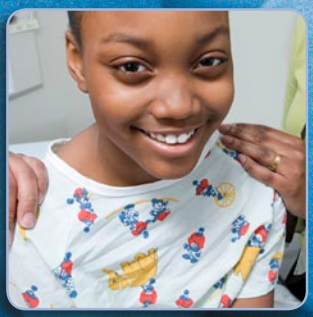
NOVEMBER 2011

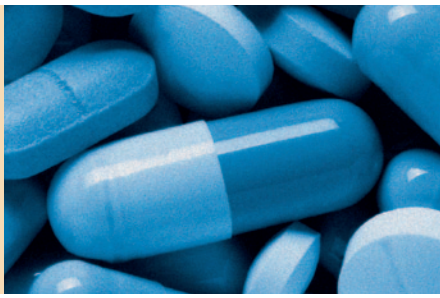
FY 2011 Innovative Drug Approvals



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. FOOD AND DRUG ADMINISTRATION

Executive Summary



The Food and Drug Administration (FDA) is entrusted with promoting and protecting the health and well-being of Americans. This means making sure that the medicines they take today are safe and that they work. But we also have another important role: promoting the innovation it takes to ensure that life-saving medicines continue to be developed and that Americans have access to new medicines as early as possible. One important means of supporting innovation is to maintain a state-of-the art drug approval process that brings important drugs to market quickly and efficiently. FDA's performance during the most recent fiscal year (October 1, 2010 – September 30, 2011) demonstrates that the FDA continues to lead the world in rapid, high-quality drug reviews.

FDA approved 35 innovative drugs in FY 2011, many of them groundbreaking. This is among the highest number of approvals in the past decade, surpassed only by 2009 (37). But few years have seen as many important advances for patients.

These drugs offer important advances in treatment for hepatitis C, late-stage prostate cancer, lupus, drug resistant skin infections, pneumonia, and other serious and life-threatening diseases including:

- Seven new medicines that provide major advances in cancer treatment.
- Ten drugs for rare ("orphan") diseases which have few or no treatments because of their small patient populations.
- Two new therapies, for lung cancer and melanoma, that are breakthrough products for personalized medicine: each was approved with a diagnostic test that helps identify patients for whom the drug is most likely to bring benefits.

FDA accelerated the review and approval of these important drugs by utilizing "expedited approval" pathways and by streamlining clinical trial requirements to permit smaller, shorter, or fewer studies wherever possible. With the help of these tools and the resources collected under the Prescription Drug User Fee Act (PDUFA), FDA was able to review these 35 important drugs quickly and efficiently.

- FDA approved 24 – almost 70% – of the 35 new drugs before any other country in the world, including the European Union (EU);
- FDA approved nearly half – 16 – of the innovative drugs under the agency's "priority review" program for drugs that may offer major advances in treatment; priority reviews carry a six-month target date for review;

The agency has made great strides forward to speed the development and availability of drugs for serious or life-threatening diseases.

- FDA approved all but one of the 35 drugs on or before the target dates for approval agreed to with industry under the PDUFA; and
- FDA approved the majority of these innovative drugs on the "first cycle," that is, without requests for additional information.

FDA's performance continued the agency's global drug-review leadership in recent years. For example, in a review of 57 novel drugs approved in both the US and EU between 2006 and 2010, FDA's median time to approval for priority review drugs was less than half that of the EU's (6 months versus13.2 months); for standard drug reviews, FDA's median time to approval was 13 months versus the EU's 14.7 months.

These results reflect many improvements in FDA's drug approval process in the last several years. The agency has made great strides forward to speed the development and availability of drugs for serious or life-threatening diseases; it has launched the Critical Path Initiative to help streamline drug testing and review; and it has sharpened its focus on methods of efficiently identifying and resolving drug safety issues.

PDUFA was established by Congress to ensure that the FDA had the necessary resources for the safe and timely review of new drugs. It played an important role in advancing the quality and speed of FDA's drug reviews. PDUFA funding has provided the agency with additional resources for hiring and training scientific reviewers, keeping FDA scientists abreast of innovative technologies, and improving the scientific basis for regulatory decisions. The current legislative authority for PDUFA expires on Sept. 30, 2012.

FDA is committed to supporting innovation in the biopharmaceutical industry. Despite its record of high-quality, efficient drug reviews, FDA recognizes that both FDA and the pharmaceutical industry face challenges in drug development. Although the approval phase of drug development (the phase in which FDA plays the biggest role) is reported to have the highest success rate of any phase of drug development, it is critical to our public health mission that we work with industry and other stakeholders to take steps to reduce uncertainty and increase success in the other phases of drug development.

Commissioner Hamburg has therefore launched the Innovation Initiative, identifying additional steps the agency can take immediately to address the most pressing concerns facing patients and industry. The agency is dedicating resources and staff to expediting drug development at every stage. The agency has made advances in regulatory science, which can reduce the length and cost of drug development and increase its predictability, a top priority. For example, FDA is working on initiatives to make clinical trials smaller, more efficient, and less uncertain, and to enhance use of pharmacogenomics and qualified biomarkers. FDA also is continuing to support the progress of personalized medicine, and is allocating more resources to expediting orphan drug development. With this effort, FDA can help speed the availability of new products, identify products that might be safer or more effective than existing therapies, and give physicians and scientists better information about how drugs work. FDA

Introduction

In Fiscal Year (FY) 2011,[1] FDA approved 35 novel medicines, many of which are groundbreaking, including two new treatments for hepatitis C, a drug that prolongs survival in patients with late-stage prostate cancer, the first new drug to treat Hodgkin's lymphoma in 30 years and the first new drug to treat lupus in 50 years. The 35 novel drugs are noteworthy for their contributions to the health of Americans and their scientific innovation.

There were breakthroughs in personalized medicine: two of the drugs, for lung cancer and melanoma, were developed and approved with diagnostic devices that will allow doctors to target the drug to those patients most likely to respond. Seven of the drugs represent major advances in cancer treatment. Still others provide important new therapies for treating drug resistant skin infections and pneumonia, and for preventing heart attack, stroke, and kidney transplant rejection. Ten of the approved treatments are for rare or "orphan" diseases, which have few or no drug treatment options because of their small patient populations (less than 200,000).

Many of these drugs were also notable for the speed with which they were approved.

Many of these drugs were also notable for the speed with which they were approved: almost 70% of them were approved first in the US, before any other country in the world. For many of these approvals, FDA used expedited approval authorities and flexible clinical trial requirements to permit shorter, smaller, or fewer studies, which can reduce the high cost of drug testing. FY 2011 continued the agency's strong track record of approving drugs on or before the target dates for application review that were agreed to under the Prescription Drug User Fee Act (PDUFA). All but one (34/35) of the innovative drugs were approved on or before their target dates for review. FDA also continued to approve over half of these drugs on the "first cycle" of review, i.e., without requests for additional information that would lead to another cycle of review.

