcine factor VIII (OBI-1) for treatment of acquired hemophilia	Individuals with acquired hemophilia A who develop immune reaction to human factor VIII	About 15% to 30% of patients with acquired hemophilia develop immune reaction to recombinant human coagulation 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 2–3 hours for the 1st 24 hours of treatment. Inspiration Biopharmaceuticals, Inc., Laguna Niguel, CA Phase II/III trial ongoing	Human coagulation factor VIIa	Adequate control of bleeding episodes

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
RenalGuard for prevention of contrast-induced nephropathy	Patients at risk of contrast-induced nephropathy (CIN)	The only standard treatment for CIN in high-risk patients with chronic kidney disease (CKD) is hydration and avoidance of nephrotoxic drugs. The RenalGuard System™ is a closed loop, single-use, software-controlled console that automatically matches fluid loss and replacement to minimize overhydration or dehydration in patients during medical procedures in which creating and maintaining high urine output is essential. The single-use urine collection set is connected to a Foley catheter and an infusion set is connected to a standard intravenous catheter. The console is managed by monitoring software that measures urine volume in the collection set and matches patient urine output with an equal volume of hydration fluid. PLC Systems, Inc., Milford, MA Pivotal trial completed. In Jun 2013, manufacturer announced receipt of expanded coverage for RenalGuard patent to include more toxic agents in additional settings.	Pharmacotherapy (e.g. deferoxamine) Hydration	Reduced occurrence and complications of CIN Reduced incidence of CIN in high-risk patients with CKD Improved quality of life
Retinal prosthesis system (Argus II) for treatment of retinitis pigmentosa	Patients with retinitis pigmentosa (RP) and a functioning optic nerve	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 1 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. The device is intended to restore a level of vision that is sufficient to improve patients' ability to function more independently. Second Sight® Medical Products, Inc., Sylmar, CA FDA approved Feb 2013; Conformité Européene (CE) marked in 2011	Standard of care No other treatments available	Improved visual acuity Improved quality of life and independence

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Smartpatch stimulator for treatment of poststroke pain	Patients in whom stroke has been diagnosed	Approximately 10% of stroke survivors experience mild to severe pain after the stroke. It can be acute or chronic. The Smartpatch peripheral nerve stimulation system is proposed as a minimally invasive therapy during which a fine wire from the patch is placed through the skin near the selected nerves to relieve pain. It purportedly differs from existing electrical stimulation modalities for treating pain because it is not an implanted stimulator device and is placed near nerves rather than touching them. SPR Therapeutics, LLC, Cleveland, OH Pivotal unphased trial currently recruiting participants; Conformité Européene (CE) marked Jan 2013	Anticonvulsants Antidepressants Corticosteroids Nonsteroidal anti-inflammatory drugs	Reduced pain Improved quality of life
SMT C1100 for treatment of Duchenne muscular dystrophy	Patients in whom Duchenne muscular dystrophy (DMD) has been diagnosed	Current treatments for DMD may reduce symptoms, but do not address the underlying cause of disease. SMT C1100 is a small molecule purported to upregulate utrophin, a naturally occurring protein that has a similar function to dystrophin. Utrophin is purported to be produced only during fetal development. The manufacturer postulates that if utrophin production can be maintained, it could act as a substitute for dystrophin to maintain muscle function. SMT C1100 is intended to complement other therapeutic approaches in development. Summit plc, Oxfordshire, UK Phase I trial ongoing; FDA granted orphan drug status	ACE-031 Corticosteroids Beta-2 agonists Eteplirsen GSK-2402968 Orthopedic devices Physical therapy Respiratory support devices	Decreased muscle degeneration Decreased need for supportive devices Improved quality of life Improved symptoms Increased survival
SOLX gold shunt for treatment-refractory glaucoma	Patients in whom treatment-refractory glaucoma has been diagnosed	Investigators have not found a cure for glaucoma, and if untreated or refractory to treatment, it leads to blindness. The SOLX® Gold Shunt gold implant uses the eye's natural pressure differential to reduce intraocular pressure (IOP). The device is a flat, perforated, rectangular-shaped implant inserted between choroid layer and sclera in the trabecular meshwork area. It is differentiated from other surgical glaucoma options because it purportedly reduces IOP without creating a bleb, which is a source of serious complications. SOLX, Inc., Waltham, MA Phase III trials ongoing; approved in Canada and parts of Europe	Pharmacotherapy (e.g., eye drops) Surgical therapy Trabectome (device)	Reduced IOP Preserved vision

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Subepidermal moisture scanner (SEM) for prevention and early detection of decubitus ulcers	Patients at risk of developing decubitus ulcers	According to The Joint Commission, about 2.5 million patients are treated for pressure ulcers in acute-care hospitals each year, and the incidence is growing at a significant rate. Prevention and early diagnosis remain a challenge; visual assessment is the current standard of detection. The Sub-Epidermal Moisture (SEM) scanner is a handheld device intended to measure a tissue's dielectric properties and estimate the subepidermal moisture to detect potential decubitus ulcers before they become visible. This device can transmit data wirelessly to a storage system for analysis. Bruin Biometrics, LLC, Los Angeles, CA Pilot trial completed; other trials ongoing	Visual assessment	Prevention or early treatment of decubitus ulcers Reduced morbidity and mortality from complications
Subretinal transplantation of human embryonic stem cell-derived retinal pigment epithelium cells for treatment of Stargardt macular dystrophy	Patients in whom Stargardt macular dystrophy has been diagnosed	Stargardt macular degeneration is a genetic eye disorder affecting the retina that causes progressive vision loss. The macular degeneration affects a small area near the center of the retina called the macula. Disease prevalence is an estimated 1 in 8,000 to 10,000 individuals, and no treatment is available. Subretinal transplantation of retinal pigment epithelial cells derived from human embryonic stem cells is under study to determine its safety and tolerability for halting or preventing the disease. Treatment is administered by subretinal injection of 50,000, 100,000, 150,000 or 200,000 cells. Advanced Cell Technology, Inc., Santa Monica, CA Phase I/II trials ongoing; FDA and EU granted orphan drug status	No treatment is available	Improved vision Reversed loss of central vision Improved functional status 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 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 are available. Given intravenously, in combination with albumin. Ikaria, Inc., Clinton, NJ Phase III trail ongoing	Liver transplantation Pharmacotherapy (e.g., dopamine, misoprostol, vasoconstrictors)	Confirmed HRS reversal Increased survival to time of transplantation Increased rates of 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
Tirasemtiv (CK-2017357) for treatment of amyotrophic lateral sclerosis	Patients in whom amyotrophic lateral sclerosis (ALS) has been diagnosed	The average life expectancy of a patient with ALS is 3–5 years, and only 10% of patients survive for more than 10 years. Only a single treatment option exists, and it has limited efficacy. Tirasemtiv is purportedly a fast skeletal muscle troponin activator. Tirasemtiv is purported to selectively activate the fast skeletal muscle troponin complex by increasing its sensitivity to calcium, leading to an increase in skeletal muscle force. Cytokinetics, Inc., South San Francisco, CA Phase II trials ongoing; FDA granted orphan drug status	Riluzole (Rilutek®)	Improved patient/investigator global assessment of symptoms
Transthyretin stabilizer (tafamidis, Vyndaqel) for treatment of transthyretin familial amyloid polyneuropathy	Patients in whom transthyretin familial amyloid polyneuropathy (TTR-FAP) has been diagnosed	TTR-FAP is a genetic neurodegenerative disease that can also affect the heart and kidneys. The disease is usually fatal within a decade in the absence of a liver transplant. Transthyretin (TTR) is a transport protein for thyroxine and retinol. It can be amyloidogenic: mutation of the TTR gene can lead to the development of unstable TTR, which forms amyloid fibrils that are deposited in various organs. Tafamidis (Vyndaqel®) purportedly is a transthyretin stabilizer intended to treat TTR-FAP. Tafamidis purportedly binds to the TTR protein to promote the stabilization of functional tetrameric molecules, slowing the formation of misfolded amyloid fibrils. Pfizer, Inc., New York, NY Phase III trials ongoing; FDA granted orphan drug status; new drug application submitted to FDA Apr 2011; FDA issued a refusal to accept letter in Jun 2012 and asked the company to conduct another trial	Supportive therapy	Improved Neuropathy Impairment Score TTR stabilization
Vesicular monoamine transporter type 2 inhibitor (NBI-98854) for treatment of tardive dyskinesia	Patients with schizophrenia who have been given a diagnosis of tardive dyskinesia	Tardive dyskinesia, involuntary movement of face or trunk muscles, can develop in patients taking long-term dopaminergic antagonist medications. Only 1 treatment is approved for this condition, and the development of the disease is not yet well understood. More and better treatments are needed. NBI-98854 is a vesicular monoamine transporter type 2 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 2 Phase II trials completed, 1 Phase II trial ongoing, additional Phase IIb trial completed enrollment in Jul 2013. FDA granted fast-track status Jan 2012	Pharmacotherapy (e.g., benzodiazepines, Cogentin®, omega-3 fatty acids, Mirapex®, Tarvil®, tetrabenazine)	Reduced abnormal involuntary movements

Table 9. AHRQ Priority Condition: 09 Infectious Disease, Including HIV-AIDS: 43 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Anthrax antitoxin monoclonal antibody raxibacumab (ABthrax) for treatment of inhalation anthrax	Patients suspected of having inhaled anthrax spores	Patients can be unaware that they have inhaled anthrax spores, leading to late treatment that may render antibiotics ineffective; treatments for later- stage inhalation anthrax are needed. Raxibacumab (ABthrax™) is a fully human, antitoxin, monoclonal antibody purported to treat inhalation anthrax by inhibiting the activity of the protective antigen of anthrax toxin, inhibiting the protein's ability to facilitate pathogenesis. Human Genome Sciences, Rockville, MD FDA approved Dec 2012 for treating adult and pediatric patients with inhalational anthrax infection due to *Bacillus anthracis* in combination with appropriate antibacterials and for prevention of inhalational anthrax when other therapies are not available or not appropriate	Anthrax vaccine Antibiotics	Protection against inhalation anthrax Rapid resolution of symptoms
Asunaprevir (NS3 protease inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic infection with hepatitis C virus (HCV) has been diagnosed	HCV treatment options are not effective in all patients and are associated with frequent adverse events, a long duration of therapy, and low patient adherence. Effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. Asunaprevir is an 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 NS5A inhibitor BMS-914143 with or without the standard-of-care pegylated interferon plus ribavirin (IFN/RBV). Bristol-Myers Squibb, New York, NY Phase III trials ongoing; FDA granted breakthrough designation for asunaprevir in combination with daclatasvir (NS5A inhibitor) BMS-791325 (non-nucleoside polymerase inhibitor)	Boceprevir IFN/RBVTelaprevir	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
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 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 purportedly eliminates ionization in physiologic pH, making PMOs uncharged. AVI-6002 uses the manufacturer's PMOplus™ technology to add position-specific, molecular charges to the PMO backbone, which purportedly improves 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) time. Sarepta Therapeutics, Inc., Cambridge, MA (purchased developer AVI BioPharma, Inc.) Phase I trial completed; manufacturer to file for FDA approval through the animal efficacy rule after completing studies in healthy human subjects; FDA granted fast-track status Sept 2012	Supportive care	Increased symptom resolution Reduced mortality
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 purportedly 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 purportedly improves 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) time. Sarepta Therapeutics, Inc. Cambridge, MA (purchased developer AVI BioPharma, Inc), with support from the U.S. Army Medical Research Institute for Infectious Diseases, Frederick, MD Phase I trial completed; manufacturer to file for approval through the animal efficacy rule after completing studies in healthy human subjects; FDA granted fast-track status Sept 2012	Supportive care	Improved symptom resolution Reduced mortality

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 hepatitis C virus (HCV) infection 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 nonnucleoside 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, 3 times a day; may also be administered in an IFN-free regimen with the faldaprevir and RBV Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing; FDA granted fast-track status in combination with faldaprevir (NS3/4 protease inhibitor) in an interferon-free combination	Boceprevir IFN/RBV 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
CMX001 for prevention of cytomegalovirus after hematopoietic stem cell transplant	Patients who recently received a hematopoietic stem cell transplant (HSCT)	In immunocompromised patients, such as those who have undergone HSCT, cytomegalovirus (CMV) infections are recognized as a significant cause of morbidity and mortality. Immunocompromised pediatric HSCT patients are particularly susceptible to serious and/or fatal CMV infections, for which no treatments are approved. CMX001 is purported to be a broad spectrum, oral antiviral for treating or preventing 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 treating CMV infection. PIM technology covalently modifies the cidofovir molecule so that it mimics a naturally occurring phospholipid metabolite that can utse 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 III trial planned; FDA granted fast-track status	Cidofovir (off label) Ganciclovir	Decreased rate of organ rejection Increased time to organ rejection Reduced HCMV load