Over the last several years, FDA has improved the quality and speed of its drug approval process through:

- The PDUFA program, which helps to provide the resources necessary to hire and train scientific reviewers, keep FDA scientists abreast of innovative technologies, allow FDA to meet with companies early in drug testing to provide advice on development programs, and develop

1. *October 1, 2010-September 30, 2011.*

guidance documents that clarify the drug development pathway for many diseases;
- Expedited approval pathways including Fast Track, Accelerated Approval, Priority Review, and Expanded Access programs, which are designed to speed the testing, availability and approval of drugs in different ways;
- Critical Path, a program started in 2004, focused on seeking the development of new test methods that can streamline drug development, testing and review; and
- A strong focus on methods of efficiently identifying and resolving drug safety issues.

In this year of strong leadership by FDA in approving innovative drugs, it is important to recognize the achievements of the biopharmaceutical industry. None of FDA's accomplishments would be possible without the innovation and hard work of large and small biopharmaceutical companies alike. Not only did the drug applications that the industry submitted to FDA represent important medical advances, but their generally high quality permitted FDA to reach an approval decision, in many cases, after a single cycle of review.

BACKGROUND

It is FDA's job to make sure that new drugs entering the U.S. market are safe and effective. At the same time, FDA must seek to ensure that Americans have access to innovative and potentially life-saving medicines as soon as possible. Although maintaining a balance between these two responsibilities can be challenging, the public health demands that FDA actively pursue both goals. FDA has recently faced criticism that drug review times have slowed due to an increased emphasis on establishing drug safety before approval. FDA's record, including FY 2011, shows instead that the agency, while ensuring the safety and effectiveness of new therapies, continues to approve innovative drugs earlier and faster than anywhere else in the world, including the European Union (EU).

This report looks at FDA's approvals of "new molecular entities" (NMEs) in FY 2011. For purposes of this report, NMEs are drugs, including biological products, with novel chemical structures that have never been approved before to treat any disease, and often represent the most innovative drugs entering the market. These drugs include products approved by FDA's Center for Drug Evaluation and Research and FDA's Center for Biologics Evaluation and Research.

More "first approvals" than any other country.

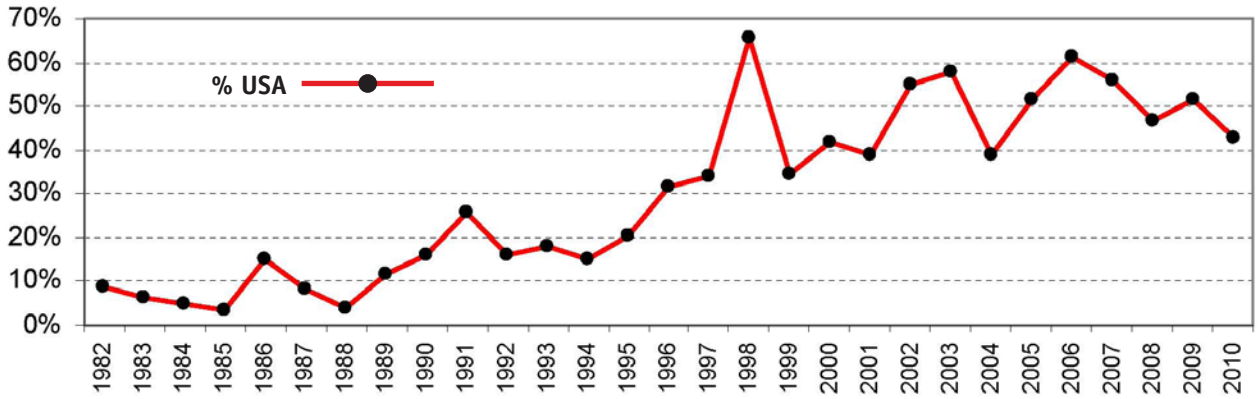
Of the 35 innovative drugs approved in FY 2011, 24 (almost 70%) were approved by FDA before any other regulatory agency in the world, including the EMA (the EU's drug regulatory agency).

Since the enactment of the Prescription Drug User Fee Act (PDUFA) in 1992, FDA has steadily increased the speed of Americans' access to important new drugs compared to the EU and the world as a whole. As shown in Figure 1, the United States now leads the world in the first introduction of new active drug substances.[2]

If the performance of the US is compared

2. *Source: Scrip NCE Review/Scrip Yearbook/Scrip Magazine (1982 -2005), PharmaProjects R&D Annual Review (2006-2010). New active substances include novel chemical or biological substances not previously approved to treat any disease. There is a close, but not complete overlap between NASs and NMEs: NASs exclude radiopharmaceuticals.*

Figure 1. US Share of New Active Substances (NAS) First Launched on the World Market



Year of NAS First Launch Worldwide

with that of the EU, of 57 novel drugs approved by both FDA and the EU between 2006 and 2010, 43 (75%) were approved first in the US.

Length of reviews shorter than the EU.

In recent years, FDA's drug review times have also been, on average, significantly faster than those in the EU. It is difficult to compare length of approvals for FY 2011 because many of the drugs approved in the US have not yet been approved in the EU. A comparison of drugs approved in the US and EU between 2006 and 2010 is illustrative, however. For "priority" drugs[3] approved between 2006 and 2010, FDA's median time to approval was 6 months (183 days), more than twice as fast as the EU, which took a median time of 13.2 months (403 days). For standard drug reviews, FDA's median time to approval was 13 months (396 days), 53 days faster than the EU time of 14.7 months (449 days).

A recent article in the journal Health Affairs also compared cancer drugs approved in the US and EU from 2003 through 2010. Thirty-five cancer drugs were approved by the US or the EU from October 2003 through December 2010. Of those, FDA approved 32—in an average time of 8.6 months (261 days). The EU approved only 26 of these products, and its average time was 12.2 months (373 days). All 23 cancer drugs approved by both agencies during this period were approved first in the United States.[4]

PDUFA has substantially reduced review times.

According to researchers at the Tufts Center for the Study of Drug Development, the time required for FDA's review of a new drug (i.e. time from submission until approval) has been cut by 60 percent since the enactment of PDUFA, from an average of 2.0 years at the start of PDUFA to an average of 1.1 years more recently.

Of the 35 the innovative drugs approved in FY 2011, 34 met their PDUFA target dates for review.

3. Priority drugs are those designated by FDA for priority reviews because of their potential therapeutic value.

4. "Despite Criticism Of The FDA Review Process, New Cancer Drugs Reach Patients Sooner In The United States Than In Europe," Samantha A. Roberts, Jeff D. Allen, and Ellen V. Sigal, Health Affairs, June 2011.

12 of 13 drugs that received a Fast Track designation were approved in the US first and achieved first cycle approvals.