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Copper surfaces in the intensive care unit for prevention of hospital-acquired infections	Patients admitted to an intensive care unit (ICU)	Hospital-acquired infections (HAIs) are the 4th 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 purportedly controls bacterial growth and lowers the rates of infections acquired in the ICU. Bacterial reduction rates are intended to achieve the same outcome as current "terminal cleaning" practices, though use of copper surfaces is not intended to obviate the need for all other infection prevention and control measures. International Copper Association, New York, NY Various manufacturers; commercially available; studies at hospitals ongoing	Terminal cleaning of standard surfaces	Reduced costs associated with HAIs Reduced infection rates Reduced bacteria isolated from surfaces Reduced morbidity and mortality from HAIs
Crofelemer (Fulyzaq) for treatment of HIV-1-associated diarrhea	Patients on HIV antiretroviral therapy with chronic diarrhea	About 40% of patients in the U.S. with HIV-1 infections have chronic diarrhea, which can reduce adherence to antiretroviral regimens. Effective antidiarrheals that do not cause adverse reactions with antiretrovirals are needed. Crofelemer (Fulyzaq™) treats diarrhea by inhibiting the cystic fibrosis transmembrane conductance regulator ion channel, which is responsible for transporting chloride ions into the intestinal lumen, drawing water into the bowel. It is thought to work by blocking chloride secretion, thereby reducing the high volume water loss seen in HIV-associated diarrhea. The drug is a delayed release formulation, and the dosage in the approved product labeling is 125 mg, twice daily. Salix Pharmaceuticals, Inc., Raleigh, NC (distributor)Napo Pharmaceuticals, Inc., San Francisco, CA (licenser) FDA approved Dec 2012 for "symptomatic relief of non-infectious diarrhea in adult patients with human immunodeficiency virus (HIV)/ acquired immune deficiency syndrome (AIDS) on anti-retroviral therapy (ART)."	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
Cyclophilin inhibitor alisporivir for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (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 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 purportedly acts as a host-targeted antiviral with enhanced cyclophilin binding but no immunosuppressive activity, which might be due to the inability of the alisporivir-cyclophilin complex to bind calcineurin which modulates proinflammatory lymphocyte signaling. Debiopharm, S.A., Lausanne, Switzerland Novartis International AG, Basel, Switzerland Phase III trials ongoing; FDA granted fast-track status	Boceprevir Pegylated interferon plus 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
Daclatasvir (NS5A inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C infection (HCV) has been diagnosed	HCV treatment options are not effective in all patients and are associated with frequent adverse events, a long duration of therapy, and low patient adherence. Effective treatments that improve clinical outcomes and safety in a shorter time are needed. Daclatasvir is a 1st-in-class inhibitor of HCV NS5A, which is a multifunctional, nonenzymatic endoplasmic reticulum (ER) membrane-associated phosphoprotein. This protein 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 known to be required for viral replication. Researchers propose that daclatasvir 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 interferon (IFN) lambda, or asunaprevir and BMS-791325. Administered orally, 60 mg, once daily. Bristol-Myers Squibb, New York, NY Phase III trials ongoing; FDA granted breakthrough status for daclatasvir in combination with asunaprevir (NS3 protease inhibitor) and BMS-791325 (non-nucleoside polymerase inhibitor)	Boceprevir Sofosbuvir (investigational) Pegylated IFN plus 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
Extracorporeal membrane oxygenation for treatment of serious influenza infections	Patients in whom serious influenza infection has been diagnosed	Influenza continues to cause significant morbidity and mortality in susceptible patients; better treatments are needed. Extracorporeal membrane oxygenation (ECMO) has been contraindicated in patients with serious infections; however, recent trials in patients with H1N1 influenza suggested some utility for the procedure. ECMO involves cannulas placed in large blood vessels to provide access to the patient's blood. An ECMO machine continuously pumps blood from the patient through a membrane oxygenator that imitates the gas exchange process of the lungs, and oxygenated blood is then returned to circulation. Management of the ECMO circuit requires a specially trained team. Far Eastern Memorial Hospital, Taipei, Taiwan, and National Taiwan University Hospital, Taipei Unphased trial ongoing; could be implemented readily	Ventilation support Treatment of comorbidities	Reduced morbidity Reduced mortality
Faldaprevir (NS3/4 protease inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic infection with hepatitis C virus (HCV) has been diagnosed	HCV treatment options are not effective in all patients, are associated with frequent adverse events, a long duration of therapy, and low patient adherence. Effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. Faldaprevir is a NS3/4 protease inhibitor intended to block the activity of HCV protease, preventing functional viral particles from cleaving and maturing. Administered orally, 120 or 240 mg, once daily in combination with the standard-of-care pegylated interferon plus ribavirin (IFN/RBV); may also be administered in an IFN-free regimen with the polymerase inhibitor BI-207127 and RBV. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing; FDA granted fast-track status in combination with standard of care and in IFN-free combination with BI-207127	Boceprevir IFN/RBV 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
Fecal microbiota transplantation for treatment of recurrent *Clostridium difficile* infection	Patients with recurrent *Clostridium difficile* infection (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 in 1 of several ways (e.g., colonoscopy, nasogastric tube) with the intended purpose of introducing healthy flora to the intestinal tract to prevent recurrence of CDI. Multiple trials ongoing at various U.S. medical centers; fecal transplantation is considered a biological product and a drug by FDA. An investigational new drug (IND) application is required to treat patients with *C. difficile* infection. However, FDA intends to exercise enforcement discretion regarding the IND requirements to use FMT for treating *C. difficile* infection not responding to standard therapies provided physicians obtains adequate informed consent.	Fidaxomicin Metronidazole Vancomycin	Reduced diarrhea Reduced dehydration Reduced reinfection
Ledipasvir (NS5A inhibitor) for treating chronic hepatitis C infection	Patients in whom chronic hepatitis C virus 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. Ledipasvir is an oral NS5A inhibitor purported to block the ability of the viral NS5A protein to attach to the endoplasmic reticulum of infected hepatocytes, which is thought to be required for the formation of functional viral particles. Ledipasvir could inhibit the activity of all HCV genotypes. Administered orally 30 mg, once daily. Intended to be used in combination with sofosbuvir in a single pill. Gilead Sciences, Inc., Foster City, CA Phase III trials ongoing	Boceprevir Pegylated interferon plus 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
Letermovir (AIC246) for prevention of human cytomegalovirus reactivation after organ transplantation	Patients undergoing organ transplantation who could be at risk of reactivation of human cytomegalovirus (HCMV)	HCMV is the primary cause of morbidity and mortality during the 1st 6 months after a patient receives an organ transplant. Ganciclovir is considered expensive and not appropriate or effective in preventing HCMV reactivation in many patients. Letermovir is a quinazoline purportedly targets the HCMV terminase enzyme. The terminase enzyme is crucial for concatemeric HCMV DNA cleavage during the replication process and its subsequent packaging into the HCMV virions. This is purported to be a novel mechanism of action that should remain effective against strains resistant to current therapy targeting the HCMV DNA polymerase. In a clinical trial, letermovir was administered orally, 120 or 240 mg, once daily AiCuris GmbH & Co. KG, Wuppertal, Germany Merck & Co Inc., Whitehouse Station, NJ Phase II trial complete; FDA granted orphan drug and fast-track statuses	Cidofovir (off label) Ganciclovir	Decreased rate of organ rejection Increased time to organ rejection Reduced HCMV load
Nitazoxanide for treatment of 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 anti-infective 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, the drug is being administered orally, 300 mg, twice a day. Romark Laboratories, L.C., Tampa, FL Phase III trial ongoing	Oseltamivir (Tamiflu®) Zanamivir (Relenza®)	Reduced complications of influenza infection Shorter duration of symptoms
Nitro-dihydro-imidazooxazole (delamanid) for treatment of tuberculosis	Patients in whom tuberculosis (TB) has been diagnosed	TB has developed resistance to existing antibiotic therapies and treatment is further complicated by a lengthy regimen. Treatments that can improve outcomes in antibiotic-resistant infections and shorten treatment duration are needed. Delamanid purportedly addresses these unmet needs. As a nitro-dihydro-imidazooxazole derivative, it purportedly inhibits the synthesis of mycolic acid, which is a component of the TB bacteria cell wall. Delamanid is administered orally, 100 mg, twice daily, or 200 mg, once daily, in addition to standard TB regimens. Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan Phase III trial ongoing	Bedaquiline (Sirturo™) Ethionamide (Trecator®) Kanamycin Ofloxacin (Floxin®) PA-824, a nitroimidazole (in development) Pyrazinamide	Improved patient adherence with therapy Reduced spread of infection Reduced time to clinical response Resolution of active TB infection Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Nitroimidazole (PA-824) for treatment of pulmonary tuberculosis	Patients in whom multidrug-resistant/drug susceptible tuberculosis (TB) has been diagnosed	TB has developed resistance to existing antibiotic therapies and treatment is further complicated by a lengthy regimen. Treatments that can improve outcomes in antibiotic-resistant infections and shorten treatment duration are needed. PA-824 is a nitroimidazole, a class of antibacterial agents that has activity in vitro against all tested drug-resistant clinical isolates. It is intended to shorten treatment time and simplify treatment. Taken orally. Novartis International AG, Basel, Switzerland Bayer AG, Leverkusen, Germany 2 phase II trials completed; additional phase I trial ongoing; FDA granted orphan drug and fast-track statuses for treating TB	Ethambutol Ethionamide Isoniazid Kanamycin Ofloxacin Pyrazinamide Rifampicin	Shorter duration of therapy Simpler dosing Improved adherence Safer method of action Lower cost of overall treatment
Nonnucleoside polymerase inhibitor (ABT-333) for treatment of chronic hepatitis C infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	HCV treatment options are not effective in all patients, are associated with frequent adverse events, a long duration of therapy, and low patient adherence. Effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. ABT-333 is a nonnucleoside NS5B polymerase inhibitor intended to bind HCV RNA-dependent RNA polymerase and inhibit replication of the viral genome. It is administered orally 250 mg twice daily. AbbVie Inc., North Chicago, Illinois Phase III trials ongoing; FDA granted breakthrough designation for treating HCV genotype 1 in combination with ABT-450/r, ABT-267, with and without ribavirin	Boceprevir Pegylated interferon plus 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
NS3/4A protease inhibitor and ritonavir (ABT-450/ritonavir) for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	HCV treatment options are not effective in all patients, and are 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. ABT-450/r is an NS3/4A HCV protease inhibitor co-administered with ritonavir and is under study in many clinical trials in combination with other HCV treatments. It is administered as ABT-450 (tablets) dosed 150 mg once daily with ritonavir (capsules) dosed 100 mg once daily. AbbVie Inc., North Chicago, Illinois Enanta Pharmaceuticals, Inc., Watertown, MA Phase III trials ongoing; FDA granted breakthrough designation for treating HCV genotype 1 in combination with ABT-333, ABT-267, with and without ribavirin	Boceprevir Pegylated interferon plus 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
NS5A inhibitor (ABT-267) for treating chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus 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. ABT-267 is an oral NS5A inhibitor purported to block the ability of the viral NS5A protein to attach to the endoplasmic reticulum of infected hepatocytes, which is thought to be required for the formation of functional viral particles.ABT-267 could inhibit the activity of all HCV genotypes. Administered orally 25 mg, once daily. AbbVie Inc., North Chicago, Illinois Phase III trials ongoing; FDA granted breakthrough designation for treating HCV genotype 1 in combination with ABT-450/r, ABT-333, with and without ribavirin	Boceprevir Pegylated interferon plus 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
Off-label maraviroc (Selzentry) for prevention of HIV infection	People at high risk of contracting HIV infection	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments. HIV-drug resistance, high lifelong cost of therapy, and adverse events continue to suggest that prophylactic HIV measures be pursued for individuals at high risk of contracting HIV infection. Maraviroc (Selzentry®) is a chemokine receptor-5 antagonist (CCR-5) that is approved for treating CCR-5-tropic HIV-1 in combination with other antiretroviral agents. CCR-5 is expressed on the surface of T cells and has been identified as 1 of the 2 co-receptors needed for HIV to enter host cells. By preventing HIV from entering T cells, maraviroc could prevent HIV infection; thus, the drug is considered an entry inhibitor. It is intended to be administered daily as preexposure prophylaxis for people at high risk of HIV infection. Administered orally, 300 mg, once daily. ViiV Healthcare, Middlesex, UK Phase II trials recruiting	Condoms Harm-reduction campaigns Preexposure prophylaxis (tenofovir/emtricitabine) Prophylactic vaccines (investigational) Vaginal microbicide gels (investigational)	Reduced transmission and incidence of HIV Reduced morbidity and mortality
OraQuick in-home rapid test for detection of HIV infection	Patients who may have been exposed to HIV	Despite advances in treatment, prevention, detection, and education, HIV continues to spread, and better, rapid, early detection methods might help limit this spread. The OraQuick® In-Home HIV Test was adapted from the FDA-approved OraQuick rapid HIV test available since 2009 for use in clinics. The new test is an over-the-counter version for home use. To perform the test, individuals swab their upper and lower gums and place the swab into a vial of test fluid. Results (colored lines on the test strip) can be read within 20 minutes. A positive result is intended to signal the need for the patient to have followup testing by a health care provider. The kit includes an information booklet with directions to call the manufacturer's support center 24 hours a day, 7 days a week for counseling on the test results and referral to medical services. OraSure Technologies, Inc., Bethlehem, PA FDA approved Jul 2012	Home-based blood tests (mail-in) Clinic-based rapid test (OraQuick)	Reduced HIV transmission Earlier intervention to control viral load Increased HIV screening rate

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Ozonated water disinfectant to prevent health care–acquired infections	Patients in a hospital or other health care facility where hospital–acquired infections (HAIs) are a concern	HAIs are a major cause of death in the U.S. About 1 in 20 hospitalized U.S. patients 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 surfaces with ozonated water purportedly cleans as effectively as using other chemicals for terminal cleaning, but ozonated water is said to be less harsh on hospital staff and patients. Additionally, ozonated water is thought to leave no harmful residue after cleaning. Ozone is a highly active form of oxygen that purportedly reacts with microorganisms leading to efficient killing. After reacting, elemental oxygen is thought to remain. Windsor Regional Hospital, Windsor, Ontario, Canada Medizone International, Inc., Sausalito, CA Manufacturer is in discussions with EPA for marketing clearance as a disinfection system	Antimicrobial copper touch surfaces Terminal cleaning procedures using bleach and cleaning of visibly soiled surfaces as necessary Ultraviolet light	Reduced costs associated with HAIs Reduced bacteria isolated from surfaces Reduced infection rates Reduced HAI morbidity and mortality
Patient-centered signage to improve hand washing among health care workers	Patients attending health care facilities	Hand-washing adherence by health care workers is only about 40% in many health care settings, leading to transmission of dangerous and costly infections. Many health care workers have purportedly expressed the opinion that because they are frequently exposed to infections, they are more immune to infection and, thus, do not wash their hands. Signage posted 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 health care-acquired infections Reduced HAI incidence Reduced HAI morbidity and mortality

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Pegylated interferon lambda (BMS-914143) 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 is ineffective in more than half of infected patients and the presence of pegylated interferon (IFN)a-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 IFN lambda) is a recombinant, pegylated form of IFN lambda, a type III IFN, which binds to a unique receptor on cells with a restricted cellular distribution and may improve tolerability when compared with treatment with type I IFNs/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 trials ongoing	IFNa-2a IFN-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
PneumoniaCheck device for detection of pneumonia	Patients in whom pneumonia is suspected	Only 40% of suspected pneumonia cases are thought to be accurately detected because organisms from the mouth and lungs contaminate the sample, leading to inappropriate treatment and increased morbidity and mortality. The PneumoniaCheck™ device purportedly uses fluid mechanics in a simple design that separates upper and lower airway aerosols, allowing contaminating organisms from the mouth to be eliminated from the lower respiratory isolates needed for appropriate diagnosis. The device consists of a plastic tube with a mouthpiece. A patient coughs into the device to fill up a balloonlike upper airway reservoir before the lung aerosols go into a filter that can be analyzed with standard polymerase chain reaction methods. MD Innovate, Inc., Decatur, GA Exempt from FDA regulatory clearance processes; classified as a class I device	Sputum and culture detection methods	Improved accuracy of diagnosis Improved treatment plan Reduced duration of symptoms through appropriate treatment

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
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 nonclinical laboratory staff in the point-of-care setting and provide results in 10–15 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 Unphased 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 1st-generation polymerase chain reaction (PCR) assay 2nd-generation quantitative PCR	Reduced transmission of MRSA Increased sensitivity and specificity of MRSA detection Faster MRSA detection
Private intensive care rooms to reduce hospital acquired infections	Patients admitted to an intensive care unit (ICU)	Despite infection-control efforts, about 1/3 of patients admitted to an ICU contract an infection, which may increase length of stay, morbidity, and cost of care. Private ICU rooms may help to better isolate patients and contain their infections or prevent them from contracting a new infection. McGill University Health Centre, Montreal, Quebec, Canada Early adoption ongoing	Antimicrobial copper touch surfaces Standard infection control practices Portable pulsed xenon ultraviolet light added to terminal cleaning Terminal cleaning with peracetic acid	Reduced hospital-acquired infection rates

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Rapid molecular detection test (Gene Xpert MTB/RIF) for *Mycobacterium tuberculosis* infection with rifampin resistance	Patients suspected of having *Mycobacterium tuberculosis* infection	According to the World Health Organization, tuberculosis (TB) is highly underdiagnosed. Current TB testing methods require weeks to deliver a definitive result. During that time, patients can be left untreated or placed on ineffective therapies, which could allow TB to continue to spread to others in the community. The automated molecular test (Xpert® MTB/RIF) for detecting *M. tuberculosis* infection is a nucleic acid test that runs on the manufacturer's GeneXpert® real-time polymerase chain reaction (PCR) system. The test detects the presence of *M. tuberculosis* complex species and simultaneously determines whether the identified bacterium is susceptible to the 1st-line antibiotic rifampicin. The assay is intended to yield results for both the presence of TB and antibiotic resistance for positive samples in about 2 hours. Traditional susceptibility testing is still required for antibiotics other than rifampicin. Cepheid, Sunnyvale, CA In the United States, the test is available only for research use as a 10-test kit; Conformité Européene (CE) marked; World Health Organization endorsed MTB/RIF in late 2010 for use in the "High Burden Developing Countries" and the Gates Foundation is supporting adoption of test in these 145 nations	Microscopy Tuberculin skin test (Mantoux test) Ziehl-Neelsen microscopy	Less lab staff training time Rapid detection Improved treatment Better control of antibacterial resistance
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 national or international guidelines do not exist for anal dysplasia screening. Anal Pap (Papanicolaou) 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 patient reaches 50 years of age) or during routine gynecologic visits for women	Earlier detection of suspicious polyps Reduced anal cancer incidence in patients with HIV Reduced anal cancer mortality in patients with HIV

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
RTS,S (Mosquirix) for prevention of malaria caused by *Plasmodium falciparum*	Patients living in or traveling to areas endemic for malaria	Almost half of the world population is at risk of contracting malaria. Current treatments to the *Plasmodium falciparum* parasite can be ineffective, particularly in young children and immunosuppressed individuals; this results in high morbidity and mortality. RTS,S (Mosquirix™) consists of a recombinant, circumsporozoite protein in which the 9 central tandem repeat and carboxyl-terminal regions are fused to the N-terminus of the hepatitis B virus S antigen in a particle expressed in yeast that also includes unfused S antigen. The vaccine is also administered with the AS02A adjuvant (proprietary oil-in-water emulsion with the immunostimulants monophosphoryl lipid A and QS21). The vaccine purportedly targets the pre-erythrocytic stage of P. falciparum growth by inducing protective immune responses against the parasite when it 1st enters the human host's bloodstream and/or when it infects liver cells, thus inhibiting the infection cycle. Administered in 3 intramuscular injections at 0, 1, and 2 months. GlaxoSmithKline, Middlesex, UK PATH Malaria Vaccine Initiative, Washington, DC Phase III trials completed; phase II/III trial ongoing	Chloroquine phosphate Mosquito nets	Reduced incidence of malaria infection Increased overall survival
Silicone-based condom (ORIGAMI Anal Condom) to prevent HIV infection during receptive anal intercourse	Persons engaging in anal intercourse	HIV remains a chronic illness associated with high morbidity and mortality in the absence of effective treatments. HIV-drug resistance, high lifelong cost of therapy, and adverse events suggest that prophylactic HIV measures to prevent infection should be pursued for individuals at high risk of infection. The ORIGAMI Anal Condom™ is purportedly the first silicone-based condom designed for receptive anal intercourse. The condom is made of medical grade silicone, which is intended to improve the safety of receptive anal sex with respect to the transmission of HIV. The manufacturer purports latex condoms are not designed for the vigor of anal intercourse. Silicone is also purported to have a novel and improved feel compared with the feel of latex condoms and might increase condom use. The condom is intended to be inserted into the anus similar to female condoms. Origami Condoms of California, Culver City, CA Trial completed	Latex condoms Harm reduction campaigns Preexposure prophylaxis (tenofovir/emtricitabine) Prophylactic vaccines (investigational)	Reduced transmission and incidence of HIV Patient satisfaction Increased use of condoms during receptive anal intercourse

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Simeprevir (protease inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	HCV treatment options are not effective in all patients and are 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. Simeprevir in an oral NS3/4a HCV protease inhibitor that may be used to limit viral replication in combination with pegylated interferon plus ribavirin (IFN/RBV). Simeprevir is also being investigated in combination with sofosbuvir and daclatasvir as an IFN-free regimen. Administered 150 mg, once daily. Janssen Research & Development, LLC, Raritan, NJ Phase III trials ongoing; FDA granted fast- track status; Janssen submitted new drug application to FDA in Mar 2013; new drug application submission accepted for priority review by FDA in May 2013	Boceprevir IFN/RBV 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
Sofosbuvir (polymerase inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	HCV treatment options are not effective in all patients and are associated with frequent adverse events, a long duration of therapy, and low patient adherence. Effective treatments that improve clinical outcomes and safety in a shorter period of time are needed. Sofosbuvir (GS-7977) is a uridine nucleotide analog intended to inhibit HCV NS5B polymerase activity, which may limit viral replication by inhibiting viral genome replication. Sofosbuvir is being evaluated in conjunction with standard-of-care pegylated interferon plus ribavirin (IFN/RBV) and in IFN-free regimens that include ribavirin, daclatasvir, simeprevir, and other agents. Administered orally 400 mg, once daily. Gilead Sciences, Inc., Foster City, CA Phase III trials ongoing; FDA granted fast-track status; new drug application submitted Apr 2013; FDA granted priority review Jun 2013; FDA decision date set for Dec 2013	Boceprevir IFN/RBV 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
Sovaprevir (NS3 protease inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	Current standard of care for HCV infection is not effective in all 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. Sovaprevir is a NS3 protease inhibitor intended to block the activity of HCV protease, preventing the cleavage and maturation of functional viral particles; sovaprevir is purported to have broad genotypic coverage and to induce high rates of rapid virologic responses irrespective of interleukin-28 genotype. It is intended to be used in combination with standard-of-care pegylated interferon plus ribavirin (IFN/RBV), and is taken orally, 200–800 mg, once daily. Sovaprevir could be taken in combination with ACH-3102 (NS5A inhibitor) and ribavirin as an IFN-free regimen. Achillion Pharmaceuticals, Inc., New Haven, CT Phase II trial ongoing; FDA granted fast-track status for chronic HCV infection; FDA placed sovaprevir on clinical hold Jul 1, 2013 due to safety concerns when the drug was administered with ritonavir-boosted atazanavir	Boceprevir IFN/RBV 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
Streaming weekly educational soap opera episodes to smartphones for people at high risk for HIV	Patients who are at high risk of contracting HIV infection	Despite HIV prevention and education efforts, the epidemic continues to spread. New methods to educate patients about how to better avoid activities associated with elevated risk of contracting HIV are needed. A 12-episode soap opera video series called “Love, Sex, and Choices” was designed to educate women about HIV risk reduction methods. Women were given a secure cell phone that streamed weekly episodes incorporating HIV risk-reduction messages. Delivering risk-reduction messages in this format could lead to better awareness. Rutgers College of Nursing, Newark, NJ Study completed	Standard risk-reduction programs Text messaging risk reduction programs	Reduced HIV incidence in women at risk of contracting the infection Increased knowledge and identification of high-risk behavior

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Surotomycin (CB-183,315) for treatment of recurrent *Clostridium difficile* infection	Patients in whom recurrent *Clostridium 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.Surotomycin is a novel cyclic lipopeptide, which purportedly disrupts bacterial membrane potential, inhibiting bacterial metabolism. Administered orally, 125–250 mg, twice daily, for 10 days. Cubist Pharmaceuticals, Inc., Lexington, MA Phase III trials recruiting participants	Fidaxomicin Metronidazole Vancomycin	Reduced CDI recurrence rate Shorter hospitalization time Faster time to resolution of diarrhea
Tenofovir and emtricitabine (Truvada) for prevention of HIV infection	People at risk of HIV infection	Although behavior-change programs have resulted in dramatic reductions in HIV transmission in the United States, there remains no truly effective means to prevent HIV infection among populations at high risk for infection. Truvada® is a combination of 2 reverse transcriptase inhibitors, tenofovir disoproxil fumarate (Viread®) and emtricitabine (Emtriva®) given as preexposure 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 both men who have sex with men and in heterosexual men. Data for prophylactic use in women have been confounding because of lack of efficacy. The 2 drugs are combined into 1 oral tablet, taken daily. Gilead Sciences, Inc., Foster City, CA FDA approved Jul 2012 to reduce the risk of HIV infection in high-risk, uninfected individuals who may engage in sexual activity with infected partners. As a condition of approval, FDA also directed Gilead to develop a Risk Evaluation and Mitigation Strategy to help ensure safe use as part of a comprehensive prevention strategy for the disease. The company will also provide vouchers for free HIV testing and condoms, an opt-in service for reminders about HIV testing, and subsidized HIV resistance testing for any person who becomes HIV-positive while taking the drug as prescribed for prevention.	Condoms Harm reduction campaigns Prophylactic vaccines (investigational) Vaginal microbicide gels (investigational)	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 disoproxil fumarate (Viread) for prevention of HIV infection	People at high risk of contracting HIV infection	HIV remains a chronic illness resulting in high morbidity and mortality in the absence of effective treatments. HIV-drug resistance, high lifelong cost of therapy, and adverse events continue to suggest that prophylactic HIV measures be pursued for individuals at high risk of infection. Tenofovir disoproxil fumarate (Viread®) is a nucleotide analog reverse transcriptase inhibitor used in combination with other antiretroviral agents for treating HIV infection. Truvada® (emtricitabine with tenofovir disoproxil fumarate) has been approved as preexposure prophylaxis for people at high risk of HIV infection. Clinical studies have suggested that daily prophylactic use of tenofovir without emtricitabine can also reduce the risk of sexual acquisition of HIV. Administered orally, 300 mg, once daily. Gilead Sciences, Inc., Foster City, CA Phase III trial completed	Condoms Harm reduction campaigns Preexposure prophylaxis (tenofovir with or without emtricitabine) Prophylactic vaccines (in development) Vaginal microbicide gels (in development)	Reduced HIV transmission Reduced HIV incidence
Universal clearance (decolonization) to prevent methicillin-resistant *Staphylococcus aureus* infections in intensive care units	Patients admitted to intensive care units (ICUs)	Hospital-acquired infections such as methicillin-resistant *Staphylococcus aureus* (MRSA) are a major cause of morbidity and death; improved infection control protocols are needed. Screening patients admitted to ICUs for MRSA colonization followed by isolation or decolonization is standard practice in many facilities. Universal decolonization consists of nasal decolonization of all patients with mupirocin for 5 days and daily chlorhexidine baths for the duration of ICU stay. Universal decolonization is purportedly more effective in reducing the incidence of MRSA in the ICU and reducing the need for surveillance cultures and isolation in the ICU. University of California Irvine School of Medicine, Orange, CA Large trial completed	Nasal screening followed by isolation Nasal screening followed by isolation and decolonization	Reduced infection rates

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vaniprevir (protease inhibitor) for treatment of chronic hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) infection has been diagnosed	HCV treatment options are not effective in all patients and are 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. Vaniprevir (MK7009) is a next-generation NS3/4 protease inhibitor intended to block the activity of HCV protease, preventing viral particles from cleaving and maturing. Vaniprevir is used in combination with pegylated interferon plus ribavirin (IFN/RBV). Administered orally 300 mg, twice daily. Merck & Co., Inc., Whitehouse Station, NJ Phase III trial ongoing	Boceprevir IFN/RBV 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
xTAG Gastrointestinal Pathogen Panel for detecting gastroenteritis	Patients suspected of having gastroenteritis	Traditional stool testing for gastroenteritis can take 2–3 days, during which time a severe gastrointestinal infection can kill a patient. Faster detection methods are needed. The xTAG Gastrointestinal Pathogen Panel (GPP) is a rapid molecular diagnostic test that simultaneously analyzes the DNA or RNA of 11 viral, bacterial, and parasitic causes of infectious gastroenteritis from a single stool sample using the Luminex xMAP® platform. Pathogens detected include norovirus and rotavirus A, the bacteria Campylobacter, *Clostridium difficile* toxin A/B, Salmonella and 3 strains of Escherichia coli, as well as the parasites Cryptosporidium and Giardia. Testing for DNA and RNA from all 11 species occurs simultaneously. The panel purportedly takes 5 hours to perform, which could improve treatment outcomes. Luminex Corp., Austin, TX FDA cleared via the de novo pathway (route to market for low to moderate risk classified in class III; not substantially equivalent to predicate device on market) in Jan 2013 for diagnosing gastroenteritis	Antibody-based detection methods Polymerase chain reaction assay Stool culture	Rapid resolution of diarrhea and symptoms Reduced mortality

Table 10. AHRQ Priority Condition: 10 Obesity: 9 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Aspiration system (AspireAssist) for treatment of obesity	Patients with body mass index (BMI) 35.0–55.0 kg/m2	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Current surgical options for treating obesity have varying degrees of invasiveness, some of which are associated with significant adverse effects, and others that have suboptimal efficacy. The AspireAssist™ Aspiration Therapy System is a weight loss device/system that reduces food portions after a meal by removing stomach food contents approximately 20 minutes after consumption, reducing the calories available for the body to absorb. Patients can control this process through an endoscopically-implanted tube that comes through the surface of the abdominal skin, where the opening is closed with a poker chip-sized valve (Skin-Port). Patients can dump "excess" food contents into a toilet. This process is reversible and the device can be implanted or explanted during conscious sedation. Aspire Bariatrics, King of Prussia, PA Pivotal trial ongoing; Conformité Européene (CE) marked Dec 2011	Endoluminal sleeve (EndoBarrier) Gastric banding surgery Gastric pacemaker (in development) Intragastric balloons (in development) Pharmacotherapy Sleeve gastrectomy surgery	Decreased comorbidities Improved quality of life Total weight loss
Controlled-release phentermine-topiramate (Qsymia) for treatment of obesity	Overweight adults with body mass index (BMI) >27 kg/m2 and a comorbidity or obese adults (BMI >30 kg/m2)	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Controlled-release phentermine-topiramate (Qsymia™) is a combination of the appetite suppressant phentermine (approved for short-term use in weight loss) and topiramate (an approved antiepileptic agent with known weight loss side effects). It is a controlled-release pill that is intended to be taken once daily, and in trials reportedly resulted in more weight loss by more patients than other available antiobesity drugs. Vivus, Inc., Mountain View, CA FDA approved Jul 2012 for “for chronic weight management in adults who are obese, or overweight with at least 1 weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia” with diet and lifestyle modification. Obesity is defined as BMI 30 kg/m2 or higher; overweight is BMI 27 kg/m2 or more. The approval included a Risk Evaluation and Mitigation Strategy requiring physician training, physician registration, pregnancy avoidance counseling for patients of reproductive age on the drug, and dose-escalation strategy.	Bariatric surgery Behavior and lifestyle modifications Combination norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (Contrave; in development) Lorcaserin (Belviq) Orlistat (Xenical®)	Decreased comorbidities Improved quality of life Total weight loss

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Fecal microbiota therapy for metabolic syndrome in obese patients	Obese patients in whom metabolic syndrome as been diagnosed	The prevalence of metabolic syndrome is increasing in the U.S., warranting the need for effective therapies aimed at reducing coronary artery disease, stroke, and diabetes mellitus. Obese patients are thought to have an imbalance in the flora of their lower intestinal tract that could be contributing to insulin resistance. A transplant of healthy flora from another person's fecal matter has been suggested as a way to treat metabolic syndrome. In an effort to treat insulin resistance and obesity, fecal matter is harvested from healthy, lean donors, processed, and transferred via enema into obese patients who have metabolic syndrome. Academic Medical Centre at the University of Amsterdam, the Netherlands Pilot trial completed; fecal microbiota therapy has also been used to treat other conditions, such as recurrent *Clostridium difficile* infection.	Antiobesity pharmacotherapy Diet and behavior changes Surgical intervention (e.g., bariatric surgery)	Improved fecal flora composition Weight loss Resolution of metabolic syndrome
Intragastric dual balloon (ReShape Duo) for treatment of obesity	Patients with a body mass index (BMI) between 30 and 40 kg/m2 who wish to lose weight	Current surgical options for treating obesity have varying degrees of invasiveness, some of which are associated with significant adverse effects, and other surgical options have suboptimal efficacy. ReShape Duo is a nonsurgical, intragastric, dual balloon that is endoscopically inserted into the stomach in an uninflated state using a guidewire. Once the guidewire positions the dual balloon appropriately, the dual balloon is inflated with 900 cc of saline, occupying stomach space with the intended purpose of increasing satiety while avoiding overdistention. The dual balloon design purportedly reduces device displacement. Endoscopic placement takes 15–30 minutes. The device can stay in the stomach for up to 6 months, and then it must be removed endoscopically using a snare to deflate and remove the balloon through the patient's mouth. ReShape Medical, Inc., San Clemente, CA Pivotal trial in the United States ongoing; Conformité Européene (CE) marked in 2007; after product revisions, launched in the United Kingdom in Mar 2012	Endoluminal sleeve (EndoBarrier) Gastric banding surgery Gastric pacemaker (in development) Pharmacotherapy Sleeve gastrectomy surgery	Decreased comorbidities Improved quality of life Total weight loss

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Liraglutide (Victoza®) for treatment of obesity	Patients at risk of developing diabetes with a body mass index (BMI) greater than 30 kg/m2 or between 27 and 30 kg/m2 with an associated comorbidity	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Liraglutide (Victoza®) is approved for treating T2DM and acts as a glucagon-like peptide 1 analog; the drug reduces blood glucose levels by increasing insulin secretion, which delays gastric emptying and suppresses glucagon secretion, potentially leading to weight loss. This once-daily treatment showed potential in preclinical studies and studies in overweight patients without diabetes to reduce food intake and induce weight loss. Novo Nordisk A/S, Bagsværd, Denmark 1 phase III trial completed and 1 phase III trial ongoing in nondiabetic obese patients.	Bariatric surgery 5-HT2C receptor agonist (Belviq®) Behavior and lifestyle modifications Combination appetite suppressant/stimulant and anticonvulsant (Qsymia®) Combination norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (Contrave; in development) Pancreatic lipase inhibitor (orlistat, Xenical®)	Decreased comorbidities Improved quality of life Total weight loss
Lorcaserin (Belviq) for treatment of obesity	Overweight adults (BMI >27 kg/m2) with a comorbidity or obese adults (BMI >30 kg/m2)	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Pharmacologic options have expanded with new drug approvals in 2012; however, competing approved drugs have significant potential side effects and work in only a proportion of patients taking them. Lorcaserin (Belviq®) is in a new class of selective serotonin 2C receptor agonists. It is taken twice daily in a 10-mg tablet. If 5% weight loss is not achieved by week 12 of therapy, labeling requires that the drug therapy be discontinued. Arena Pharmaceuticals, Inc., San Diego, CA (manufacturer) Eisai, Inc., U.S., a subsidiary of Eisai Co., Ltd., Tokyo, Japan (U.S. distributor) FDA approved Jun 2012 on basis of 3 completed phase III trials “as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 kg/m2 or greater (obese), or 27 kg/m2 or greater (overweight) in the presence of at least 1 weight related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes).” In Jun 2013, manufacturer announced the launch of Belviq® in the US.	Behavior and lifestyle modifications Combination appetite suppressant/stimulant and anticonvulsant (Qsymia®) Combination norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (Contrave; in development) Pancreatic lipase inhibitor (orlistat, Xenical®) Surgical therapy (e.g., bariatric surgery)	Decreased comorbidities Improved quality of life Total weight loss

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	Adults with body mass index (BMI) >30 kg/m2 or >27 kg/m2 with comorbidities	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Pharmacologic options have expanded with new drug approvals in 2012; however, the approved drugs have significant potential side effects and work in only a proportion of patients taking them. Additional pharmacologic options are needed. Contrave is a fixed-dose combination of naltrexone sustained-release (SR) and bupropion SR. Bupropion purportedly acts on weight control by stimulating the POMC neuron. Naltrexone purportedly prevents inhibition of POMC neurons by blocking the action of beta-endorphin. Naltrexone and bupropion extended release (Contrave SR®) is taken orally, once a day. Orexigen Therapeutics, Inc., La Jolla, CA FDA rejected new drug application Feb 2011; requested additional trial on cardiovascular effects; the trial began enrollment in Jun 2012 and the company announced it had enrolled more quickly than anticipated and that it expects to complete data collection by end of 2013; The company anticipates a resubmission of data in early 2014. In Jan 2013, company announced it made progress with FDA on faster path to resubmission.	Bariatric surgery Behavior and lifestyle modifications Combination appetite suppressant/stimulant and anticonvulsant (Qsymia®) Lorcaserin (Belviq) Orlistat (Xenical)	Decreased comorbidities Improved quality of life Total weight loss
Off-label exenatide for treatment of pediatric obesity	Children and adolescents receiving a diagnosis of “extreme” obesity (body mass index [BMI] ≥1.2 times the 95th percentile or BMI ≥35 kg/m2)	A single weight-loss pharmacotherapy is available for adolescents older than 12 years of age: orlistat (Xenical). However, prescription medications are not recommended for child or adolescent use. Exenatide is a glucagon-like peptide-1 receptor agonist approved for type 2 diabetes mellitus treatment that purportedly reduces BMI, waist circumference, and body weight in addition to improving the glycemic index. Exenatide purportedly increases satiety sensation and appetite suppression. In trials, exenatide was administered subcutaneously, twice daily, 5 mcg/dose for the 1st month and then 10 mcg/dose for 2 months. University of Minnesota, Minneapolis Pilot trial completed; phase II trial completed	Bariatric surgery Behavior and lifestyle modifications Pancreatic lipase inhibitor (orlistat, Xenical®) Surgical therapy (e.g., bariatric surgery)	Decreased comorbidities Improved quality of life Total weight loss

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vagus nerve blocking (Maestro system VBLOC) for treatment of obesity	Adults with body mass index (BMI) between 40 and 45 kg/m2 or ≥35 kg/m2 with comorbidities	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. Available pharmacologic and surgical options can have serious side effects or adverse events, warranting the need for more novel approaches for treating obesity. The VBLOC is an implanted device that emits high-frequency, low-energy electrical impulses, which are intended to block the vagus nerve (VBLOC™) in an effort to inhibit gastric motility and increase feelings of fullness. Electrical impulses are delivered by the 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, with expected completion in 2013; Jun 2013, company announced it had submitted a premarket approval application to FDA for Maestro RC System	Bariatric surgery Behavior and lifestyle modifications Combination appetite suppressant/stimulant and anticonvulsant (Qsymia®) Combination norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (Contrave; in development) Lorcaserin (Belviq®) Pancreatic lipase inhibitor (orlistat, Xenical®)	Decreased comorbidities Improved quality of life Total weight loss

Table 11. AHRQ Priority Condition: 11 Peptic Ulcer Disease and Dyspepsia: 14 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 experience damage to their bowels and require surgery; no regenerative therapies are approved. Remestemcel-L (Prochymal®) consists of allogeneic, bone marrow–derived human mesenchymal stem cells (MSCs), which purportedly 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. In clinical trials, administered 3 times, 200 million cells per infusion, 42 days apart. Osiris Therapeutics, Inc., Columbia, MD Phase III trials ongoing; FDA granted fast-track status	Autologous bone marrow–derived MSC stromal cells (in development) Teduglutide	Increased disease remission Improved disease symptoms Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Fecal microbiota transplantation for treatment of ulcerative colitis	Patients in whom ulcerative colitis (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 anti-inflammatory drugs with varied success, and investigators have not found a 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. Phase II/III trial ongoing; procedure may be adopted by gastroenterologists who are using the procedure for treating recurrent *Clostridium difficile* infection	Aminosalicylates (mesalazine) Antibiotics (for acute flares) Corticosteroids (e.g., prednisone) Immunomodulators (e.g., azathioprine) Monoclonal antibodies (e.g., natalizumab, infliximab)	Reduced relapse frequency Reduced use of medications Reduced symptoms Reduced or postponed need for surgery Improved quality of life
Helminthic therapy (pig whipworm) for treatment-resistant ulcerative colitis	Patients in whom treatment-resistant ulcerative colitis has been diagnosed	The rationale for pig whipworm therapy using *Trichuris suis* ova is that inflammatory bowel diseases are uncommon in developing countries where helminths are common and that people with helminth infection have an altered immunological response to antigens. In animal models, helminthes prevent or improve colitis by the induction of regulatory T cells and modulatory cytokines. Parasites are obtained from U.S. Department of Agriculture. Patients ingest 2,500 pig whipworm eggs, every 2 weeks, for 3 months. University of California, San Francisco Trial ongoing at NYU School of Medicine; 2 trials completed; 1 for ulcerative colitis and 1 for Crohn's disease	Aminosalicylates (mesalazine) Antibiotics (for acute flares) orticosteroids (e.g., prednisone) Immunomodulators (e.g., azathioprine) Monoclonal antibodies (e.g., natalizumab, infliximab	Increased safety Reduced flare symptoms Maintained remission 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
Linx Reflux Management System for treatment-refractory gastroesophageal reflux disease	Patients in whom treatment-refractory gastroesophageal reflux disease (GERD) has been diagnosed	GERD is a progressive disease that is not always managed by pharmacologic treatments, and many patients undergoing surgical treatment remain on pharmacologic therapy. The Linx® Reflux Management System purportedly augments the activity of the weak lower esophageal sphincter of patients with GERD, which may restore the body's natural barrier to reflux. The system comprises a small flexible band of interlinked titanium beads with magnetic cores. The magnetic attraction between the beads is intended to help the lower esophageal sphincter remain closed in response to gastric pressures to prevent reflux from the stomach into the esophagus. Swallowing force temporarily breaks the magnetic bond of the beads, allowing food and liquid to pass normally into the stomach; after swallowing, the lower esophageal sphincter closes. The system is implanted via laparoscopic surgery. Torax Medical, Inc., Shoreview, MN FDA approved Mar 2012 for patients with treatment-refractory GERD despite use of optimal medical therapy	Antacid medications FundoplicationH2 antagonists Proton pump inhibitors	Reduced GERD symptoms Reduced risk of GERD-related cancer Improved quality of life
Magnetically guided capsule endoscopy for diagnosis of gastrointestinal disorders	Patients appropriate for gastrointestinal (GI) endoscopic examinations	Current GI endoscopic procedures are invasive, require sedation, and have low rates of patient acceptance and satisfaction. Additionally, existing capsule endoscopy technology does not let clinicians guide the capsule as it travels through the patient's GI tract to ensure images of desired areas are captured. Magnetically guided capsule endoscopy 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 AG, Munich, Germany Olympus Corp., Tokyo, Japan Unphased trial ongoing	Endoscope procedure Pill Cam	Increased sensitivity and specificity Positive and negative predictive values Improved diagnostic accuracy Impact on clinical decisionmaking for managing symptoms