Expedited approval and flexible trial requirements used to speed access. FDA has several programs to expedite the development and availability of important new drugs. The most important of these are Fast Track, Accelerated Approval, and Priority Review.[5]

Fast Track is designed to facilitate the development and expedite the review of drugs to treat serious diseases that fill an unmet medical need. Its purpose is to get important new drugs to the patient earlier. Once a drug receives *Fast Track* designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients. Fast Track drugs are also eligible for rolling review, in which a company can submit portions of its application as they are completed, and FDA may begin review without waiting for the full application. More than a third (13/35) of the innovative drugs approved in 2011 were given a Fast Track designation. Of the 13 drugs that received a Fast Track designation, 12 (92%) were approved in the US before any other country, and 12 (92%) were approved on the first review cycle.

Nearly half (16 of 35) of the FY 2011 drugs received "Priority Review," which means that FDA gave itself a 6-month target date to review the drug. Priority reviews are given to drugs that may offer major advances in treatment or that provide a treatment when no adequate therapy exists. Under PDUFA, FDA has agreed to a 6-month review goal for priority drugs compared to a 10-month review goal for non-priority or "standard" drugs. Of the 16 drugs given a priority review, 11 (69%) were approved in the US before any other country, and 13 (81%) were approved on the first cycle.

Three of the novel drugs approved in FY 2011 were approved under FDA's "Accelerated Approval" authority. Accelerated approval allows the agency to approve a drug to treat a serious disease based on clinical data showing, for example, that the drug has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients (such as evidence that a drug shrinks cancer tumors), but does not demonstrate the clinical benefit itself (that patients actually live longer). Clinical trials to establish an effect on surrogate endpoints are frequently shorter and less costly than those establishing a longer-term clinical benefit. The program is designed to provide patients with earlier access to promising new drugs, followed by further studies to confirm the drug's clinical benefit conducted after approval.

Several of the drugs were also approved with flexible clinical trial requirements, for example, on the basis of a single study (in contrast to the usual requirement that a finding of effectiveness be replicated in a second study) and studies using small patient populations.

5. For more information on these expedited approval processes, go to: http://www.fda.gov/forconsumers/byaudience/forpatientadvocates/speedingaccesstoimportantnewtherapies/ucm128291.htm.

FDA has also taken steps to speed the development and approval of safe and effective drugs for Americans with rare diseases. Therapies for rare diseases—those affecting fewer than 200,000 people in the United States—represent the most rapidly expanding area of drug development. Although each disease affects a relatively small population, collectively rare diseases affect about 25 million Americans. Approximately 30% of the NMEs approved in the last five years have been drugs for rare diseases. Because of the small numbers of patients who suffer from each disease, FDA often allows non-traditional approaches to establishing safety and effectiveness. The National Organization for Rare Disorders has just released a report concluding that FDA has consistently allowed flexible clinical trial designs in approving drugs for rare diseases.[6] FDA

Notable FY 2011 Approvals

In FY 2011, FDA approved 35 "new molecular entities" (NMEs). Of the 35 novel drugs, 17 were particularly notable for their significant contributions to the health of patients. In this subset of drugs that offer real promise for serious and life-threatening diseases, FDA's record on speeding access was the strongest. 12/17 (71%) were approved first in the US, 13/17 (76%) gained approval after a single review cycle, and 100% were approved on or before their PDUFA target dates. A complete list of the 35 NMEs approved in FY 2011 can be found in the appendix to this report. The following notable NME's were approved in FY 2011.

A. Cancer

1. Zytiga (albiraterone acetate) for late-stage prostate cancer.

Importance: Prostate cancer is the most commonly diagnosed cancer in men, and second only to lung cancer in the number of cancer deaths. In 2007, over 200,000 men were diagnosed with prostate cancer, and almost 30,000 died from it. Zytiga is the first in a new class of drugs to treat late-stage prostate cancer.

6. Frank J. Sasinowski, National Organization for Rare Disorders, Quantum of Effectiveness Evidence in FDA's Approval of Orphan Drugs: Cataloguing FDA's Flexibility in Regulating Therapies for Persons with Rare Disorders. Released October 11, 2011.

The ability of Zytiga to prolong survival in these patients is significant because they have few other treatment options.

Zytiga was shown to prolong the survival of certain late-stage prostate cancer patients, whose cancer is "castration-resistant," when given in combination with prednisone (a steroid). Castration-resistant cancers are those that grow even when drugs or surgery are used to reduce testosterone levels or block its effects in the body. The ability of Zytiga to prolong survival in these patients is significant because they have few other treatment options.

Actions by FDA to speed drug testing and review: Zytiga's safety and effectiveness were established in a clinical trial of 1,195 patients with late-stage castration-resistant prostate cancer who had received prior treatment with docetaxel chemotherapy. FDA did not require the sponsor to replicate the study findings in a second trial. The study was designed to measure overall survival, the length of time from when the treatment started until a patient's death. A planned mid-study analysis showed that patients who received the Zytiga and prednisone combination had a median overall survival of 14.8 months compared to 10.9 months for patients receiving the placebo and prednisone combination. Because of these convincing findings, the trial was terminated early, and approval was based on the early results. Zytiga was reviewed under the FDA's priority review program, which provides for an expedited six-month review of drugs.

Safety issues: FDA concluded that the benefits of Zytiga outweighed the risk of reported side effects, which include joint swelling or discomfort, low levels of potassium in the blood, fluid retention (usually of the legs and feet), muscle discomfort, hot flashes, diarrhea, urinary tract infection, cough, high blood pressure, heartbeat disorders, urinary frequency, increased nighttime urination, upset stomach or indigestion and upper respiratory tract infection.

Time from submission to approval: 4.2 months
First approved in: U.S.
Review cycles before approval: 1
PDUFA target date met: Yes. Zytiga was approved ahead of its target date.

Zytiga 1

2. Zelboraf (vemurafenib) and companion genetic test for late-stage melanoma.

Importance: Zelboraf was the first drug in a new class of drugs to treat patients with late-stage (metastatic) or unresectable (cannot be removed by surgery) melanoma, the most dangerous type of skin cancer. Melanoma is the leading cause of death from skin disease. An estimated 68,130 new cases of melanoma were diagnosed in the United States during 2010, and about 8,700 people died from the disease last year, according to the National Cancer Institute. 2011 was an important year for patients with late-

Because of convincing early results, FDA scientists encouraged early submission of Zelboraf.

stage melanoma. Zelboraf was the second new cancer drug (after Yervoy approved in March 2011) ever approved by FDA that demonstrated an improvement in overall survival.

Zelboraf was also the first important approval of FY 2011 in the quest for targeted or "personalized" medicine, in this case allowing for the identification of patients most likely to respond to this drug therapy. Zelboraf is specifically indicated for the treatment of patients with melanoma whose tumors express a gene mutation called BRAF V600E. Zelboraf is being approved with a first-of-a-kind genetic test called the cobas 4800 BRAF V600 Mutation Test, a companion diagnostic that will help determine if a patient's melanoma cells have the BRAF V600E mutation. This type of melanoma is an orphan disesase.