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
MuDelta (JNJ-27018966) for treatment of diarrhea-predominant irritable bowel syndrome	Patients in whom diarrhea-predominant irritable bowel syndrome (IBS-d) has been diagnosed	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 III trials ongoing; FDA granted fast-track status Jan 2011	Antispasmodic drugs Opioids Serotonin agonists Tricyclic antidepressants	Reduced abdominal pain and bloating symptoms Long-term relief
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 5 abdominal incisions to access the blocked esophageal pathway. PerOral endoscopic myotomy is a procedure proposed for treating 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 purportedly is less invasive, thereby potentially reducing complications, recovery time, and pain. Northwestern Memorial Hospital, Chicago, IL Phase IV trial ongoing	Heller myotomy	Improved Esophageal Function Tests (upper endoscopy, barium swallow, esophageal manometry, pH test) scores 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, 0.3–9.0 mg, once daily. Synergy Pharmaceuticals, Inc., New York, NY Phase II/III trial completed	Enemas Laxatives Lubiprostone	Decreased straining and abdominal discomfort Increased frequency of bowel movements Improved stool consistency Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Rifaximin (Xifaxan) for treatment of nonconstipating irritable bowel syndrome	Patients in whom nonconstipating irritable bowel syndrome has been diagnosed	Rifaximin (Xifaxan®) is a nonabsorbable oral antibiotic approved for treating traveler's diarrhea. Salix Pharmaceuticals, Inc., Morrisville, NC Phase III trial ongoing; 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
Spherical carbon adsorbent (AST-120, Zysa) for treatment of diarrhea-predominant irritable bowel syndrome	Patients in whom diarrhea-predominant irritable bowel syndrome (IBS-d) has been diagnosed	Current treatments for IBS-d are purported to be ineffective in many patients, and no new treatment options have been available for decades. The only approved treatment in the U.S. for IBS-d is alosetron, and this intervention is associated with safety issues. Other treatments include off-label antispasmodic agents and antidepressants and probiotics. AST-120 (Zysa™) is an oral spherical carbon adsorbent that purportedly binds to and neutralizes the activity of several compounds associated with IBS-d pathogenesis as well as ammonia, indoles (serotonin), histamine, bile acids, advanced glycation endproducts, and certain bacterial toxins. By binding and neutralizing toxins in the gut, AST-120 could relieve IBS-d symptoms. Ocera Therapeutics, Inc., San Diego, CA Phase II trial completed; FDA granted fast-track status	Antispasmodic drugs Opioid receptor agonist in development Opioids Serotonin agonists Tricyclic antidepressants	Reduced abdominal pain and bloating symptoms Long-term relief
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 purportedly increases nutrient absorption and intestinal cell growth in patients with SBS. NPS Pharmaceuticals, Inc., Bedminster, NJ FDA approved Dec 2012 for treating SBS	Intravenous fluids Parenteral nutrition	Improved hydration Improved nutritional status Weight gain Reduced diarrhea Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Tofacitinib (JAK 3 kinase inhibitor) for treatment of ulcerative colitis	Patients in whom ulcerative colitis (UC) has been diagnosed	Current therapies for UC temporarily control symptoms and are poorly tolerated in some patients. Tofacitinib is an oral tyrosine kinase inhibitor specifically targeting the 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 might suppress the inflammatory reactions that are the basis of UC. Tofacitinib has been administered twice daily (0.5, 1, 3, 5, 10, and 15 mg) doses. Pfizer, Inc., New York, NY Phase III trials ongoing	Aminosalicylates (mesalazine) Antibiotics (for acute flares) Corticosteroids (e.g., prednisone) Immunomodulators (e.g., azathioprine) Monoclonal antibodies (e.g., natalizumab, infliximab)	Improved clinical response Reduced flare symptoms Reduced or postponed need for surgery Improved quality of life
Vedolizumab for treatment of moderate to severe ulcerative colitis	Patients in whom moderate to severe ulcerative colitis (UC) has been diagnosed	Vedolizumab is an infused monoclonal antibody; current treatments for UC have limited effectiveness; the only cure is surgery. This may provide an alternative treatment. In June 2013, the manufacturer announced that it had submitted a Biologics License Application (BLA) to United States (U.S.) Food and Drug Administration (FDA) for this intervention. Millennium Pharmaceuticals unit of Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trial completed (Gemini I)	Aminosalicylates (mesalazine) Antibiotics (for acute flares) Corticosteroids (e.g., prednisone) Immunomodulators (e.g., azathioprine) Monoclonal antibodies (e.g., natalizumab, infliximab)	Reduced flare symptoms Maintained remission Reduced or postponed need for surgery Improved quality of life
Vercirnon (Traficet-EN) for treatment of Crohn's disease	Patients in whom moderate to severe Crohn's disease has been diagnosed	Vercirnon (Traficet-EN™, GSK1605786) 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, Vercirnon selectively impairs the movement of activated T cells that are involved in causing inflammation of the digestive tract. In phase III trials, administered 500 mg twice daily. GlaxoSmithKline, Middlesex, UK 4 phase III trials ongoing (SHIELD 1, 2, 3, and 4)	Aminosalicylates (mesalazine) Antibiotics (for acute flares) Corticosteroids (e.g., prednisone) Immunomodulators (e.g., azathioprine) Monoclonal antibodies (e.g., natalizumab, infliximab)	Delayed or avoided surgery Reduced flares Reduced side effects Disease remission Symptom improvement Improved quality of life

Table 12. AHRQ Priority Condition: 12 Pregnancy, Including Preterm Birth: 7 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Bi-directional communication for personalized body weight management (SmartMoms) for pregnant women	Pregnant women	Pregnant women in the U.S. are at increased risk of exceeding pregnancy weight goals at term as recommended by current Institute of Medicine guidelines, leaving both mother and child susceptible to poor postpartum health outcomes. SmartMoms is a pregnancy weight-management program consisting of screening visits, weight management advice, 2nd and 3rd trimester health testing, and postnatal followup. The most recent SmartMoms intervention involves weekly delivery of weight management strategies from a weight management counselor via a smartphone. The patient will also be asked to submit weight data (using a provided scale) and nutritional information via smartphone. Pennington Biomedical Research Center, Baton Rouge, LA Phase III trial ongoing	Other perinatal weight-management strategies	Improved perinatal weight management Reduced morbidityImproved maternal and fetal health outcomes Improved quality of life
Blood test (ProNid) to predict spontaneous preterm birth	Pregnant women	About 1 in 10 pregnant women have a spontaneous preterm birth in the U.S. each year; however, no screening or diagnostic test is available to identify women at risk of preterm birth early in pregnancy—having results of such a test would allow clinicians and their patients to plan preterm birth prevention strategies. ProNid™ a panel of proteomic markers that purportedly indicates 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 Validation study ongoing on 4,000 patients to develop as a commercial assay	Assessment of cervical length Detection of bacterial vaginosis Fetal fibronectin levels Home uterine activity monitoring Salivary estriol testing	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
Elagolix (gonadotropin-releasing hormone antagonist) for treatment of endometriosis	Patients in whom endometriosis has been diagnosed	Elagolix is the 1st oral nonpeptide gonadotropin-releasing hormone (GnRH) antagonist that, unlike available 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 make it possible to maintain appropriate levels of estrogen, thus preventing menopausal-like hormonal levels and the need for managing bone loss while treating endometriosis. AbbVie Inc., North Chicago, IL Phase III trials ongoing	Pharmacotherapy (e.g., hormonal contraceptives, steroids) Surgical intervention (e.g., endometrial growth and scar tissue excision, hysterectomy)	Improved composite pelvic signs and symptoms score (measures dysmenorrhea, nonmenstrual pelvic pain, dyspareunia, pelvic tenderness and induration) Maintained bone mineral density Improved patient global impression of change Less pain (visual analog scale)
In utero fetal catheterization procedure for treatment of hypoplastic left heart syndrome	Pregnant women receiving a diagnosis of fetal hypoplastic left heart syndrome (HLHS)	HLHS is a congenital condition in which parts of the heart's left side (i.e., aorta, aortic valve, mitral valve) do not completely develop. It occurs in about 1 in 6,000 live births. Once a baby with HLHS is born, treatment protocol involves admitting the patient to the neonatal intensive care unit, placing the neonate on a ventilator, and giving prostaglandin E1 to keep the ductus arteriosus patent. Texas Children's Fetal Center has created a fetal in utero catheterization program to better stabilize the baby at time of birth before undergoing phase I of HLHS surgery. Each fetal intervention procedure is specialized to the needs of the patient and depends on the specific cardiac malformation. For example, catheterization could occur in the aortic valve for a fetus with severe aortic stenosis that typically develops into HLHS, allowing blood to circulate throughout the entire body. Catheterization could also occur across the atrial valve (AV septum), connecting the 2 atrial chambers and allowing blood to pass through the heart's other side. In this case, a stent may also be placed to help sustain the patency of the hole created between the atrial chambers. These techniques can help blood pass to the left side of the heart, allowing the baby to become more oxygenated and increasing odds of postnatal survival. Texas Children's Fetal Center of Texas Children's Hospital, Houston, TX 4-patient surgery trial completed	Neonatal surgery	Increased oxygenation to fetus Increased survival to live birth Increased postnatal survival

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Preconception Care System (Gabby) for improving health outcomes in pregnancy	Women of reproductive age with potential for pregnancy	Despite overall improvement in contraceptive methods and access to early prenatal care, poor maternal and infant mortality rates persist in the United States, disproportionately affecting minority and socially disadvantaged populations. Preconception care (PCC) is a concept that aims to mitigate poor reproductive health outcomes by addressing a broad range of issues, including family planning, previous health condition history, environmental or nutritional exposure to teratogens, and behavior practices. Health information technology innovations have been used to improve the preconception care model. Gabby is a virtual patient advocate (VPA), or animated computer character, that mimics the behavior of a health provider to simulate a face-to-face encounter between patient and clinician. The Gabby system delivers health educational information individually tailored to the patient's needs, based on previous medical records and information collected. In this case, this VPA is designed to engage in educational dialogue with the patient about PCC, particularly delivering culturally competent and appropriate information to underprivileged populations. This system first screens individuals for preconception risks, do an individual assessment of acceptance to behavior change, educate individuals about preconception risks, and create an action plan to reduce those risks. Researchers hypothesize this delivery innovation could mitigate poor birth outcomes, both for mother and child. Boston University School of Medicine's Department of Family Medicine/Boston Medical Center, MA Pilot trial completed	Educational therapy Routine care	Reduced maternal and infant mortality rates Improved health outcomes
Ulipristal acetate (CDB-2914) for treatment of uterine fibroids and excessive uterine bleeding	Premenopausal women in whom symptomatic uterine fibroids have been diagnosed	Uterine fibroids are the most common benign tumor in women, with some fibroids causing excessive pain and bleeding. Available therapies can work with limited efficacy, marking a need for more novel treatment. Ulipristal acetate (CDB-2914; EllaOne®) is a selective P receptor modulator with antiprogestin effects. Administered orally, 10 or 20 mg, once daily. Laboratoire HRA Pharma, SA, Paris, France Phase III trials completed, 1 phase III trial ongoing	Cryomyolysis 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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Vending machine dispensers for emergency oral contraceptives (Plan B One Step) to prevent pregnancy	Women at risk of pregnancy	According to the U.S. Centers for Disease Control and Prevention, about 50% of pregnancies in the U.S. are unintended. Women in underserved areas are at increased risk of unintended pregnancies. Access, fear of others' perception, and cost are several determinants in emergency contraceptive use. Shippensburg University in Pennsylvania has incorporated an emergency contraceptive, or "morning after pill," vending machine into the student health center, charging $25 for each dose for students 17 years of age or older. The vending machine also includes other reproductive health products, including condoms and pregnancy test kits. Shippensburg University, Shippensburg, PA Dispensers not subject to FDA approval; FDA approved; FDA announced in Jun 2013 that Plan B One Step became available for purchase without age restrictons	Over-the-counter access to emergency contraceptives	Decreased risk of pregnancy Increased emergency contraceptive use Increased risk of adverse events associated with emergency contraception

Table 13. AHRQ Priority Condition: 13 Pulmonary Disease, Asthma: 17 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
AeriSeal for treatment of emphysema	Patients in whom emphysema has been diagnosed	Treatment for advanced emphysema involves lung volume reduction surgery, which has risk of serious complications; less invasive treatment options are needed. The AeriSeal System® purportedly achieves lung volume reduction using a minimally invasive approach. Damaged areas of the patient's lungs are targeted with a bronchoscope to deliver a proprietary foam sealant that purportedly seals and collapses, through reabsorption, the treated area, resulting in reduced lung volume. Lung volume reduction purportedly creates more space for healthier, adjacent lung tissue to function more effectively. Aeris Therapeutics, Woburn, MA Phase III trials ongoing	Antibiotics Bronchodilators Corticosteroids Oxygen Pulmonary rehabilitation program Surgery: lung-reduction volume surgery, bullectomy, lung transplantation	Improved lung function Improved activities of daily living Improved quality of life
Ataluren for treatment of nonsense mutation cystic fibrosis	Patients age 6 and older 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 cases in the United States and Europe and more than 50% of CF cases in Israel. The drug is intended to improve lung function and is given orally 3 times daily in clinical trials. PTC Therapeutics, Inc., South Plainfield, NJ 1 phase III trial completed, 1phase III trial ongoing; FDA granted orphan drug status	Antibiotics Bi-level positive airway pressure ventilators Bronchodilators Chest physiotherapy DNase (such as Pulmozyme®) Gene therapies (viral vector or liposome delivery of normal CFTR; investigational) Hypertonic saline Mucolytics (acetylcysteine)	Improved lung function Increased survival Reduced need for additional therapies Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Endobronchial valve system (Zephyr) for treatment of heterogeneous emphysema	Patients in whom heterogeneous emphysema has been diagnosed	This implanted endobronchial valve system (Zephyr®) is intended as a minimally invasive method to treat hyperinflation in the lungs. The device is intended to reduce a patient's diseased lung volume without surgery. According to the company, the procedure involves placing "small, one-way valves in targeted airways to direct the flow of air out of diseased portions of the lung." Clinicians typically place 3–4 valves per lobe during a procedure, and the total procedural time purportedly takes 15–30 minutes, depending on the number of valves placed. The valves are coated with medical-grade silicone to prevent tissue growth through the nitinol retainer. Pulmonx, Inc. (formerly Emphasys), Redwood City, CA Multicenter pivotal investigational device exemption (IDE) clinical trial ongoing	Antibiotics Bronchodilators Corticosteroids Oxygen Pulmonary rehabilitation program Surgery: lung-reduction volume surgery, bullectomy, lung transplantation	Improved lung function Improved activities of daily living Improved quality of life
Inhaled amikacin (Arikace) for treatment of nontuberculous Mycobacteria infection	Patients in whom pulmonary nontuberculous mycobacterial (NTM) lung infection has been diagnosed	Most NTM infections are resistant to many common antibiotics, and NTM infection requires treatment with lengthy multidrug regimens. Few effective treatments exist. 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 using an optimized, investigational eFlow® Nebulizer System. 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. Administration is via inhalation, once daily. Insmed, Inc., Monmouth Junction, NJ Phase II trial ongoing; results expected in 2013; FDA granted orphan drug and fast-track statuses. Arikace is approved for other indications; sometimes used off-label for treating NTM, but existing formulation is not intended for that use and trials are ongoing for the NTM indication.	Amikacin (injectable) Other antibiotics such as: Amoxicillin/clavulanate Capreomycin Clarithromycin Clofazimine Ethionamide Fluoroquinolones Imipenem/cilastatin Isoniazid Kanamycin Linezolid 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 oxygen saturation Extended time before need for rescue antimycobacterial drugs

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Interleukin-5 antagonist (mepolizumab, Bosatria) for treatment of eosinophilic asthma	Patients in whom eosinophilic asthma has been diagnosed	Eosinophilic asthma occurs in about 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 purportedly plays 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, or 750 mg, every 4 weeks. GlaxoSmithKline, Middlesex, UK Phase III trials ongoing	Bronchial thermoplastyInhaled corticosteroids Ipratropium (Atrovent) Leukotriene modifiers Long-acting beta agonists Omalizumab (Xolair) Reslizumab (in development) Short-acting beta agonists Theophylline	Improved asthma control Improved asthma exacerbation rate Reduced emergency room visits Reduced hospitalization Improved quality of life
Interleukin-5 antagonist (reslizumab, Cinquil) for treatment of eosinophilic asthma	Patients in whom eosinophilic asthma has been diagnosed	Eosinophilic asthma occurs in about 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 interleukin-5 (IL-5). IL-5 purportedly plays 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. Teva Pharmaceutical Industries, Ltd., Petach Tikva, Israel (acquired developer Cephalon, Inc., Oct 2011) Phase III trials ongoing	Bronchial thermoplastyInhaled corticosteroids Ipratropium (Atrovent) Leukotriene modifiers Long-acting beta agonists Mepolizumab (in development) Omalizumab (Xolair) Short-acting beta agonists Theophylline	Improved asthma control Improved asthma exacerbation rate Reduced emergency room visits Reduced hospitalization Improved quality of life
Ivacaftor (Kalydeco) for treatment of cystic fibrosis in patients with G551D-CFTR mutation	Patients 6 years of age or older with cystic fibrosis (CF) who have the G551D-CFTR gene mutation (10% to 15% of patients with CF)	Ivacaftor (Kalydeco™) is intended to improve lung function by improving function of mutant cystic fibrosis transmembrane conductance regulator (CFTR) protein; regulator protein is an epithelial ion channel involved in salt and fluid transport. Administered orally, 150 mg, twice daily, with fat-containing food. Vertex Pharmaceuticals, Inc., Cambridge, MA Phase III trial ongoing; FDA approved Jan 2012 for patients with CF who are age 6 years or older with the G551D mutation	No treatment available for 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
KIT tyrosine kinase inhibitor masitinib for treatment of severe asthma	Patients in whom severe persistent asthma has been diagnosed	About 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 purportedly targets 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	Bronchial thermoplastyInhaled corticosteroids Ipratropium (Atrovent) Leukotriene modifiers Long-acting beta agonists Omalizumab (Xolair) Short-acting beta agonists Theophylline	Improved asthma control Improved asthma exacerbation rate Reduced emergency room visits Reduced hospitalization Improved quality of life
KL4 synthetic lung surfactant (Aerosurf combination drug/device) for prevention of neonatal respiratory distress syndrome	Very-low- and low-birthweight premature infants at risk of respiratory distress syndrome (RDS)	KL4 surfactant is a synthetic peptide-containing surfactant intended to closely mimic the essential attributes of human lung surfactant. Aerosurf® is a combination drug and device administered in conjunction with noninvasive nasal continuous positive airway pressure in neonates at risk of RDS. Discovery Laboratories, Inc., Warrington, PA Phase IIa trial for aerosolized Aerosurf formulation completed; company received 2010 National Institutes of Health fast-track small business innovation research grant	Surfaxin (lucinactant) Animal-derived surfactants delivered by endotracheal intubation with or without mechanical ventilation	Improved survival Reduced pulmonary complications Reduced intubation and mechanical ventilation Prevented risks associated with intubation and mechanical ventilation
Lumacaftor (VX-809) for treatment of cystic fibrosis	Patients with cystic fibrosis (CF) who have the delta F508-CFTR gene mutation	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. VX-809 is considered a corrector of the cystic fibrosis transmembrane regulator (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 ivacaftor (Vertex's other CF drug). Vertex Pharmaceuticals, Inc., Cambridge, MA 2 phase III trials and 1 phase II trial ongoing; FDA granted orphan drug and fast- track statuses	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