Actions by FDA to speed drug testing and review. Zelboraf was given a Fast Track designation because it had the potential to improve overall survival in melanoma patients. Zelboraf's safety and effectiveness were established in a single international trial of 675 patients with late-stage melanoma with the BRAF V600E mutation who had not received prior therapy. FDA did not require the sponsor to replicate the study findings in a second trial. Patients were assigned to receive either Zelboraf or dacarbazine, another anti-cancer therapy. The trial was designed to measure overall survival (the length of time between start of treatment and death of a patient). The median survival (the length of time a patient lives after treatment) of patients receiving Zelboraf has not been reached (77 percent still living) while the median survival for those who received dacarbazine was 8 months (64 percent still living).

Because of convincing early findings with this drug, FDA scientists worked proactively with the sponsor during drug testing to encourage early submission of the application. FDA also encouraged the sponsor to open an expanded access protocol to permit patients earlier access to Zelboraf. Zelboraf was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: About 24 percent of patients developed a skin-related cancer called cutaneous squamous cell carcinoma, which was managed with surgery. Other common side effects reported in patients receiving Zelboraf included joint pain, rash, hair loss, fatigue, nausea, itching, and skin sensitivity when exposed to the sun. FDA concluded that the benefits of Zytiga outweighed these risks.

Zelboraf

Time from submission to approval: 3.6 months

First approved in: U.S.

Review cycles before approval: 1

PDUFA/MDUFA[7] target dates met: Zelboraf and the companion diagnostic test were approved substantially ahead of the target dates for both the drug and the companion diagnostic device.

7. As a device, the companion diagnostic had its target date assigned under the Medical Device User Fee Act (MDUFA).

The approval of Xalkori with a specific test allows the selection of patients who are more likely to respond to the drug.

3. Xalkori (crizotinib) and companion genetic test for late-stage lung cancer.

Importance: 1-7% of lung cancer patients have an abnormal ALK gene. Patients with this abnormality are generally non-smokers. Xalkori was the first in a new class of drugs that targets lung cancer in these patients. This type of cancer is an orphan disease.

In addition to providing a new treatment for lung cancer, Xalkori represented the second important "personalized" medicine approval of FY 2011. Xalkori was approved with a companion genetic test that will allow the drug to be targeted to the patients it is most likely to help. The genetic test, a first-of-a-kind genetic test called the Vysis ALK Break Apart FISH Probe Kit, helps determine if a patient has the abnormal ALK gene. The approval of Xalkori with a specific test allows the selection of patients who are more likely to respond to the drug. Targeted therapies such as Xalkori are important options for treating patients with this disease and may ultimately result in fewer side effects.

Actions by FDA to speed drug testing and review. In July 2011, FDA issued a draft guidance industry on the agency's policy for reviewing a companion diagnostic and the corresponding drug therapy. The purpose of the guidance was to help manufacturers navigate the approval process for companion drug/diagnostics more quickly and efficiently.

Xalkori's testing and review were expedited in several ways. The drug received a Fast Track designation, and was given a rolling review. Xalkori was reviewed under the FDA's priority review program, which provides for an expedited six-month review of drugs. The drug was also approved under FDA's accelerated approval program, which allowed approval of the drug based on surrogate endpoints (in this case tumor shrinkage) rather than a demonstration of improved survival. Altogether, the development time for this drug was just 5 years from first-in-human Phase 1 studies to FDA approval, a significant reduction over the average development time for cancer drugs.

Safety issues: Xalkori use has been associated with inflammation of the lung tissue (pneumonitis), which can be life-threatening. FDA concluded that the benefits of Xalkori outweighed this risk and the risk of other reported side effects. The most common side effects included vision disorders, nausea, diarrhea, vomiting, swelling (edema), and constipation. Vision disorders included visual impairment, flashes of light, blurred vision, floaters, double vision, sensitivity to light, and visual field defects.

Xalkori

Time from submission to approval: 4.9 months

First approved in: U.S.

Review cycles before approval: 1

PDUFA target date met: Yes. Xalkori and the companion Vysis ALK Break Apart FISH Probe Kit were approved ahead of their review target dates.

Yervoy, the first in a new class of immune-boosting drugs, was the first drug approved by FDA that was clearly demonstrated to prolong the life of patients with late-stage melanoma.

4. *Yervoy (ipilimumab) for late-stage melanoma (skin cancer).*

Importance: Melanoma is the leading cause of death from skin disease. An estimated 68,130 new cases of melanoma were diagnosed in the United States during 2010, and about 8,700 people died from the disease last year, according to the National Cancer Institute. Late-stage melanoma is devastating, with very few treatment options for patients. Prior to this year, none of the existing treatments prolonged a patient's life. Yervoy, the first in a new class of immune-boosting drugs, was the first drug approved by FDA that was clearly demonstrated to prolong the life of patients with late-stage melanoma.

Actions to speed drug testing and review: Yervoy was given a Fast Track designation for its potential to address an unmet medical need—prolonging survival in patients with metastatic melanoma. Yervoy's safety and effectiveness were established in a single international trial of 676 patients. All patients in the trial had stopped responding to other FDA-approved or commonly used treatments for melanoma. Patients who received Yervoy alone, or in combination with an experimental vaccine, lived an average of about 10 months, while those who received only the experimental vaccine lived an average of 6.5 months. Yervoy was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: Yervoy poses a risk of serious side effects, including severe to fatal autoimmune reactions in 12.9 percent of patients treated with Yervoy, as well as a range of milder side effects. FDA decided that the benefits of Yervoy outweigh its risks, because no other treatment had been shown to prolong a patient's life. FDA determined, however, that a Risk Evaluation and Mitigation Strategy (REMS) was required to inform health care professionals and patients about these serious risks.

Time from submission to approval: 9.0 months (PDUFA date was extended by the submission of a late major amendment by the sponsor)

First approved in: U.S.

Review cycles before approval: 1

PDUFA target date met: Yes

Adcetris was approved on a single clinical trial involving 102 patients.

5. Adcetris (brentuximab vedotin) to treat two types of lymphoma.

Importance: Adcetris is the first new FDA-approved treatment for Hodgkin's lymphoma (HL) since 1977, and the first specifically indicated to treat a rare lymphoma known as systemic anaplastic large cell lymphoma (ALCL).

These cancers are orphan diseases. The National Cancer Institute estimates that 8,830 new cases of HL will be diagnosed in the United States in 2011 and about 1,300 people will die from the disease. Systemic ALCL is a rare malignant tumor (non-Hodgkin's lymphoma) that may appear in several parts of the body including the lymph nodes, skin, bones, soft tissue, lungs or liver.

Actions to speed drug testing and review: Adcetris was given a Fast Track designation for its potential to address an unmet medical need in patients with Hodgkin's lymphoma. The effectiveness of Adcetris in patients with HL was evaluated in a single clinical trial involving 102 patients. In the single-arm trial, patients were only treated with Adcetris. FDA did not require a concurrent control group or second trial to replicate the results. The study's primary endpoint was objective response rate--the percentage of patients who experienced complete or partial cancer shrinkage or disappearance after treatment—rather than improved survival. Seventy-three percent of patients achieved either a complete or partial response to the treatment. On average, these patients responded to the therapy for 6.7 months.

The effectiveness of Adcetris in patients with systemic ALCL was evaluated in a single clinical trial in 58 patients. In the single-arm trial, patients were only treated with Adcetris. FDA did not require a concurrent control group or second trial to replicate the results. Similar to the HL trial, the trial's primary endpoint was objective response rate. Of the patients receiving Adcetris for ALCL, 86 percent experienced either a complete or partial response and responded on average for 12.6 months.

Adcetris was reviewed under the FDA's priority review program, which provides for an expedited six-month review of drugs, and was approved under FDA's accelerated approval program, which allowed approval of the drug based on surrogate endpoints (tumor shrinkage) rather than a demonstration of improved survival. The data on safety and effectiveness were limited because of the small number of patients tested and the lack of a control group, but FDA granted accelerated approval with a commitment from the sponsor to provide additional data after approval.

Safety issues: FDA concluded that the benefits of Adcetris outweighed the risk of reported side effects, including a decrease in infection-fighting white blood cells (neutropenia), nerve damage (peripheral sensory neuropathy), fatigue, nausea, anemia, upper respiratory infection, diarrhea, fever, cough, vomiting, and low blood platelet levels (thrombocytopenia). Pregnant women should be aware that Adcetris might cause harm to their unborn baby.

Time from submission to approval: 5.7 months
First approved in: US
Review cycles before approval: 1
PDUFA target date met: Yes

Adcetris 5

Caprelsa is the first drug ever approved to treat medullary thyroid cancer.

6. Caprelsa (vandetanib) to treat thyroid cancer.

Importance: Caprelsa was the first drug approved to treat medullary thyroid cancer. There were previously no FDA-approved treatments for this type of cancer, a cancerous growth of the thyroid gland, which is located in the neck. Medullary thyroid cancer involves specific types of cells that are found in the thyroid gland and can occur spontaneously, or be part of a genetic syndrome. Medullary thyroid cancer is estimated to represent 3 to 5% of thyroid cancers, and is an orphan disease. It is estimated to affect about 1,300 to 2,200 patients in the U.S, making it one of the rarest forms of thyroid cancer. Caprelsa's approval underscores FDA's commitment to approving treatments for patients with rare and difficult to treat diseases.

Actions to speed drug testing and review: Caprelsa was given a Fast Track designation for its potential to treat a cancer with no approved treatments. Caprelsa's safety and effectiveness were established in a single, randomized international trial of 331 patients with late-stage medullary thyroid cancer. FDA did not require the sponsor to replicate the study findings in a second trial. Patients who received Caprelsa had a longer period of time without disease progression when compared to patients receiving placebo. Median progression-free survival was at least 22.6 months in the patients given vandetanib compared to 16.4 months in the patients given placebo. Caprelsa was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: Caprelsa was shown to affect the electrical activity of the heart, which in some cases can cause irregular heart beats that could lead to sudden death. The drug was therefore approved with a REMS to inform health care professionals about these serious heart-related risks, without which the benefits of Caprelsa would not have been considered to outweigh the risks. Only health care professionals and pharmacies certified through the vandetanib REMS program, a restricted distribution program, will be able to prescribe and dispense the drug. Patients will also receive an FDA-approved Medication Guide informing them of the potential risks.

Time from submission to approval: 9.0 months (PDUFA target date extended by the submission of a late major amendment by the sponsor)

First approved in: U.S.

Review cycles before approval: 1

PDUFA target date met: Yes

The approval of Halaven is important because of the limited options currently available to women with aggressive forms of late-stage breast cancer.

7. Halaven (eribulin mesylate) for metastatic breast cancer.

Importance: Breast cancer is the second leading cause of cancer related death among women, according to the National Cancer Institute. This year, an estimated 230,480 women will be diagnosed with breast cancer, while 39,520 women will die from the disease. Halaven was approved to treat breast cancer patients whose cancer has metastasized (spread) and who have already been treated with at least two other chemotherapeutic regimens for metastatic breast cancer. Halaven is the first single agent to show an overall improvement in survival in these patients. The approval of this drug is important because of the limited options currently available to women with aggressive forms of late-stage breast cancer.

Actions to speed drug testing and review: Halaven was given a Fast Track designation for its potential to treat advanced relapsed or refractory breast cancer. Halaven's safety and effectiveness were established in a single trial in 762 women with metastatic breast cancer who had received at least two prior chemotherapy regimens for late-stage disease. FDA did not require the sponsor to replicate the study findings in a second trial. Patients were randomly assigned to receive treatment with either Halaven or a different single agent therapy chosen by their oncologist. The trial was designed to measure the length of time from when this treatment started until a patient's death (overall survival). On average, patients treated with Halaven lived 2.5 months longer than those treated with an alternate therapy. Halaven was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: FDA concluded that the benefits of Halaven outweighed the risk of reported side effects, including a decrease in infection-fighting white blood cells (neutropenia), anemia, a decrease in the number of white blood cells (leukopenia), hair loss (alopecia), fatigue, nausea, weakness (asthenia), nerve damage (peripheral neuropathy), and constipation.

Time from submission to approval: 7.6 months (PDUFA target date extended by the submission of a late major amendment by the sponsor)

First approved in: U.S.

Review cycles before approval: 1

PDUFA target date met: Yes

B. Hepatitis C

1. *Victrelis (boceprevir) to treat chronic Hepatitis C*

Importance: Chronic hepatitis C is a serious public health problem, both globally and domestically. 170 million people are estimated to be infected worldwide and approximately 3 million in the United States. Hepatitis C is caused by a virus, and results in inflammation of the liver that can lead to reduced liver function, cirrhosis, liver cancer, and liver failure. Most liver transplants in the U.S. are due to liver disease caused by hepatitis C. Most people with hepatitis C have no symptoms until liver damage occurs. People can get the hepatitis C virus in a number of ways, including: exposure to blood that is infected with the virus; being born to a mother with HCV; sharing a needle; having sex with an infected person; sharing personal items such as a razor, toothbrush with someone who is infected with the virus, or from unsterilized tattoo or piercing tools. Although cases of chronic hepatitis C in the U.S. are declining, the number of serious complications of advanced disease is on the rise.

Victrelis is an important advance for patients with hepatitis C, and should have a significant impact on their lives. Victrelis was the first drug approved in its class and offers a greater chance of cure for some patients' hepatitis C infection compared to previously available therapy. Patients given Victrelis with two other drugs (pegylated interferon and ribavirin) had an increased sustained virologic response (the hepatitis C virus is no longer detectable in the patient's blood). Sustained virologic response can result in decreased cirrhosis and complications of liver disease, decreased rates of liver cancer (hepatocellular carcinoma), and decreased mortality.

Actions to speed drug testing and review: Victrelis was designated as a Fast Track drug and was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: FDA concluded that the benefits of Victrelis outweighed the risk of reported side effects which include fatigue, low red blood cell count (anemia), nausea, headache and taste distortion (dysgeusia).