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 with upper and/or lower lobe heterogeneous emphysema and/or multiple emphysematous lobes with focal tissue defects	Treatment for advanced emphysema involves lung volume reduction surgery, and a less invasive approach to lung volume reduction 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 for healthier lung tissue to function. RePneu is a wirelike 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, improving breathing. PneumRx, Inc., Mountain View, CA Pivotal phase III trial ongoing; Conformité Européene (CE) marked Oct 2010	Antibiotics Bronchodilators Corticosteroids Oxygen Pulmonary rehabilitation program Surgery: lung-reduction volume surgery, bullectomy, lung transplantation	Improved lung function, physical endurance, and activities of daily living Improved scores in St. George's Respiratory Questionnaire (which measures impaired health and perceived well-being in airways disease)
Nintedanib (multikinase inhibitor) to preserve lung function in idiopathic pulmonary fibrosis	Patients in whom idiopathic pulmonary fibrosis (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 2–5 years; 5-year survival rate is about 20%. No approved treatments are available. Nintedanib (BIBF-1120) is a tyrosine kinase inhibitor that has activity against vascular endothelial growth factor receptor, platelet-derived growth factor receptor, and fibroblast growth factor receptor tyrosine kinases, which regulate tumor growth and angiogenesis. Nintedanib is under study for treating IPF and slowing of disease progression and symptoms. Boehringer Ingelheim GmbH, Ingelheim, Germany Phase III trials ongoing	Azathioprine Bosentan Corticosteroids Cyclophosphamide Cyclosporine Methotrexate Penicillamine Pirfenidone (investigational) Pulmonary rehabilitation Supplemental oxygen	Improved lung function measured by forced vital capacity Improved ability to perform activities of daily living 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 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 anti-inflammatory properties. Administered orally, 250 mg, once daily, for 1 year to prevent COPD exacerbations. University of Colorado Denver Health Sciences Center Phase III trials completed; FDA approved in 1992 for treating community-acquired respiratory infections and skin infections	Glucocorticoids Long-acting anticholinergic agents Long-acting beta-2 agonists Roflumilast	Reduced cost due to exacerbations Reduced incidence of exacerbations Increased survival Improved quality of life
Off-label thalidomide for treating cough associated with idiopathic pulmonary fibrosis	Patients in whom idiopathic pulmonary fibrosis (IPF) with persistent cough 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 2–5 years; 80% of patients have a dry nagging cough, for which no approved treatments are available. Thalidomide is considered to be a potent anti-inflammatory drug and is thought to suppress excessive tumor necrosis factor alpha production and down-modulate adhesion molecules involved in leukocyte migration. Thalidomide is also purported to suppress prostaglandin synthesis by macrophages, and modulate interleukin-10 and interleukin-12 production by peripheral blood mononuclear cells. These immunomodulatory effects could improve cough symptoms. Administered orally, 50–100 mg, daily. Celgene Corp., Summit, NJ Phase III trial completed; can be used off label	Azathioprine Bosentan Corticosteroids Cyclophosphamide CyclosporineIntedanib (investigational) Methotrexate Penicillamine Pirfenidone (investigational)	Improved ability to perform activities of daily living Improved lung function measured by forced vital capacity 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
Pirfenidone (Esbriet) for treatment of idiopathic pulmonary fibrosis	Patients in whom idiopathic pulmonary fibrosis (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 2–5 years; 5-year survival rate is about 20%. No approved treatments are available. Pirfenidone (Esbriet®) is a small molecule that inhibits the synthesis of transforming growth factor-beta, which purportedly is involved in fibrosis, and tumor necrosis factor alpha, which is involved in mediating inflammation. The drug is administered orally. InterMune, Inc., Brisbane, CA 2 Phase III trials completed and 2 Phase III trials ongoing; FDA advisory panel voted 9-3 in Mar 2013 to recommend; FDA granted fast-track and orphan drug statuses	Azathioprine Bosentan Corticosteroids Cyclophosphamide CyclosporineIntedanib (investigational) Methotrexate Penicillamine Pulmonary rehabilitation Supplemental oxygen	Improved ability to perform activities of daily living Improved lung function measured by forced vital capacity Slowed disease progression Improved quality of life
School-based preventive asthma care technology (SB-PACT) program for management of asthma in school children	School children in whom asthma has been diagnosed	Children in inner city areas are more likely to have their asthma poorly controlled. The School-Based Preventive Asthma Care Technology (SB-PACT) program is comprised of directly-observed administration of preventive asthma treatments in school, combined with the use of a Web-based technology that helps coordinate systematic symptom screening, electronic report generation, and medication authorization from providers. University of Rochester School of Medicine and Dentistry, Rochester, NY Pilot study completed. Program developers received NIH grant funding in Feb 2013.	Standard care	Fewer days missed from school Increased symptom-free days Reduced symptoms at night Reduced rescue medication use Reduced exhaled nitric oxide (inflammation)
Temperature controlled laminar air-flow device (Airsonett) for treatment of atopic asthma	Patients in whom atopic asthma has been diagnosed	Despite pharmaceutical treatment and lifestyle modification, many patients continue to have difficulty controlling asthma symptoms. Airsonett is a temperature-controlled laminar air-flow device that is positioned over the patient while he or she sleeps. The device purportedly creates a downward flow of filtered air that surrounds the sleeping patient's breathing zone with the intention of providing air in convection currents that is free of allergens and irritants. Airsonett AB, Ängelholm, Sweden Phase III trials completed. Received patent US patent approval Jun 2013	Air purifiers Antiallergenic pillow/mattress encasements Home heating, ventilation, and air conditioning systems	Reduced asthma symptoms Improved peak nasal inspiratory flow Improved sleep quality Improved quality of life

Table 14. AHRQ Priority Condition: 14 Substance Abuse: 8 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	Many patients with opioid dependence attempt abstinence, but relapse rates remain high. Sublingual buprenorphine-naloxone tablet induction followed by buprenorphine implants. Buprenorphine is a 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 (manufacturer) Braeburn Pharmaceuticals subsidiary of Apple Tree Partners, New York, NY (licensee) Phase III confirmatory trial completed; new drug application submitted Oct 2012; FDA advisory panel recommended approval Mar 2013; FDA issued complete response letter stating that it could not grant approval, requested more efficacy data Apr 2013	Opioid maintenance/ replacement therapy (e.g., buprenorphine, methadone, naltrexone) Psychotherapy (e.g., cognitive behavior therapy)	Resolution of problems with adherence, diversion Reduced illicit use of opioids Improved health outcomes associated with abstinence Improved quality of life
Community-based overdose prevention program (Project Lazarus)	Patients with chronic opioid use or opioid dependence	Opioid overdose is an increasingly common issue with the problematic rise of prescription opioid use and abuse in communities across the U.S. Project Lazarus is a community-targeted overdose prevention program developed in Wilkes County, North Carolina, in response to extremely high rates of overdose deaths. The program offers 5 components: community activation and coalition building, monitoring and surveillance data, prevention of overdoses, use of rescue medication for reversing overdoses by community members, and evaluating project components. Primary care physicians receive an educational tool kit on chronic pain management and safe opioid prescribing practices. Project Lazarus in collaboration with the Community Care of North Carolina's Chronic Pain Initiative After success in Wilkes County, ongoing expansion efforts are bringing this program and care model statewide. Program site reports this program has been implemented in over 30 counties to date.	Other substance abuse prevention and treatment programs; various combinations of opioid replacement therapy and detoxification treatment	Decreased incidence of overdose and overdose-related death Improved chronic pain management Improved opioid prescribing practices

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Handheld, portable fingerprinting device (Intelligent Fingerprinting Technology) to detect substance abuse	Individuals suspected of illicit drug use	Detection of drugs and their metabolites in body fluids (e.g., blood, urine, saliva) is limited by invasiveness, biohazard risks, cross reactivity with other substances in the samples, a requirement for cold or frozen sample transport and storage, susceptibility to contamination leading to false positives and the potential for a person to undermine the test. To address these limitations, a manufacturer has developed Intelligent Fingerprinting Technology, a handheld fingerprint drug testing device that analyzes the minute traces of sweat deposited in subjects' fingerprints. According to the manufacturer, the technology detects drug metabolites, not the drug itself. Additionally, the company purports that samples are quick and easy to collect, are impossible to cheat, are stable at room temperature, and do not require additional sample preparation. The company is positioning this product for use by law enforcement and in workplaces and institutions (e.g., prisons, the military). SmartStart, Inc., Irving, TX, with Intelligent Fingerprinting, Norwich, UK U.S. launch planned for 2013	Other body fluid testing (urine, saliva, blood) Field sobriety tests	Improved detection of illicit substances Reduced invasiveness of drug testing Reduced turnaround time for drug testing Reduced biohazard risk Reduced risk of cross reactivity Improved health outcomes
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	No therapies are indicated specifically for alcoholism secondary to PTSD disorder. Aprepitant (Emend®, approved for use in chemotherapy-induced nausea and vomiting) is a substance P antagonist that blocks neurokinin 1 receptor. Substance P, released in amygdala in response to stress, acts at neurokinin 1 receptors to mediate 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. Merck & Co., Inc., Whitehouse Station, NJ (manufacturer) National Institute on Alcohol Abuse and Alcoholism (investigator) Phase II trial ongoing	Off-label pharmacotherapy (e.g., acamprosate, disulfiram, naltrexone) Psychotherapy (e.g., cognitive behavior therapy)	Reduced alcohol consumption Reduced relapse Improved health outcomes associated with abstinence 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 deep brain stimulation for treatment of alcohol dependence	Patients in whom treatment-refractory alcohol dependence has been diagnosed	Only 36% of patients with alcohol dependence experience full remission when using available pharmacotherapy. Deep brain stimulation (DBS) uses permanently implanted electrodes to electrically interfere with activity in targeted parts of the brain. DBS is approved for use in conditions such as Parkinson's disease and obsessive-compulsive disorder. Researchers have suggested that DBS may have utility in treating alcohol dependence because the electrodes can be placed in the ventral striatum/nucleus accumbens, which is an area known to play a role in upholding addictive behaviors.Medtronic, Inc., Minneapolis, MN (manufacturer)University of Cologne, Cologne, Germany (investigator)Tangdu Hospital, Xi'an, China (investigator)National Institute on Alchohol Abuse and Alcoholism (investigator)Several small pilot studies completed and ongoing internationally; it does not appear that the manufacturer of the equipment used in these studies is seeking a labeled indication change for this product Medtronic, Inc., Minneapolis, MN (manufacturer) University of Cologne, Cologne, Germany (investigator) Several small pilot studies completed internationally; it does not appear that the manufacturer of the equipment used in these studies is seeking a labeled indication change for this product	Pharmacotherapy (e.g., acamprosate, disulfiram, naltrexone) Psychotherapy (e.g., cognitive behavior therapy)	Reduced alcohol craving Reduced alcohol consumption Reduced relapse Improved health outcomes associated with abstinence Improved quality of life
Off-label mifepristone (Mifeprex) for treatment of cocaine dependence	Patients in whom cocaine dependence has been diagnosed	No agents are approved for treating cocaine dependence. Mifepristone is a glucocorticoid receptor antagonist. Because cocaine dependence has been associated with glucocorticoid hormone hyperactivity, and because the glucocorticoid receptor has been found to mediate adaptation to environmental challenges and stress, mifepristone may have utility in reducing cocaine dependence. New York State Psychiatric Institute, New York The Scripps Research Institute, La Jolla, CA Phase II/III trial ongoing. Mifepristone is FDA approved to end early pregnancy and is marketed under the brand name Mifeprex® (Danco Laboratories, New York, NY); the manufacturer does not appear to be seeking a labeled indication for cocaine dependence; thus, it would be used off label for this indication	Off-label pharmacotherapy (e.g., disulfiram) Psychotherapy (e.g., cognitive behavior therapy)	Reduced reward associated with cocaine use Reduced cocaine consumption Reduced relapse Improved health outcomes associated with abstinence 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 mifepristone for treatment of alcohol dependence	Patients in whom alcohol dependence has been diagnosed	Only 36% of patients with alcohol dependence experience full remission when using available pharmacotherapy. Research has suggested that pharmacotherapy efficacy is linked to the protracted abstinence phase, a phase where impaired glucocorticoid receptor feedback and other central nervous system dysregulation can influence alcohol relapse. Mifepristone is a glucocorticoid receptor antagonist. Because alcohol dependence has been associated with glucocorticoid hormone hyperactivity, and because the glucocorticoid receptor has been found to mediate adaptation to environmental challenges and stress, mifepristone may have a use in reducing alcohol dependence. In a clinical trial, mifepristone was orally administered at a dosage of 600 mg/day for 1 week. The Scripps Research Institute, La Jolla, CA Phase II trial ongoing; preliminary results available	Pharmacotherapy (e.g., acamprosate, disulfiram, naltrexone) Psychotherapy (e.g., cognitive behavior therapy)	Reduced alcohol consumption Reduced relapse Improved health outcomes associated with abstinence Improved quality of life
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 available pharmacotherapy; serotonin 5-HT3 receptors are a novel therapeutic target for this population. Ondansetron is a serotonin 5-HT3 receptor antagonist, approved for treating chemotherapy-induced nausea and vomiting and 1st marketed by GlaxoSmithKline (Middlesex, UK) as Zofran®. The drug is intended to exert its effects on alcohol dependency through cortico-mesolimbic dopamine system modulation. The 5-HT 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 Drug Abuse, Bethesda, MD; University of Virginia, Charlottesville; and Medical University of South Carolina, Charleston. (No ondansetron manufacturers are sponsoring these studies.) 1 phase III trial completed; several phase II and III trials ongoing	Pharmacotherapy (e.g., acamprosate, disulfiram, naltrexone) Psychotherapy (e.g., cognitive behavior therapy)	Reduced alcohol craving Reduced alcohol consumption Reduced relapse Improved health outcomes associated with abstinence Improved quality of life

Table 15. AHRQ Priority Condition: 15 Cross-Cutting: 8 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Implantable drug delivery microchip for chronic conditions requiring medication	Patients with chronic conditions who must take daily, long-term medication	In postmenopausal women, bone density significantly decreases, leading to diagnosis of osteoporosis and osteopenia. Although current osteoporosis treatments can be effective, low compliance because of subcutaneous injection limits efficacy and leads to poorer health outcomes. The implantable microchip is a flashdrive-sized drug delivery system inserted abdominally to administer calcitonin, a naturally occurring hormone involved in calcium regulation that binds to osteoclasts to slow the rate of bone breakdown and resulting bone loss, for an extended periods of time. The device is programmed to wirelessly allow drug delivery from the resorvoir every 24 hours. In current trials, the microchip's drug resorvoir lasts 20 days, but manufacturers are in the process of developing a 365-day resorvoir. MicroCHIPS Inc., Waltham, MA Pilot trial completed	BisphosphonatesInjectable calcitonin Intranasal calcitonin Raloxifene Estrogen Teriparatide	Slowed rate of bone breakdown Decreased bone loss Decreased numbers of hip and spine fractures Improved compliance Improved quality of life
Ingesitble sensor (Proteus Digital Health Feedback System, formerly the Raisin System) for monitoring long-term drug therapy	Patients in whom long-term drug therapy is needed for various chronic conditions	According to the World Health Organization, the average medication adherence rate among patients with chronic diseases in developed nations is only 50%. The Proteus Digital Health System™ (formerly the Raisin System), a form of smart-pill technology, is being used in an attempt to improve medication adherence by patients being treated for chronic diseases and requiring ongoing medication, such as tuberculosis, diabetes, heart failure, AIDS, hepatitis C virus infection, and mental health disorders. This is an edible microchip affixed to oral drugs (tablets) to monitor patient adherence; wearable data recorder in the form of a patch adhered to the skin captures actual drug consumption and vital statistics, reminds patients of missed doses, and transmits patient data to clinicians through a mobile device. Proteus Digital Health, Inc., Redwood City, CA FDA granted marketing clearance for the monitoring device Mar 2010; Jul 2012, the company also received marketing clearance for the ingestible sensor	Conventional oral drug therapy Patient medication reminders via telephone, text message, and/or email	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
Postdischarge clinics to provide transition care after hospital stay	Patients who have been recently discharged from the hospital and require followup care but do not have access to timely primary care	1/3 of patients discharged from the hospital do not see an outpatient physician within 30 days of their hospital visit, resulting in exacerbation of conditions and a high number of hospital readmissions. Barriers to visiting an outpatient physician (e.g., primary care physician) for followup include lengthy wait times for appointments and lack of health insurance. To address this unmet need, some hospitals have created postdischarge clinics. Postdischarge clinics are located in proximity to the hospital, are staffed by hospitalists, and are available for patients who are unable to get a followup appointment with their primary care physician within a week or 10 days after discharge, especially those who have been identified as being at high risk of readmission. The clinics are not intended to offer a substitute for primary or other outpatient care and are only intended to be used for a short amount of time (although times vary from clinic to clinic) until the patient can get care from a primary care physician. Various hospitals across the country, including Beth Israel Deaconess Medical Center, Boston, MA; University of California, San Francisco; and University of New Mexico Health Sciences Center, Albuquerque Several clinics have been launched in the United States	Outpatient followup care (e.g., with primary care physician)	Improved patient outcomes Reduced hospital readmissions
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 3rd-party payers. Pilot programs ongoing in several states, including Colorado, Texas, and Minnesota	No care because of 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

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Remote monitoring project (Improving Healthcare One Patient at a Time) to improve access to care for rural residents	Patients in rural or otherwise underserved areas who have suboptimal access to health care	Patients in rural or otherwise underserved areas are unable to reach traditional care facilities regularly and easily. The Improving Healthcare One Patient at a Time remote monitoring project is intended to improve access to care for this population. The project uses kiosks (placed in rural schools and churches) and home touch-screen devices to monitor patients' vital signs and other information (e.g., blood pressure, blood sugar, symptoms, weight). Clinicians can access both the home and the kiosk information via the Internet to review patient information, monitor vital signs, manage care plans and medication reminders, and further enhance in-person visits. University of Utah and the Utah Telehealth Network, Salt Lake City Pilot demonstration project launched Jun 2011; funded by a 3-year grant from the Health Resources and Services Administration's Office for the Advancement of Telehealth	Check-up appointments onsite at health facilities	Improved access to medical care Reduced health care disparities Decreased hospitalizations Decreased visits to emergency departments Improved health outcomes
Senior-specific emergency departments for treatment of elderly patients	Senior or elderly patients who visit an emergency department ED	20% 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 of 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). Senior-specific EDs have been opened in Colorado, Missouri, New Jersey, New York, and Texas First senior-specific ED launched in 2008	General EDs	Improved health outcomes for seniors Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Sublingual patient-controlled analgesia system (Zalviso) for treatment of pain following major surgery	Patients who have undergone major abdominal or orthopedic surgery	Patient-controlled analgesia (PCA) systems have led to significant improvements in postoperative pain management, but many approaches rely on intravenous (IV) medication delivery. Limitations associated with IV delivery of analgesic medications include IV-related analgesic gaps, pump programming or system errors, limited patient mobility, and catheter-related infections. Zalviso is a preprogrammed, sublingual, patient-controlled sufentanil delivery device (15 mcg/dose) that is intended to address many of these issues. AcelRx Pharmaceuticals, Inc., Redwood City, CA Phase III trials completed (major abdominal or orthopedic surgery)	Intravenous opiates Intravenous PCA systems Nonopiate analgesics	Improved pain control Increased ease-of-use for patients and providers Reduced dosing frequency
Wireless monitoring program (Care Beyond Walls and Wires) for rural patients with chronic conditions	Patients with chronic conditions who have been recently discharged from the hospital	Up to 1/2 of patients with heart failure discharged from the hospital are rehospitalized within 3–6 months. Reasons for this include not taking medications as prescribed, improper diet, lack of awareness of heart failure signs, and lack of planned followup with a doctor. These issues are particularly salient for rural populations, such as Native Americans, who often don't have access to cars or other transportation, running water, or electricity. The Care Beyond Walls and Wires program is intended to overcome these barriers and improve hospital readmission outcomes. The program uses smart phones and in-home monitoring equipment to collect data on weight, blood pressure, activity, and other important health indicators and transfer the data to nurses at a medical center. The nurses monitor the data daily and work with physicians to detect declines in a patient's health status and intervene early, potentially reducing unnecessary travel, physician office visits, costs, and hospital readmissions. The cell phones and monitoring equipment are donated by manufacturers. For rural residents without electricity, solar-powered batteries are used. Flagstaff Medical Center, Flagstaff, AZ 50-patient trial ongoing; the program is a National Institutes of Health Public-Private Partnership	In-person patient-monitoring visits Kiosk monitoring programs Other rural health programs in development (e.g., Project ECHO)	Fewer office visits and hospital readmissions Improved patient monitoring Improved patient outcomes Reduced costs

Section 2. Interventions Added Since Last Update: 5 Interventions

Table 16. AHRQ Priority Condition: 01 Arthritis and Nontraumatic Joint Disease: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 17. AHRQ Priority Condition: 02 Cancer: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Duloxetine (Cymbalta) for treatment of chemotherapy-induced peripheral neuropathy	Patients experiencing chemotherapy-induced peripheral neuropathy	Up to 40% of patients who receive neurotoxic chemotherapy treatment develop painful peripheral neuropathy that can persist for long periods of time after chemotherapy treatment is completed. Effective, non-narcotic treatment options are needed to manage chemotherapy-induced neuropathic pain. Duloxetine is a selective serotonin and norepinephrine reuptake inhibitor (SNRI) that reduced chemotherapy-induced neuropathy symptoms more effectively than placebo in a recent clinical trial. Duloxetine was administered as a oral dose of 30–60 mg for 5 weeks. Eli Lilly and Co., Indianapolis, IN (manufacturer) Cancer and Leukemia Group B (CALGB), Chicago, IL, in collaboration with the National Cancer Institute, Rockville, MD (investigators) Phase III trial (NCT00489411) completed; drug may be prescribed off label	Anticonvulsants Antidepressants (i.e., SNRIs) Opiates	Decreased pain Decreased analgesic intake Improved neuropathy-related functional status Improved nonpainful symptoms (i.e., numbness and tingling) Improved quality of life

Table 18. AHRQ Priority Condition: 03 Cardiovascular Disease: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Autologous bone marrow–derived stem cell therapy (C-Cure) for heart failure	Patients in whom severe heart failure (HF) has been diagnosed	No treatments are available that can repair heart tissue to reverse HF. Patients with end-stage HF have few options—ventricular assist device implant, total artificial heart implant, or a heart transplant. C-Cure® consists of stem cells derived from a patient's bone marrow and cultured in a proprietary laboratory process to become cardiac lineage cells intended to improve heart function when injected into the patient's heart. The company states that the process "reprograms" cells so they become heart precursor cells with "the aim of replicating the normal process of cardiac development in the embryo" and purportedly stimulating heart-tissue repair. The company has developed a proprietary catheter called C-Cath®ez® to deliver the processed cells to the patient. Cardio3 BioSciences, S.A., Mont-Saint-Guibert, Belgium Phase III trial (CHART-1) began in Jun 2013	Cardiac rhythm therapy devices Heart transplant Implanted cardioverter defibrillator Medical therapy Total artificial heart implantation Ventricular assist device	Increased left ventricular ejection fraction and other heart-function outcomes Improved activities of daily living Increased survival Improved quality of life

Table 19. AHRQ Priority Condition: 04 Dementia (including Alzheimer's: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 20. AHRQ Priority Condition: 05 Depression and Other Mental Health Disorders: 0 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 21. AHRQ Priority Condition: 06 Developmental Delays, Attention-Deficit Hyperactivity Disorder, and Autism: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 22. AHRQ Priority Condition: 07 Diabetes Mellitus: 0 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 23. AHRQ Priority Condition: 08 Functional Limitations and Disability: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
RNS system for treatment of refractory partial epilepsy	Patients in whom refractory epilepsy has been diagnosed	An estimated 3 million people in the U.S. have some form of epilepsy, with about 1 million cases resistant to medical therapy. Pharmacological therapies have helped treat epilepsy, but recurrence is common. Surgical procedures, such as craniotomy, may leave the brain susceptible to unintended injury and resultant neurological complications. The NeuroPace RNS system is a device that uses electrical stimulation to suppress the incidence of seizure before symptoms occur. It is surgically implanted underneath the patient's scalp by a surgeon. The neurostimulating portion of the device is then connected to the surface of the brain by one or two wires which contain electrodes. The RNS system continuously monitors electrical activity of the brain and delivers brief electrical stimulation when "signatures" of onset are detected. The manufacturer purports that the device suppresses seizure activity by delivering responsive stimulation. NeuroPace, Inc., Mountain View, CA Phase III trial completed. In Feb 2013, FDA advisory panel voted unanimously to recommend approval of the RNS System.	Pharmacotherapy (e.g., ezogabine, lamotrigine, levetiracetam, perampanel, tiagabine, tricyclics, valproate)	Reduced frequency of seizures Improved quality of life

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Stroke Inpatient Rehabilitation Reinforcement of Activity (SIRRACT) monitoring system for poststroke patient monitoring	Patients who are undergoing inpatient stroke rehabilitation	Stroke affects about 795,000 individuals annually in the U.S. Patients who have survived stroke are required to undertake rehabilitation to achieve the best possible outcomes. Monitoring patient compliance to standard physical and occupational therapies has been a challenge for health care providers and measuring the effectiveness of treatment for patients who perform home-based therapies has been difficult. Stroke Inpatient Rehabilitation Reinforcement of Activity (SIRRACT) is a program that uses simple accelerometers in conjunction with Medical Daily Activity Wireless Network (MDAWN) wireless monitoring system to measure the patient's movement in the home setting. Small sensors are attached to the patient's arms or legs via Velcro wrist or ankle bands. The information is automatically recorded, and it can be wirelessly retrieved by the health care provider for analysis. University of California, Los Angeles Phase II trial completed; additional unphased trial registered in Jun 2013, not yet open for recruitment	Robot-assisted rehabilitative therapy Standard occupational therapy Standard physical therapy	Improved care monitoring Improved patient self-care motivation

Table 24. AHRQ Priority Condition: 09 Infectious Disease, Including HIV-AIDS: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 25. AHRQ Priority Condition: 10 Obesity: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 26. AHRQ Priority Condition: 11 Peptic Ulcer Disease and Dyspepsia: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 27. AHRQ Priority Condition: 12 Pregnancy, Including Preterm Birth: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 28. AHRQ Priority Condition: 13 Pulmonary Disease, Asthma: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 29. AHRQ Priority Condition: 14 Substance Abuse: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts

Table 30. AHRQ Priority Condition: 15 Cross-Cutting: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts
Diffusion tensor imaging–brain mapping for guidance of neurosurgical procedures	Patients undergoing neurosurgical procedures that involve resection of brain tissue	Many complicated neurosurgical procedures (i.e., tumor resection, epilepsy surgery) pose the risk of damaging critical brain structures and fiber tracts, resulting in loss of function and impairment. Standard MRI imaging and intraoperative electrophysiology allow basic anatomical and functional brain mapping, but these approaches fail to provide information about white matter connectivity within the brain. Diffusion tensor imaging (DTI) tracks water molecules as they travel along axonal fibers in the brain. DTI enables neurosurgeons to build a 3-dimensional, directional map of the fiber pathways connecting critical brain structures. This information can be overlaid with structural and functional MRI to provide enhanced brain-mapping guidance for neurosurgery. Imaging modality available through multiple device manufacturers Examined by multiple academic research institutions, including Memorial Sloan-Kettering Cancer Center, New York, NY; University of Pennsylvania, Philadelphia; and UT Southwestern Medical Center, Dallas, TX Clinical trials ongoing	Intraoperative electrophysiology Functional MRI Structural MRI	Improved surgical outcomes

Section 3. Interventions Tracked but Archived Since Last Update: 55 Interventions

Table 31. AHRQ Priority Condition: 01 Arthritis and Nontraumatic Joint: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Atacicept for treatment of systemic lupus erythematosus	Patients in whom systemic lupus erythematosus (SLE) has been diagnosed	Investigators have not found a permanent cure for SLE, and current treatments provide only partial relief of symptoms. Atacicept is a biologic that purportedly decreases 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 TAC Ig. Atacicept is purportedly 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 completed	AGS-009 Belimumab Rituximab Rontalizumab	Delayed disease progression Reduced symptoms Reduced flare-ups Improved quality of life	Atacicept competes with and has a similar target to belimumab, which was approved Mar 2011

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Tofacitinib (Xeljanz) for treatment of rheumatoid arthritis	Patients in whom rheumatoid arthritis (RA) has been diagnosed	RA is a chronic inflammatory disease causing polyarthritis with frequent progression to permanent joint damage, deformity, and functional disability. Tofacitinib (Xelijanz) is a selective and potent oral tyrosine kinase inhibitor that is a new targeted disease-modifying antirheumatic drug (DMARD) for treating RA. Tofacitinib inhibits a Janus kinase (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. A therapy targeted to reducing RA-specific inflammatory processes in the way tofacitinib purports to might provide better symptom control with fewer adverse events than other DMARDs or nonsteroidal anti-inflammatory drug (NSAID)-activated anti-inflammatory pathways. FDA approved the drug for a dosage of 5 mg, twice daily, for adults with moderate to severe, active RA whose disease has had an inadequate response or who are intolerant to methotrexate. Tofacitinib may be used alone or in combination with methotrexate or other nonbiologic DMARDs. Pfizer, Inc., New York, NY FDA approved Nov 2012 as 1st new oral DMARD for RA in more than 10 years and 1st JAK inhibitor approved	Corticosteroids DMARDS: hydroxychloroquine, methotrexate, sulfasalazine NSAIDS Tocilizumab Tumor necrosis factor-alpha inhibitors	Reduced inflammation Improved symptoms Improved activities of daily living Improved quality of life	Poor diffusion indicates no potential for high impact

Table 32. AHRQ Priority Condition: 02 Cancer: 21 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Antibody-drug conjugate (inotuzumab ozogamicin) for treatment-refractory 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 a poor prognosis. 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. Although an anti-CD20 antibody (rituximab) has been used in treating NHL for several years, an effective treatment targeting CD22 is not yet 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/m2 of body surface area 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 chemotherapy including 1 or more of the following: Cisplatin Cyclophosphamide Dexamethasone Doxorubicin Etoposide Gemcitabine Lenalidomide Prednisone, Procarbazine Rituximab Vincristine	Increased overall survival Increased progression-free survival Improved quality of life	Phase III trial halted after interim analysis suggested no potential to improve overall survival.
Axillary reverse mapping–guided breast cancer treatment for prevention of lymphedema	Patients with breast cancer who are undergoing sentinel lymph node biopsy, axillary lymph node dissection, or radiation therapy with exposure to the axillary nodes	Procedures to stage and treat breast cancer (e.g., lymph node dissection and radiation therapy) can disrupt the lymphatic system of the axilla. When arm-draining lymphatic structures are damaged, chronic swelling and soreness in the arm (lymphedema) may result. 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; it is considered generally incurable and can severely restrict activity. The treatment-related risk of developing lymphedema might be mitigated by identification and selective preservation of the critical lymph nodes that drain the limb. In recent clinical trials, lymphatic tracers were used to identify the arm-draining nodes, and treatment procedures were modified to minimize damage to these structures. City of Hope Medical Center, Duarte, CA; Mayo Clinic, Rochester, MN; University of Arkansas for Medical Sciences, Little Rock, AR; and University of Kansas Medical Center in Kansas City, KS Several clinical trials ongoing	Standard external beam radiation therapy Standard axillary lymph node dissection	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	Expert comments indicated no potential for high impact.

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Belagenpumatucel-L (Lucanix) for treatment of nonsmall cell lung cancer	Patients with advanced or metastatic nonsmall cell lung cancer (NSCLC) whose disease has responded to 1st-line platinum-based chemotherapy	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. Belagenpumatucel-L (Lucanix™) is an allogeneic tumor-cell vaccine intended to delay disease progression after successful 1st-line treatment with platinum-based chemotherapy. The vaccine consists of 4 NSCLC cell lines that are administered intradermally once monthly for up to 2 years. The tumor-cell lines have been genetically modified to express an antisense version of transforming growth factor beta 2 (TGFB2), which is intended to inhibit the expression of TGFB2. TGFB2 has been shown to have antagonistic effects on various components of the immune system, and the developer hypothesizes that its inhibition could enhance an immune response generated by the tumor-cell vaccine. In clinical trials, belagenpumatucel-L is given as a monthy intradermal injection at a dose of 25 million cells in 0.4 ml. NovaRx, San Diego, CA Phase III trial ongoing under a special protocol assessment with FDA, enrollment complete; FDA granted fast-track status	Watchful waiting after successful 1st-line therapy Maintenance therapy (various chemotherapy regimens determined according to NSCLC subtype)	Increased overall survival Increased progression-free survival Improved quality of life	Phase III trial halted for futility; manufacturer has not updated status of product for 4 years.
Brentuximab vedotin (Adcetris) for treatment of Hodgkin's lymphoma	Patients in whom Hodgkin's lymphoma has been diagnosed	Hodgkin's lymphoma is a CD30-positive hematologic malignancy with limited salvage therapy options. Brentuximab vedotin (Adcetris™, SGN-35 or cAC10-vcMMAE) is a monoclonal antibody-drug conjugate that targets CD30-expressing cells. Seattle Genetics, Inc., Bothell, WA FDA approved Aug 2011, for treating patients with Hodgkin's lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not ASCT candidates. Supplemental biologics license application submitted to FDA in Mar 2013 covering extended treatment duration and re-treatment.	Standard of care	Increased overall survival Increased progression-free survival Improved quality of life	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Brentuximab vedotin (Adcetris) for recurrent or treatment-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; the 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 2 indications: (1) treating patients who have Hodgkin's lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not ASCT candidates, and (2) treating patients who have systemic ALCL after failure of at least 1 prior multi-agent chemotherapy regimen. Seattle Genetics, Inc., Bothell, WA FDA approved Aug 2011 for treating systemic ALCL after failure of at least 1 prior multi-agent chemotherapy regimen; supplemental biologics license application submitted to FDA in Mar 2013 for extended treatment duration and re-treatment	Autologous stem cell transplantation Allogeneic stem cell transplantation	Increased overall survival Increased progression-free survival Improved quality of life	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Cabozantinib (Cometriq) 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 medullary thyroid cancer (MTC) that target MET, which may be responsible for drug resistance in patients treated with current receptor tyrosine kinase inhibitors. Cabozantinib (Cometriq™) is an oral, small-molecule, receptor tyrosine kinase inhibitor that targets MET and vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2). MET plays key roles in proliferation, migration, invasion, and angiogenesis; overexpression of the hepatocyte growth factor ligand of MET and activation of the MET pathway supports tumors; VEGFR2 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. The recommended dose on the labeling approved by FDA in Nov 2012 is for 140 mg orally, taken once daily. Exelixis, Inc., South San Francisco, CA FDA approved Nov 2012 for treating progressive metastatic MTC; labeling carries a black box warning for risk of gastrointestinal perforations, fistulas, and hemorrhage	Radiotherapy Sorafenib Sunitinib Vandetanib	Increased overall survival Increased progression-free survival Improved quality of life	No potential for high impact; offers minimal impact over close comparator vandetanib, which was approved in Apr 2011
CD56-specific antibody-drug conjugate (lorvotuzumab mertansine) 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. Lorvotuzumab mertansine (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 ongoing trials, lorvotuzumab mertansine is being administered by intravenous infusion as an adjunct to a conventional cytotoxic chemotherapy regimen of lenalidomide and dexamethasone. ImmunoGen, Inc., Waltham, MA Phase I trial estimated completion Jan 2013; FDA granted orphan drug status	Lenalidomide plus dexamethasone	Increased overall survival Increased progression-free survival Improved quality of life	Company halted development.