Time from submission to approval: 5.9 months
First approved in: U.S.
Review cycles before approval: 1
PDUFA target date met: Yes

2. *Incivek (teleprevir) to treat chronic hepatitis C*

Importance: Incivek is a protease inhibitor in the same class as Victrelis and was approved 10 days after Victrelis for treatment of chronic hepatitis C infection. Just like Victrelis, Incivek provides an important new therapy for patients with chronic hepatitis C infection and offers a greater chance of cure than previously available therapies.

Actions to speed drug testing and review: Incivek was designated as a Fast Track drug and was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Benlysta is the first new drug to treat systemic lupus in 50 years.

Safety issues: FDA concluded that the benefits of Incivek outweighed the risk of reported side effects which include rash, low red blood cell count (anemia), nausea, fatigue, headache, diarrhea, itching (pruritus), and anal or rectal irritation and pain. Rash can be serious and can require stopping Incivek or all three drugs in the treatment regimen.

Time from submission to approval: 5.7 months
First approved in: US
Review cycles before approval: 1
PDUFA target date met: Yes

Incivek 2

C. Lupus

1. Benlysta (belimumab) to treat systemic lupus

Importance: Lupus is a serious, potentially fatal, autoimmune disease that attacks healthy tissues. It disproportionately affects women, and usually develops between ages 15 and 44. The disease affects many parts of the body including the joints, the skin, kidneys, lungs, heart, and the brain. Estimates vary on the number of lupus sufferers in the United States ranging from approximately 300,000 to 1.5 million people. Benlysta is the first in a new class of drugs to treat systemic lupus, and the first new treatment for lupus in over 50 years. Patients who received Benlysta together with standard medicines experienced less disease activity than those who received a placebo (sugar pill) and standard medicines. Study results suggested, but did not definitively establish, that some patients had a reduced likelihood of a severe "flare," i.e., a significant increase in disease signs or symptoms.

Actions by FDA to speed drug testing and review: Benlysta received a Fast Track designation and was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: FDA concluded that the benefits of Benlysta outweighed the risk of reported side effects, including nausea, diarrhea, and fever (pyrexia). Patients also commonly experienced infusion reactions, so pre-treatment with an antihistamine should be considered.

Time from submission to approval: 9.0 months (PDUFA target date extended by submission of a late major amendment by the sponsor)
First approved in: U.S.
Review cycles before approval: 1
PDUFA target date met: Yes

Benlysta

D. Heart Attack and Stroke

1. *Pradaxa (dabigatran etexilate) to reduce risk of stroke*

Importance: Pradaxa was the first oral anticoagulant approved since warfarin in the 1950s to prevent stroke and blood clots in patients with abnormal heart rhythm (atrial fibrillation). Stroke is the leading cause of serious, long-term disability in the US. In the clinical trials of Pradaxa, patients taking Pradaxa had fewer strokes than those taking warfarin. Although not the first member of its drug class, Pradaxa was the first that could be administered orally, rather than by injection. In addition, patients taking Pradaxa, unlike warfarin, are not required to undergo periodic monitoring with blood tests.

Actions by FDA to speed drug testing and review: Pradaxa was reviewed under the FDA's priority review program which provides for an expedited six-month review of drugs.

Safety issues: As with other approved anti-clotting drugs, bleeding, including life-threatening and fatal bleeding, was among the most common adverse reactions reported by patients treated with Pradaxa. Gastrointestinal symptoms, including an uncomfortable feeling in the stomach (dyspepsia), stomach pain, nausea, heartburn, and bloating also were reported. Because of the serious bleeding risks associated with Pradaxa, FDA determined that Pradaxa's benefits would not outweigh its risks unless a Medication Guide was distributed to patients at the time of each prescription to help them understand the risks.

Time from submission to approval: 6.0 months
First approved in: E.U.
Review cycles before approval: 1
PDUFA target date met: Yes

Pradaxa 1

2. *Brilinta (ticagrelor) to reduce cardiovascular death and heart attack*

Importance: Brilinta was shown to reduce the risk of cardiovascular death and heart attack in patients with acute coronary syndromes (ACS) better than Plavix. ACS includes conditions such as unstable angina or heart attack that could result from reduced blood flow to the heart. Brilinta works by preventing the formation of new blood clots, thus maintaining blood flow in the body to help reduce the risk of another cardiovascular event. It should be noted that in the clinical trials maintenance doses of aspirin were comparably effective to Brilinta.

Actions by FDA to speed drug testing and review: Because of its serious risks, FDA approved the drug with a REMS. Without the special safety conditions imposed under the REMS, Brilinta's benefits would not have been considered to outweigh its risks.

Safety issues: A Boxed Warning to health care professionals and patients in Brilinta's label warns that aspirin doses above 100 milligrams per day decrease the effectiveness of the

medication. The Boxed Warning also says that, like other blood-thinning agents, Brilinta increases the rate of bleeding and can cause significant, sometimes fatal, bleeding. The most common adverse reactions reported by people taking Brilinta in clinical trials were bleeding and difficulty breathing (dyspnea). As part of the REMS, the company must conduct educational outreach to physicians to alert them about the risk of using higher doses of aspirin. In addition, Brilinta will be dispensed with a Medication Guide that informs patients of the most important information about the medication.

Time from submission to approval: 20.1 months
First approved in: E.U.
Review cycles before approval: 2
PDUFA target date met: Yes (PDUFA target dates met on both review cycles)

Brilinta

2

E. MRSA Infections

1. *Teflaro (ceftaroline fosamil) to treat bacterial skin infections and pneumonia*

Importance: Teflaro is an injectable antibiotic approved to treat bacterial skin infections and community-acquired bacterial pneumonia, including infections caused by MRSA (methicillin-resistant Staphylococcus aureus). MRSA infections are resistant to treatment with traditional antibiotics and can be serious or life-threatening. They can also be spread to others. Life-threatening MRSA infections are acquired most commonly in hospitals. Because of MRSA's multi-drug resistance, it is important to have new antibiotics available to which the bacteria have not become resistant. This approval is part of FDA's commitment to facilitating new antibiotic drug development.
Actions taken by FDA to speed drug testing and review: Teflaro was granted a Fast Track designation. FDA conducted independent analyses of the trial data in addition to those submitted by the sponsor. FDA's analyses provided essential support for the recommendation of the FDA Advisory Committee to approve Teflaro.

Safety issues: FDA concluded that the benefits of Teflaro outweighed the risks of reported side effects, including diarrhea, nausea and rash. Teflaro should not be used in patients with sensitivities to cephalosporin antibiotics.

Time from submission to approval: 10.0 months
First approved in: U.S.
Review cycles before approval: 1
PDUFA target date met: Yes

Teflaro

F. Kidney Transplant Rejection

1. Nulojix (belatacept) to prevent rejection of transplanted kidneys

Importance: Nulojix is the first drug in a new class of primary immunosuppressants to prevent acute organ rejection in adult kidney transplant patients. It represents the first new class of drugs for rejection of organ transplants in more than a decade. Without immunosuppression, the body will reject a transplanted organ because the immune system recognizes the new organ as foreign (transplant rejection). Nulojix works with other immunosuppressants to control the immune system and keep the new kidney working. It offers an important new option for kidney transplant patients.