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Crizotinib (Xalkori) for treatment of nonsmall cell lung cancer	Patients with nonsmall cell lung cancer (NSCLC) that harbors a genetic rearrangement that leads to constitutive activation of anaplastic lymphoma kinase (ALK)	The 5-year survival rate for patients with advanced NSCLC is less than 15% with current treatments. 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, it may reduce tumor growth and survival. In June 2013, phase III trial results showed that crizotinib was superior to chemotherapy for patients with previously-treated ALK+ NSCLC. Pfizer, Inc., New York, NY FDA approved Aug 2011 for treating locally advanced or metastatic NSCLC that is ALK-positive as detected by an FDA-approved test	1st-line: Combination chemotherapy (e.g., pemetrexed plus cisplatin) Targeted immunotherapy (e.g., bevacizumab, cetuximab, erlotinib) 2nd-line: Erlotinib Single agent chemotherapy (e.g., docetaxel, pemetrexed)	Increased overall survival Increased progression-free survival Improved quality of life	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria
Everolimus (Afinitor) for treatment of pancreatic neuroendocrine tumors	Patients with surgically unresectable pancreatic neuroendocrine tumors (PNETs) that have progressed within the past year	Patients with PNETs have few treatment options, and existing treatments are of limited efficacy. The mTOR/phosphoinositide 3-kinase pathway is a central regulator of cell growth, proliferation, death, and migration. Inhibition of mTOR has exhibited anticancer activity in a number of disease settings. Everolimus (Afinitor®) is an mTOR inhibitor FDA approved for treating renal cell carcinoma and subependymal giant cell astrocytomas. It is proposed for treating PNETs. In clinical trials of patients with PNETs, everolimus was administered in a daily, oral dose of 10 mg. Novartis International AG, Basel, Switzerland FDA approved May 2011 for treating PNETs	5-Fluorouraci Capecitabine Dacarbazine Doxorubicin Streptozocin Sunitinib Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Fosbretabulin tromethamine (Zybrestat) for treatment of anaplastic thyroid cancer	Patients in whom anaplastic thyroid cancer has been diagnosed	Few treatment options exist for patients with anaplastic thyroid cancer, and these patients often die from the disease within a year of diagnosis. Fosbretabulin tromethamine (Zybrestat®) is a vascular disrupting agent under study for treating patients with this condition. Vascular-disrupting agents such as fosbretabulin tromethamine purportedly act as tubulin depolymerizing agents that selectively disrupt the cytoskeleton of proliferating endothelial cells. Proliferating endothelial cells are often found in the disordered vasculature of tumors, and abnormal endothelial cell function caused by cytoskeletal manipulation is thought to disrupt tumor blood supply, potentially leading to cell death within the tumor. In trials, fosbretabulin tromethamine is administered by intravenous infusion in combination with cytotoxic chemotherapy of carboplatin plus paclitaxel. OXiGENE, Inc., South San Francisco, CA Phase II/III trial complete; FDA granted orphan drug status; special protocol assessment for phase III trial negotiated with FDA	Carboplatin and paclitaxel regimen	Increased overall survival Increased progression-free survival Improved quality of life	No longer in development for U.S. market.
Integrated positron emission tomography and magnetic resonance imaging system (Biograph mMR) for diagnosis and monitoring of cancer	Patients in whom cancer has been diagnosed	This system combines positron emission tomography (PET) with MRI (Biograph™ mMR) to provide simultaneous acquisition of morphologic, functional, and metabolic imaging data. The integration of these technologies is intended to enable imaging exams to be taken in 30 minutes, compared with 60 minutes or more for sequential PET with MRI exams. The system may be used individually for MR or PET procedures, as well as combined imaging. Siemens AG, Munich, Germany Received FDA 510(k) clearance Jun 2011	Stand-alone MRI and PET exams CT/PET exams	Improved imaging Decreased radiation exposure (compared to CT/PET) Improved patient throughput Increased patient satisfaction	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
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 antiulcer compound). It uses proprietary NexACT drug delivery technology, which is designed to reduce by 7 times the dose needed. The drug has shown strong anticancer activity in mice bearing human liver tumors. It is taken orally. Apricus Biosciences, Inc., San Diego, CA, licensed from Innovus Pharmaceuticals, Inc., La Jolla, CA Phase III trial special protocol assessment under discussion with FDA; FDA granted orphan drug status	Doxorubicin Sorafenib	Increased overall survival Increased progression-free survival Improved quality of life	Apricus acquired license to develop this drug in 2010, but there has been no movement in 3 years and the drug is no longer listed in the company's pipeline. No trials are registered with National Clinical Trials database.
Liver chemosaturation drug/device combination (melphalan-Chemosat) for treatment of melanoma metastases to the liver	Patients with ocular melanoma that has metastasized to the liver	Liver cancer is largely refractory to standard systemic chemotherapy. Although targeted chemotherapy delivery options are available for treating 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, Inc., New York, NY Phase III trial completed; FDA returned new drug application (NDA) in Feb 2011 asking for further safety data; pre-NDA held with FDA in Jan 2012 and company intended to refile NDA in 2nd quarter 2012; Conformité Européene (CE) marked for liver cancer. Company submitted a new NDA in Aug 2012 which was accepted by FDA in Oct 2012. FDA advisory panel voted unanimously against approval in May 2013.	Hepatic artery-delivered chemotherapy Trans-arterial chemoembolization	Increased overall survival Increased progression-free survival Improved quality of life	In May 2013, FDA advisory panel voted unanimously against approval because of efficacy and safety concerns.

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Microtubule destabilizing agent (ombrabulin) for treatment of soft tissue sarcoma	Patients with advanced soft tissue sarcoma who have undergone prior systemic chemotherapy with anthracycline (e.g., doxorubicin) and ifosfamide	Doxorubicin is the only FDA-approved treatment for soft tissue sarcomas (excluding gastrointestinal stromal tumors and liposarcomas), and no consensus on treatment exists for patients whose disease has progressed during doxorubicin-based chemotherapy. Ombrabulin (AVE8062) is a novel, small-molecule agent that purportedly functions through the depolymerization of microtubules. Although the exact antitumor mechanism of ombrabulin is unclear, it is thought bind tubulin and preferentially disrupts immature tumor vasculature, leading to ischemia and subsequent tumor necrosis. In a late-phase trial, ombrabulin is being administered by intravenous infusion in combination with cisplatin. Sanofi, Paris, France, licensed from Ajinomoto Phase III trial completed; FDA granted orphan drug status for sarcoma	Pazopanib Sorafenib (off label) Sunitinib (off label)	Increased overall survival Increased progression-free survival Improved quality of life	No longer listed in company pipeline; investigators concluded it did not show sufficient clinical benefit to warrant further study; no other registered trials ongoing.
Zoledronic acid (Zometa) for treatment of breast cancer	Postmenopausal women with stage II/III breast cancer who have undergone surgery and/or surgical resection	Despite successful 1st-line therapy, a significant number of patients with breast cancer experience recurrence. Zoledronic acid (Zometa®) is a bisphosphonate used to prevent skeletal fractures in cancer patients at risk of 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., postmenopausal patients). Given that the drug is commercially available, its off-label use for this may be an option exercised by oncologists. Based on clinical trial data, the manufacturer has decided not to pursue a label expansion. Novartis International AG, Basel, Switzerland Multiple phase III trials completed; based on AZURE trial results, Novartis decided not to pursue expanded label for zoledronic acid; additional phase III data reported Jun 2013	Chemoradiation therapy Hormone therapy	Increased overall survival Increased progression-free survival Improved quality of life	Company decided to not pursue expanded label

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Orteronel (TAK 700) for treatment of castration-resistant prostate cancer	Patients in whom castration-resistant prostate cancer (CRPC) has been diagnosed	Median overall survival for patients with CRPC is only about 18 months. 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 forming dehydroepiandrosterone (DHEA) and androstenedione, which may ultimately be metabolized into the testosterone that is needed for the growth of many prostate tumors. Orteronel may be used in chemotherapy-naïve patients or after docetaxel, in combination with prednisone. Millennium Pharmaceuticals subsidiary of Takeda Pharmaceutical Co., Ltd., Osaka, Japan Phase III trials ongoing	Abiraterone Cabazitaxel Docetaxel Enzalutamide Sipuleucel-T	Increased overall survival Increased progression-free survival Improved quality of life	This has become a "me too" given the prior recent approvals of other new drugs for mCRPC.
Poly ADP-ribose polymerase inhibitor (iniparib) for treatment of metastatic nonsmall cell lung cancer	Patients in whom stage IV metastatic nonsmall cell lung cancer (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 adenosine diphosphate (ADP)-ribose polymerase (PARP), which functions in 1 type of DNA repair. Researchers have observed that cancers are often deficient in a 2nd type of DNA repair, and loss of both types of DNA repair is hypothesized to result in cancer cell lethality in response to DNA damage. No PARP inhibitors are on the market. Iniparib is being administered to patients with a new diagnosis who have not received treatment with any other agent. It is given in combination with a DNA- damage-inducing chemotherapy regimen (gemcitabine, carboplatin). BiPar Sciences unit of Sanofi, Paris, France Phase III trial ongoing	Cytotoxic chemotherapy (e.g., gemcitabine, carboplatin) alone	Increased overall survival Increased progression-free survival Improved quality of life	Manufacturer halted development following phase III trial failure.

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Protein kinase C-beta inhibitor (enzastaurin) for treatment of diffuse large B-cell lymphoma	Patients with diffuse large B-cell lymphoma (DLBCL) who have achieved complete remission after R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone) chemotherapy	The majority of patients with DLBCL achieve complete remission after 1st-line therapy; however, disease recurs in about 25% to 30% of patients. Enzastaurin is a small-molecule inhibitor of protein kinase C beta (PKC-beta) that is being studied as maintenance therapy to prevent DLBCL recurrence. PKC family members play a central role in a diverse range of cellular functions including the passage of signals from receptor tyrosine kinases controlling cell growth, cell survival, and endothelial cell migration. Inhibition of PKC-beta by enzastaurin is hypothesized to limit tumor growth and survival and angiogenesis. In a phase III trial, enzastaurin is being administered in a daily oral dose of 500 mg. Eli Lilly and Co., Indianapolis, IN Phase III trial ongoing	No maintenance therapy is available for DLBCL	Increased overall survival Increased progression-free survival Improved quality of life	Failed to meet primary endpoint in phase III trial. Company has ceased development.
Radiopharmaceutical (tilmanocept) for sentinel lymph node detection	Selected patients undergoing surgical resection of primary breast, melanoma, or head and neck tumors	The radiopharmaceuticals used to detect tumor-site draining lymph nodes for sentinel lymph node biopsy have several shortcomings, such as slow injection-site clearance, a relatively long half-life, and significant lymph node pass-through. Tilmanocept (Lymphoseek®) is a novel radiopharmaceutical preparation that is intended to improve on these by using a technetium-99 radiolabel. This radiolabel is coupled to a macromolecule that contains multiple units of mannose, which bind to the surface of dendritic cells and macrophages present in lymph nodes. Tilmanocept is administered by injection before the procedure. Navidea Biopharmaceuticals, Inc. (formerly NeoProbe Corp.), Dublin, OH Received FDA approval on Mar 13, 2013 for use in breast cancer and melanoma; phase III trial in head and neck cancers ongoing, positive topline results reported Apr 2013	Technetium sulfur colloid Vital blue dye (e.g., isosulfan blue)	Increased sentinel node detection sensitivity and specificity Improved patient outcomes Optimized treatment selection	Expert comments indicated no potential for high impact.

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Sunitinib (Sutent) for treatment of pancreatic neuroendocrine tumors	Patients with surgically unresectable pancreatic neuroendocrine tumors (PNETs) that have progressed within the past year	Patients with PNETs have few treatment options, and existing treatments are of limited efficacy. Like many tumors, PNETs depend on receptor tyrosine kinase activity to drive angiogenic and mitogenic processes. PNETs have been shown to express a range of receptor tyrosine kinases that could mediate these processes, such as certain platelet-derived growth factor receptors, vascular endothelial growth factor receptors, and stem-cell factor receptors. Sunitinib (Sutent®) is a small-molecule inhibitor of the kinase activity of these receptors. In clinical trials, it was administered orally, at a daily dose of 37.5 mg. Pfizer, Inc., New York, NY FDA approved May 2011 for treating PNETs	5-Fluorouracil Capecitabine Dacarbazine Doxorubicin Everolimus Streptozocin Temozolomide	Increased overall survival Increased progression-free survival Improved quality of life	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria
Therapeutic vaccine (BiovaxID) for indolent follicular non-Hodgkin's lymphoma	Patients in whom indolent follicular non-Hodgkin's lymphoma has been diagnosed and who are in their 1st complete remission	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 granulocyte macrophage colony-stimulating factor 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	Watchful waiting	Increased overall survival Increased progression-free survival Improved quality of life	Development has not progressed for two years; company in chapter 11.

Table 33. AHRQ Priority Condition: 03 Cardiovascular Disease: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Icatibant (Firazyr) for treatment of acute hereditary angioedema	Patients 18 years of age or older in whom acute hereditary angioedema (HAE) has been diagnosed	HAE is a genetic disorder caused by dysfunction or deficiency of the plasma protein C1 inhibitor (C1INH). C1INH inhibits 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 beta-receptor-1, bradykinin beta-2 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 beta-2 receptors. Administered by subcutaneous injection. Shire Pharmaceuticals, plc, Dublin, Ireland FDA approved Aug 2011 for treating 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	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Table 34. AHRQ Priority Condition: 04 Dementia (including Alzheimer's): 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Intravenous immunoglobulin (Gammagard) for treatment of Alzheimer's disease	Patients in whom mild to moderate Alzheimer's disease (AD) has been diagnosed	No approved disease-modifying agents are available for treating AD; available therapy options are limited to symptom management. Intravenous immunoglobulin (IVIG) infusion (Gammagard) is approved for treating many immune disorders. In patients with AD, IVIG is intended to clear beta amyloid from the brain, thereby purportedly blocking beta amyloid's detrimental effects on the brain. Clinical trials are testing low- and high-dose IVIG infusions, given every 2 weeks for 18 months. Baxter International, Inc., Deerfield, IL May 2013, completed phase III trial failed to meet co-primary endpoints. Remaining trials for this indication discontinued	Cholinergic agents (e.g., donepezil, galantamine, tacrine) NMDA inhibitor (e.g., memantine)	Reduced beta-amyloid load in brain Halted or slowed disease progression Improved quality of life	No development ongoing for this indication.

Table 35. AHRQ Priority Condition: 05 Depression and Other Mental Health Disorders: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
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	25% to 40% of citizen soldiers (National Guard, Reserves) develop posttraumatic stress disorder, clinical depression, sleep disturbances, or suicidal thoughts, but when veterans return home, barriers exist to receiving appropriate care. About 1/2 of those needing medical or psychological intervention are not receiving care. The Buddy-to-Buddy 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. 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; University of Michigan, Ann Arbor; 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	Other peer support group programs (e.g., Vet-to-Vet)	Increased access for veterans to medical and psychological support resources Improved mental health outcomes Improved substance abuse outcomes Improved quality of life	Program has not diffused outside of state of origin after two years

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Lisdexamfetamine (Vyvanse) for treatment of negative symptoms in schizophrenia	Patients in whom schizophrenia has been diagnosed	Existing pharmacotherapies for schizophrenia may have limited efficacy and are associated with unwanted side effects in many patients. Additionally, available treatment options inadequately address the negative and cognitive symptoms of schizophrenia. Negative symptoms are an absence of normal responses and include blank stares, monotone and monosyllabic speech, few gestures, and disengagement or disinterest. Lisdexamfetamine (Vyvanse®) is a prodrug of dextroamphetamine and induces release of dopamine and norepinephrine, which contribute to maintaining alertness, focus, thought, effort, and motivation. In clinical trials, the drug is being tested in once daily oral doses of 40mg, 100mg, and 160mg. Shire, plc, Dublin, Ireland Phase III trial was terminated; lisdexamfetamine is already indicated for treating attention-deficit hyperactivity disorder	Pharmacotherapy (e.g., atypical antipsychotics)	Reduced negative symptoms Improved social functioning Improved quality of life	Development halted after trial was canceled

Table 36. AHRQ Priority Condition: 06 Developmental Delays, Attention-Deficit Hyperactivity Disorder, and Autism: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Arbaclofen (STX209) for treatment of fragile X syndrome	Patients in whom fragile X syndrome (FXS) has been diagnosed	No cure exists for FXS; medications and behavior interventions alleviate individual symptoms but do not address the syndrome's cause. Pharmacologic treatments that address FXS social deficits are needed because impairments in social function are a core feature of the condition. 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 restore the normal balance at the synapse and correct abnormalities associated with FXS. Seaside Therapeutics, Inc., Cambridge, MA Phase III trials	Physical and behavior interventions Medications: Antipsychotics Central nervous system stimulants Clonidine (Catapres®) Folic acid Selected serotonin reuptake inhibitors To address sleep disturbances To treat seizures and mood instability	Improved behavior and cognitive measures Increased sociability and communication	Company halted trials and development because of lack of funding
Arbaclofen (STX209) for treatment of social withdrawal in autism spectrum disorder	Patients in whom an autism spectrum disorder (ASD) has been diagnosed	Most individuals with an ASD are treated through highly structured behavior programs to try to improve social cognition and functioning. Pharmacologic treatments to address ASD-related social deficits are lacking because 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 communication, repetitive behaviors, and restricted interests is needed. Research suggests an imbalance in gamma aminobutyric acid (GABA)/glutamate transmission underlies behavior deficits of ASD. Arbaclofen is intended to improve synaptic functioning by regulating glutamate and increasing GABA, the main inhibitory neurotransmitter in the central nervous system and 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 5 or 10 mg, twice a day; 10 or 15 mg, 3 times a day. Seaside Therapeutics, Inc., Cambridge, MA Phase IIb trial	Off-label pharmacotherapy Physical and behavior interventions including speech and language, behavior, cognitive development, sensory integration, gross motor development, and activities of daily living Pharmacotherapy (e.g., risperidone, anti-inflammatories, melatonin, naltrexone, oxytocin, tetrahydrobiopterin)	Improvement in Aberrant Behavior Checklist Social Withdrawal Subscale	Company halted trials and development because of lack of funding

Table 37. AHRQ Priority Condition: 07 Diabetes Mellitus: 1 Intervention

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Service dogs (diabetic alert dogs) for detection of hypoglycemia in patients with insulin-dependent diabetes mellitus	Patients with diabetes mellitus (type 1 or type 2) who are insulin dependent	Patients with diabetes mellitus who are insulin dependent can often experience hypoglycemic episodes as a side effect to insulin therapy. Hypoglycemia can cause confusion, clumsiness, or fainting, and severe hypoglycemia can lead to seizures, coma, and even death. Attending to the hypoglycemia at the onset of symptoms can prevent severe consequences; however, children and seniors may not be fully aware of their symptoms or they may be unable to communicate their symptoms. Additionally, many patients with type 1 diabetes develop hypoglycemia unawareness, a condition in which the patient no longer experiences many of the warning symptoms associated with low blood sugar. Service dogs are being trained to detect and react to a scent associated with a drop in patients' blood sugar levels. Placed with patients, these dogs alert patients when their blood sugar level is dropping or even before the drop occurs. Diabetic alert dogs are provided by several training centers including nonprofit training centers. Diabetic alert dogs are currently being placed in households of patients with insulin-dependent diabetes mellitus.	Conventional glucose monitoring Diabetes management education	Decreased hospitalizations for acute complications Decreased hypoglycemic episodes Improved quality of life	Expert comments indicated no potential for high impact