More than 89,000 patients are waiting for a kidney transplant in the United States, according to the Organ Procurement and Transplantation Network, which is overseen by HHS' Health Resources and Services Administration.

Actions taken by FDA to speed drug testing and review: Nulojix was designated as a Fast Track drug.

Safety issues: Nulojix carries a Boxed Warning that patients face an increased risk of developing post-transplant lymphoproliferative disorder (PTLD), a type of cancer where white blood cells grow out of control after an organ transplant. Another Boxed Warning on the Nulojix label, as well as labels of other immunosuppressants, warns of an increased risk of serious infections and other cancers. FDA concluded that the benefits of Nulojix outweighed these risks as well as the risks of other reported side effects, which included low red blood count (anemia), constipation, kidney or bladder infection, and swollen legs, ankles, or feet.

Nulojix

Time from submission to approval: 23.5 months

First approved in: U.S.

Review cycles before approval: 2

PDUFA target date met: Yes (PDUFA target dates met on both review cycles)

G. Hereditary Angioedema (HAE)

1. Firazyr to treat acute attacks of hereditary angioedema (HAE)

Importance: HAE is a rare disease is caused by low levels or the improper function of a protein called C1 inhibitor, which is involved in regulating how certain immune system and blood clotting pathways function. Fewer than 30,000 people in the United States have HAE. People with HAE can develop rapid swelling of the hands, feet, limbs, face, intestinal tract, voice box, or windpipe, which may result in disfigurement, disability, or death. Swelling of the digestive tract may cause abdominal pain, nausea, and vomiting, while airway swelling puts patients at risk of suffocation.

Firazyr is the first in a new class of drugs to treat this condition and provides a new option to treat acute attacks of HAE. Firazyr is the third drug approved in the United

Because Firazyr can be self-administered through an injection in the abdominal area, patients can treat themselves.

States to treat HAE attacks. In October 2009 the FDA approved Berinert to treat facial and abdominal attacks of HAE, and Kalbitor was approved in December 2009 to treat acute attacks of HAE in patients ages 16 years and older. Because Firazyr can be self-administered through an injection in the abdominal area, patients can treat themselves upon recognition of an HAE attack.

Actions taken by FDA to speed drug testing and review: The safety and efficacy of Firazyr was demonstrated in three small controlled clinical trials, with open-label extension periods, in which 225 patients received 1,076 doses of 30 mg Firazyr. The median time for patients treated with Firazyr to report onset of symptom relief was two hours compared with almost 20 hours with placebo.

Safety issues: FDA concluded that the benefits of Firazyr outweigh the risks of reported side effects, including injection site reactions, fever, increased liver enzymes, dizziness, and rash.

Time from submission to approval: 46 months (new clinical trial necessary to gain approval was conducted after submission of the application).

First approved in: E.U.

Review cycles before approval: 2

PDUFA deadlines met: Yes (PDUFA target dates met on both review cycles)

Firazyr

H. Clotting Disorder

1. *Corifact (Factor XIII Concentrate [Human]) intended to prevent bleeding in people with the rare genetic defect congenital Factor XIII deficiency.*

Importance: Corifact is the first specific treatment approved in the U.S. to prevent bleeding in people with congenital Factor XIII deficiency. This rare clotting disorder affects 1 out of every 3 to 5 million people in the United States. Patients with congenital Factor XIII deficiency don't make enough Factor XIII, a substance that circulates in the blood and is important for normal clotting. The deficiency may lead to soft tissue bruising, mucosal bleeding and fatal intracranial bleeding; newborns with Factor XIII deficiency may have umbilical cord bleeding. Without treatment, people with the condition are at risk for life-threatening bleeding.

Actions taken by FDA to speed drug testing and review: Corifact received orphan-drug designation by the FDA, a Fast Track designation, and was given a priority review. It was approved for marketing under

FDA's accelerated approval regulations. FDAzapproved Corifact based on results of a clinical trial of 14 people, including children, with congenital Factor XIII deficiency.

Safety issues: FDA concluded that the benefits of Corifact outweigh the risks of reported side effects, the most common of which were hypersensitivity reactions (allergy, rash, pruritus and erythema), chills, fever, arthralgia, headache, elevated thrombin-antithrombin levels, and an increase in liver (hepatic) enzymes. Safety was evaluated in 187 individuals, most of whom were enrolled in open-label studies.

Time from submission to approval: 6 months.
First approved in: E.U.
Review cycles before approval: 1
PDUFA target date met: Yes

Corifact

I. Scorpion Stings

1. Anascorp (Centruroides [Scorpion] Immune F(ab')2 [Equine]) to treat clinical signs of scorpion envenomation.

Importance: Anascorp is the first specific treatment approved in the U.S. for scorpion stings, and represents an important—and potentially life-saving—medical intervention. Most reports of envenomation from scorpions in the U.S. are from Arizona. Severe stings, which occur most frequently in infants and children, can cause shortness of breath, fluid in the lungs, breathing problems, excess saliva, blurred vision, slurred speech, trouble swallowing, abnormal eye movements, muscle twitching, difficulty walking, and other uncoordinated muscle movements. Cases that are untreated can be life-threatening.

Actions taken by FDA to speed drug testing and review: Anascorp received orphan-drug designation by the FDA, and received priority review. FDA approved Anascorp based on results of a randomized, double-blind, placebo-controlled trial of 15 children with neurological signs of scorpion stings. These signs resolved within four hours of treatment in the eight subjects who received Anascorp, but in only one of the seven participants who received placebo.

Safety issues: FDA concluded that the benefits of Anascorp outweigh the risks of reported side effects, the most common of which were vomiting, fever, rash, nausea, itchiness, headache, runny nose and muscle pain. Safety was evaluated in 1,534 individuals, most of whom were enrolled in open-label studies. FDA

Time from submission to approval: 30.3 months.
First approved in: Mexico
Review cycles before approval: 2
PDUFA target date met: Yes (PDUFA target dates met on both review cycles)

Anascorp

Ongoing Support of Innovation

FDA's record in FY 2011 shows that the agency is continuing to make innovative drugs available to American patients faster than other countries, while upholding its reputation as the "gold standard" for safety and effectiveness decisions. Despite this record of high-quality, efficient drug reviews, FDA recognizes that both FDA and the pharmaceutical industry face challenges in drug development.

FDA is committed to working with the US pharmaceutical industry as it continues to develop innovative treatments for serious diseases and to help ensure that patients continue to have access to safe and effective drugs at the earliest possible time. Among other initiatives, FDA is working to make sure that user fees are sufficient in PDUFA V to:

- Increase the percentage of drugs that get through the review process in the first cycle; and
- Increase communication between FDA and sponsors throughout the drug testing and review process.