Table 38. AHRQ Priority Condition: 08 Functional Limitations and Disability: 8 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Autologous knee bone and cartilage transfer for surgical treatment of wrist injuries	Patients with wrist fractures, chronic wrist pain, and ligament tears that require surgical intervention	About 1/6 of fractures evaluated in U.S. emergency rooms are wrist fractures. Some wrist injuries are unstable, with ligament tears and dissociation of the wrist bones. Conventional ligament reconstruction surgery often does not alleviate pain, warranting the need for better surgical procedures. Knee bone and cartilage transfer represents an innovative surgical procedure that involves resecting, shaping, and transferring the patient's own cartilage-bearing bone from the knee to the wrist, with the intent of eliminating the previously existing gap caused by the torn ligament(s). Union Memorial Hospital's Curtis National Hand Center, Baltimore, MD First reported procedure completed Aug 2011	Conventional ligament reconstruction surgery	Decreased wrist pain Decreased risk of wrist arthritis Improved wrist function Improved quality of life	Horizon scanning team determined upon further investigation that procedure is not novel; is used for a variety of joint injuries

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Peginesatide (Omontys) for treatment of anemia from chronic renal failure	Patients with chronic kidney disease (CKD) who are on dialysis and 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 (ESAs) 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 (Omontys®) is a long-acting, parenteral formulation being developed for treating anemia in patients on dialysis (i.e., with CKD). 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 ESAs. Peginesatide is administered once monthly, by subcutaneous or intravenous injection, 0.04–0.16 mg/kg of body weight per dose. It is not intended for use in patients with CKD who are not on dialysis or for use in patients with anemia from other conditions, such as cancer. Affymax, Inc., Palo Alto, CA, in collaboration with Takeda Pharmaceutical Co., Ltd., Osaka, Japan FDA approved Mar 2012; approval required Risk Evaluation and Mitigation Strategy for treating anemia in adults on dialysis; was 1st agent approved since 2001 for this condition. Labeling included warning: “ESAs increase the risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access and tumor progression or recurrence.”	Diet and lifestyle modifications ExenatideInsulinInsulin sensitizers (pioglitazone, rosiglitazone) Metformin Renal transplantation Sitagliptin Sulfonylurea drugs (glimepiride)	Reduced frequency of drug administration Resolution of anemia Improved quality of life	Manufacturer voluntarily recalled product in late Feb 2013 due to serious adverse effects

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Levadex (MAP-0004) orally inhaled for treatment of migraine headaches	Patients in whom migraine headaches have been diagnosed	A derivative (Levadex™ [MAP-0004]) of the available dihydroergotamine; intended to alleviate migraine headache symptoms quickly through oral inhalation using the company's Tempo inhaler. Allergan, Inc., Irvine, CA; Allergan acquired original developer MAP Pharmaceuticals, Inc., Mountain View, CA, in Feb 2013 Positive phase III results reported; new drug application (NDA) accepted by FDA Aug 2011; Mar 2012, FDA issued complete response letter citing chemistry, manufacturing, and control issues, but did not request additional efficacy or safety information. Company resubmitted NDA in Oct 2012, filing accepted by FDA Nov 2012. In Apr 2013, FDA issued 2nd complete response letter, citing concerns about the inhaler canisters. The manufacturer is addressing these concerns.	Pharmacotherapy (e.g., pain relievers, triptans, ergot, anti-nauseates, opiates, dexamethasone)	Quicker reduction in pain and light/noise sensitivity Reduced recurrence of symptoms Reduced side effects	Expert comments indicated no potential for high impact; incremental improvement over existing forms of the drug available as nasal spray and injection
Perampanel (Fycompa) for treatment of partial-onset epilepsy	Patients aged 12 or older in whom partial-onset epilepsy has been diagnosed	Some patients with partial-onset epilepsy do not respond to current therapy. Perampanel (Fycompa®) represents a new mechanism of action/class of drugs for this disease state. It is a highly selective, noncompetitive alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (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. The drug is taken as an oral tablet, once daily, 8 or 12 mg. Eisai Co., Ltd., Tokyo, Japan FDA approved Oct 2012 as adjunct treatment for partial-onset seizures with or without secondarily generalized partial-onset seizures in patients with epilepsy aged 12 years or older. Approval included a warning "to alert prescribers and patients about the risk of serious neuropsychiatric events, including irritability, aggression, anger, anxiety, paranoia, euphoric mood, agitation, and mental status changes." FDA recommended the drug be classified by the U.S. Drug Enforcement Administration as a scheduled drug; DEA will review the recommendation and determine the final scheduling designation. The drug was approved by the European Medicines Agency in Jul 2012.	Pharmacotherapy (e.g., lamotrigine, levetiracetam, tiagabine, tricyclics, valproate)	Reduced frequency of partial seizures Improved quality of life	FDA raised significant safety concerns; no potential for high impact

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Robotic navigation aid (Guide Vest) to assist visually impaired people	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 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 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 1st-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 and Viterbi School of Engineering, Los Angeles, CA Pilot study completed at Braille Institute	Long canes Remote Infrared Audible Signage (RIAS) "Sighted" wheelchair	Decreased risk of falls and injury Improved mobility Increased independence	Device was developed as a graduate student engineering project and no further development activity has been reported for 2 years
Tabalumab, (LY2127399) for treatment of systemic lupus erythematosus	Patients in whom systemic lupus erythematosus (SLE) has been diagnosed	Investigators have not found a permanent cure for SLE, and current treatments provide only partial relief of symptoms. Tabalumab 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 later. BAFF overexpression was found in a diseased brain and BAFF was subsequently referred to as a B cell–targeted therapy. The drug is delivered by subcutaneous injection every 2 or 4 weeks and taken with standard care. Eli Lilly and Co., Indianapolis, IN Phase III trials ongoing	Belimumab Corticosteroids Cyclophosphamide Methotrexate TNF-alpha inhibitors Rituximab	Improved SLE Responder Index Improved quality of life	No potential for high impact; mechanism of action similar to belimumab approved Mar 2011

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Vanquix (diazepam) auto-injector for treatment of epilepsy seizures	Patients in whom epilepsy has been diagnosed	About 3 million people in the U.S. are living with epilepsy, and another 200,000 cases are being diagnosed per year. Currently, patients are being treated pharmacologically; however, a more effective treatment is needed for patients who experience seizure. Vanquix (diazepam) is an intramuscular injection administered via auto-injector technology, which purports to overcome the inconsistency of injectable diazepam. In clinical trials, the diazepam auto-injector is provided in doses that are based on patient's weight (5, 10, 15, or 20 mg). Vanquix purports to reduce the frequency of epileptic seizures, fulfilling an unmet need. Vanquix purports to be the only available injectable form of diazepam that can be administered without the help of a healthcare professional. Vanquix is intended for the emergency treatment of acute, repetitive epileptic seizures, and the selected dose is administered by caregiver. The dose of diazepam is purported to fully deliver within 10 seconds. Pfizer, Inc., New York, NY Phase III trial ongoing	Lamotrigine Levetiracetam Tiagabine Tricyclics Valproate	Reduced frequency of partial-onset seizures Improved quality of life	No potential for high impact; determined to be incremental benefit only
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 strength Improved quality of life	Tracked 2 years in horizon scanning system and innovation has diffused widely; no longer meets horizon scanning criteria

Table 39. AHRQ Priority Condition: 09 Infectious Disease, Including HIV-AIDS: 6 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Bedaquiline (Sirturo) for treatment of drug-resistant tuberculosis	Patients in whom drug-resistant tuberculosis (TB) is inspected	TB has developed resistance to existing antibiotic therapies and treatment is further complicated by a lengthy regimen. Treatments that can improve outcomes in antibiotic-resistant infections and shorten treatment duration are needed. Bedaquiline (Sirturo™) is a diarylquinoline antituberculosis drug that is intended to achieve clinical response rates twice as fast as standard treatment. The dosage on the approved product labeling is 400 mg once daily for 2 weeks followed by 200 mg 3 times per week for 22 weeks with food. Janssen Therapeutics, Division of Janssen Products, LP, Titusville, NJ FDA approved Dec 28, 2012 for treating pulmonary, multidrug-resistant tuberculosis (MDR-TB) in adults as part of combination therapy when an effective treatment regimen cannot otherwise be provided. The drug carries a boxed warning alerting patients and health care professionals that the drug can affect the heart (i.e., QT prolongation), which could lead to an abnormal and potentially fatal heart rhythm. An increased risk of death was seen in the patients taking bedaquiline compared to patients taking placebo in one placebo- controlled trial.	Ethambutol Ethionamide Isoniazid Kanamycin Ofloxacin Pyrazinamide Rifampicin	Resolution of active TB infection Reduced time to clinical response Improved patient adherence with therapy Reduced spread of infection Improved quality of life	No potential for high impact after safety concerns emerged including cardiac abnormalities and increased risk of death.
Boceprevir (Victrelis) for treatment of hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) genotype 1 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. Boceprevir (Victrelis™) 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, 800 mg, 3 times daily, in combination with pegylated interferon and ribavirin (IFN/RBV). Merck & Co., Inc., Whitehouse Station, NJ FDA approved May 2011	IFN/RBV 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	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Collaborative care model (HITIDES) for treatment of depression secondary to HIV	Patients in whom depression secondary to HIV has been diagnosed	Major depressive disorder (MDD) is the most common mental illness that patients with HIV experience, yet is both underdiagnosed and undertreated in this patient population. HIV patients with co-occurring MDD are likely to have accelerated HIV disease progression, decreased immune function, decreased adherence to HIV medication regimens, and increased risk of mortality.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. A 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 careImproved health status Decreased HIV symptom severity Improved HIV medication and antidepressant adherence Improved patient satisfaction Improved health-related quality of life	Tracked more than 2 years in horizon scanning system with little further evidence of diffusion
Fidaxomicin (Dificid) for treatment of *Clostridium difficile* infection	Patients in whom *Clostridium difficile*–associated diarrhea has been diagnosed	Because of antibiotic resistance, new antibacterials that can improve clinical cure rates and reduce *C. difficile* infection (CDI) recurrence are needed. Fidaxomicin (Dificid®) is an antibiotic that is 1st in a new class, called macrocyclics, that 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 2011	Fecal microbiota transplant Metronidazole Vancomycin	Increased clinical cure rates Reduced CDI recurrence	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
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 that 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 5–10 days. BioCryst Pharmaceuticals, Inc., Research Triangle Park, NC Phase III trials terminated for administrative reasons; approved for emergency use in patients with confirmed or suspected H1N1 influenza	Oseltamivir (Tamiflu®; for influenza) Zanamivir (Relenza®; for influenza)	Decreased length of hospitalization Reduction in virus titers Relieved symptoms	Expert comments indicated no potential for high impact; incremental benefit relative to oseltamivir and zanamivir
Telaprevir (Incivek) for treatment of hepatitis C virus infection	Patients in whom chronic hepatitis C virus (HCV) genotype 1 infection has been diagnosed	HCV treatment with pegylated interferon plus ribavirin (IFN/RBV) is generally ineffective in more than half of infected patients; effective treatments that improve clinical outcome in a shorter period of time are needed. Telaprevir (Incivek™) 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, 750 mg, 3 times daily, in combination with IFN/RBV. Vertex Pharmaceuticals, Inc., Cambridge, MA FDA approved May 2011	Boceprevir IFN/RBV	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	Diffused 2 years after FDA approval; no longer meets horizon scanning system criteria

Table 40. 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	Reason
Food-based polymer (Attiva) for treatment of obesity	Adults with body mass index (BMI) >30 kg/m2	The World Health Organization estimates that more than 1.5 billion adults are overweight and 500 million are considered obese. 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 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 pursuing FDA 510(k) clearance	Bariatric surgery Behavior and lifestyle modifications Combination appetite suppressant/stimulant and anticonvulsant (Qsymia) Combination norepinephrine/dopamine reuptake inhibitor and opioid receptor antagonist (Contrave; in development) Lorcaserin (Belviq) Pancreatic lipase inhibitor (orlistat, Xenical®)	Decreased comorbidities Improved quality of life Total weight loss	Company has no clear path to regulatory approval.

Table 41. AHRQ Priority Condition: 11 Peptic Ulcer Disease and Dyspepsia: 0 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason

Table 42. AHRQ Priority Condition: 12 Pregnancy, Including Preterm Birth: 3 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Daily text messaging to encourage oral contraceptive continuation	Patients using an oral contraceptive pill (OCP)	63% of reproductive-age women who practice contraception use nonpermanent methods, with OCP as the leading method for women younger than 30 years of age. On average, 6-month OCP continuation rates in young women range from 12% to 58%. In the U.S., OCP discontinuation and misuse lead to about 1 million unintended pregnancies a year. The OCP daily text messaging study evaluates the efficacy of a 2-way text-messaging program intended to deliver educational content on OCP continuation. This intervention is intended to reduce OCP discontinuation rates, especially for women in urban settings. Columbia University Medical Center Department of Obstetrics and Gynecology, New York, NY One pilot trial completed, one phase I trial ongoing	Educational therapy Routine care	Increased OCP continuation Decreased risk of pregnancy	Expert comments indicated no potential for high impact; incremental benefit only
Donor human milk program to feed very-low-birthweight infants	Very-low-birthweight infants (VLBW; less than 1,501 g weight at birth)	Women who give birth to infants of VLBW who must remain in the neonatal intensive care unit often are unable to supply sufficient breast milk. Donated breast milk for infants of VLBW whose mothers cannot supply sufficient breast milk purportedly leads to better health and neurodevelopmental outcomes for premature infants than those outcomes in preterm infants fed fortified formula. The milk is collected from lactating volunteers and screened for safety before being given to infants. University of Iowa, Iowa City Available through the Human Milk Banking Association of North America and commercially through Prolacta Bioscience, City of Industry, CA Phase III trials ongoing	Standard infant formula	Reduced health care costs Normal Bayley Scales of Infant Development, III (at 18–22 months of age)	Tracked more than 2 years in horizon scanning system; program has diffused widely

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Fetal programming to prevent 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 Pilot trial ongoing	Nutritional programs alone for pregnant women Prenatal vitamins alone Routine prenatal care	Improved health in newborns Decreased risk of development of metabolic disorders	Tracked more than 2 years in horizon scanning system; diffusing

Table 43. AHRQ Priority Condition: 13 Pulmonary Disease, Asthma: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
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. The 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 1 reading per inhaler use. Asthmapolis, Madison, WI FDA 510(k) cleared Jul 2012	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	Horizon scanning system subsequently identified other similar tracking systems; does not meet criteria
Heparin (VR-496) dry inhaled powder for treatment of cystic fibrosis	Patients in whom cystic fibrosis (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 is a proprietary formulation of dry powder heparin sodium; it is intended to be the first agent to treat CF that can potentially provide anti-inflammatory, mucolytic, antibronchoconstrictor, and anti-infective activity. The formulation's 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, plc, Chippenham, UK Phase II trial completed; FDA granted orphan drug status. Manufacturer pipeline lists VR-496 as available for licensing.	Hypertonic saline (to clear mucus Mucolytics: Pulmozyme Tobramycin (TOBI) solution for inhalation antibiotic treatment Physical therapy for mucolysis Investigational: Ataluren, Denufosol, VX-770, VX-809	Reduced chest infections Reduced anti-inflammatory activity Improved mucolysis	No longer in development by manufacturer; manufacturer wants to license development to another company

Table 44. AHRQ Priority Condition: 14 Substance Abuse: 2 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Vigabatrin (CPP-109) for treatment of cocaine dependence	Patients in whom cocaine dependence has been diagnosed	No pharmacotherapies for cocaine dependence are approved. Vigabatrin (CPP-109) 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. For this indication, the drug is intended to be administered dissolved in orange juice. Catalyst Pharmaceutical Partners, Inc., Coral Gables, FL Phase III trial failed to meet primary endpoints. Manufacturer discontinued development for this and all other indications. Vigabatrin is approved for use in patients with epilepsy.	Off-label pharmacotherapy (e.g., disulfiram) Psychotherapy (e.g., cognitive behavior therapy)	Reduced reward associated with cocaine use Reduced cocaine consumption Prevented relapse Improved health outcomes associated with abstinence Improved quality of life	Development halted after trial failed to meet primary endpoints
Interactive cell phone text message program (Text2Quit) for smoking cessation	Patients attempting smoking cessation	Although 75% of smokers want to quit smoking, fewer than 5% who attempt to quit are successful. Text2Quit is an interactive cell phone text-messaging program intended to help smokers stop 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 users 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, both of Washington, DC; several other institutions manufacturers have developed bi-directional text messaging platforms Clinical trials completed; program launched Jun 2011	1-way text messaging smoking cessation plans (not diffused) Hardcopy patient education Internet-based patient education Patient support groups Psychotherapy (e.g., cognitive behavior therapy)	Increased number of successful smoking cessation attempts Improved health outcomes associated with abstinence Reduced health disparities and improved access to cessation program Improved quality of life	Program has diffused widely after 2 years of tracking in horizon scanning system; no longer meets inclusion criteria

Table 45. AHRQ Priority Condition: 15 Cross-Cutting: 3 Interventions

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
Integrated positron emission tomography and magnetic resonance imaging system (Biograph mMR) for diagnosis and monitoring of neurologic conditions	Patients in whom neurologic conditions have been diagnosed	Imaging exams that combine positron emission tomography (PET) with MRI (Biograph™ mMR) to provide simultaneous acquisition of morphologic, functional, and metabolic imaging data. The exam is intended to take 30 minutes to perform, compared with 60 minutes or more for sequential PET with MRI exams. Siemens AG, Munich, Germany Received FDA 510(k) clearance Jun 2011	Stand-alone MRI and PET exams	Improved imaging Improved patient throughput Increased patient satisfaction	2 years after FDA approval; no longer meets horizon scanning system criteria
Motivational interviewing in the pharmacy setting to improve patient medication adherence	Patients who are at risk of nonadherence or are nonadherent to prescribed medication regimen(s)	According to the New England Healthcare Institute, medication nonadherence is responsible for about $290 billion annually in avoidable medical spending. Motivational interviewing 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. Motivational interviewing 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 (2–5 minutes) motivational interviews with patients may cultivate patient self-efficacy and improve medication adherence. Pharmacists are taught overall interviewing techniques and strategies for dealing with patient resistance to medication adherence. University of Missouri, Columbia; 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 adhere to regimen Improved medication adherence Reduced costs of medical care from treating noncompliant patients	Program has diffused widely after 2 years of tracking; no longer meets horizon scanning inclusion criteria

Topic Title	Potential Patient Population	Intervention Developer/Manufacturer(s) Phase of Development	Potential Comparators	Potential Health or Other Impacts	Reason
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 uses 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 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	Program diffused after 2.5 years of tracking in horizon scanning system; no longer meets inclusion criteria