Although the NDA/BLA approval phase of drug development (the phase in which FDA plays the biggest role) is reported to have the highest success rate of any phase of drug development, it is critical to our public health mission that we work with industry and other stakeholders to take steps to reduce uncertainty and increase success in the other phases of drug development.

To promote the development of innovative new therapies, FDA has made advances in regulatory science a top priority. FDA is pursuing a number of scientific goals whose purpose is to expedite drug development. For example, FDA is working to improve the science behind certain clinical trial designs. FDA issued a draft guidance document on "adaptive trial designs" that make use of early results of a trial to modify the design, making the study more likely to detect whether the drug works. FDA is now working on a guidance document on "enrichment designs," studies that make use of patient characteristics to identify people for whom the drug is likely to be effective. These designs allow smaller studies to be successful and target the treatment to patients who will benefit most. FDA encouraged the involvement of the scientific community in the development of these guidances, discussing them at many public meetings and putting them out for public comment. These advances can make drug testing more efficient, encouraging the development of novel products, and speeding new therapies to patients.

FDA has also built a computational science center to give reviewers advanced tools to analyze clinical data—tools that have already been used to support approval of drugs that might not otherwise have been approved. And

the agency has issued an innovative "drug development tools" guidance document that will facilitate use of new, more efficient methods of establishing drug safety and effectiveness. The goal of this guidance, which has been enthusiastically received in the scientific community, is to encourage and support the development of methods that can speed the availability of new products, help identify products that might be safer or more effective than existing therapies, and give physicians and scientists better information about how the products act on the human body. FDA intends to support the development of these tools with dedicated staff and resources.

FDA is also working to:

- Support the enhanced use of pharmacogenomics and qualified biomarkers, each of which has the potential to decrease drug development time;
- Improve its capacity to assess drug benefits as measured by "patient reported outcomes,"
- Continue to support new developments in personalized medicine;
- Develop a more systematic and expansive approach to benefit-risk determinations; and
- Allocate more resources to facilitating orphan drug development, by developing guidance on drug development and reaching out to the rare disease patient community.

FDA is also exploring a range of new partnerships with the National Institutes of Health and academic institutions to develop the science needed to maximize advances in biomedical research and bring the development and assessment of promising new therapies into the 21st century. With this effort, FDA is poised to support a wave of innovation to transform medicine and save lives.

Appendix

I. Priority Drugs

Drug Name	Approval Date	Indication	Orphan Drug	Approved First in U.S.	PDUFA Date Met	Approved 1st Cycle	Sponsor
Adcetris (brentuximab vedotin)	8/19/11	For treatment of Hodgkin's lymphoma and ALCL (systemic anaplastic large cell lymphoma).	✓	✓	✓	✓	Seattle Genetics Bothell, WA
Anascorp (Centruroides [Scorpion] Immune F(ab')2 [Equine])	8/3/11	For treatment of clinical signs of scorpion envenomation.	✓		✓		Rare Disease Therapeutics, Inc., Franklin, TN
Benlysta (belimumab)	3/9/11	To treat patients with active, autoantibody-positive lupus (systemic lupus erythematosus) who are receiving standard therapy, including corticosteroids, antimalarials, immunosuppressives, and nonsteroidal anti-inflammatory drugs.		✓	✓	✓	Human Genome Sciences, Inc., Rockville, MD co-marketed with GlaxoSmithKline, Philadelphia, PA

I. Priority Drugs (continued)

Drug Name	Approval Date	Indication	Orphan Drug	Approved First in U.S.	PDUFA Date Met	Approved 1st Cycle	Sponsor
Caprelsa (vandetanib)	4/6/11	To treat adult patients with metastatic (late-stage) medullary thyroid cancer who are ineligible for surgery and who have disease that is growing or causing symptoms.	✓	✓	✓	✓	AstraZeneca Pharmaceuticals LP, Wilmington, DE
Corifact (Factor XIII Concentrate [Human])	2/17/11	For routine prophylactic treatment of congenital Factor XIII deficiency.	✓		✓	✓	CSL Bhering GmbH, King of Prussia, PA
DaTscan (ioflupane i-123)	1/14/11	For brain imaging to assist in the evaluation of adult patients with suspected Parkinsonian Syndrome.			✓		GE Healthcare, Inc., Princeton, NJ
Dificid (fidaxomicin)	5/27/11	For treatment of Clostridium difficile-associated diarrhea (CDAD).		✓	✓	✓	Optimer Pharmaceuticals Inc., San Diego, CA
Firazyr (icatibant)	8/25/11	For treatment of acute attacks of a rare condition called hereditary angioedema (HAE) in people ages 18 years and older.	✓		✓		Shire Human Genetic Therapies Inc., Cambridge, MA
Halaven (eribulin mesylate)	11/15/10	For treatment of patients with metastatic (late-stage) breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease		✓	✓	✓	Eisai, Inc., Woodcliff Lake, NJ
Incivek (telaprevir)	5/23/11	For treatment of certain adults with chronic hepatitis C infection.		✓	✓	✓	Vertex Pharmaceuticals, Cambridge, MA
Pradaxa (dabigatran etexilate)	10/19/10	To reduce the risk of stroke and blood clots in patients with abnormal heart rhythms (non-valvular atrial fibrillation).			✓	✓	Boehringer Ingelheim Pharm, Inc, Ridgefield, CT
Victrelis (boceprevir)	5/13/11	To treat certain adults with chronic hepatitis C infection.		✓	✓	✓	Merck, Whitehouse Station, NJ

I. Priority Drugs (continued)

Drug Name	Approval Date	Indication	Orphan Drug	Approved First in U.S.	PDUFA Date Met	Approved 1st Cycle	Sponsor
Xalkori (crizotinib) and companion genetic test	8/26/11	To treat certain patients with late stage (locally advanced or metastatic), non-small cell lung cancers (NSCLC) who express the abnormal anaplastic lymphoma kinase (ALK) gene.	✓	✓	✓	✓	Xalkori is marketed by Pfizer, New York, NY, and the Vysis ALK Break Apart FISH Probe Kit is marketed by Abbott Molecular Inc. of Des Plaines, IL.
Yervoy (ipilimumab)	3/25/11	To treat patients with metastatic melanoma (late-stage skin cancer).	✓	✓	✓	✓	Bristol-Meyers Squibb, New York, NY
Zelboraf (vemuranfenib) with companion diagnostic	8/17/11	To treat patients with metastatic (late-stage) or unresected (cannot be removed by surgery) melanoma (skin cancer) in patients whose tumors express a gene mutation called BRAF V600E.	✓	✓	✓	✓	Zelboraf is marketed by Genentech, a member of the Roche Group, South San Francisco, CA.
Zytiga (albiraterone acetate)	4/28/11	To use In combination with prednisone (a steroid), to treat patients with metastatic (late-stage) castration-resistant prostate cancer who have received prior docetaxel (chemotherapy).		✓	✓	✓	Centocor Ortho Biotech, Inc., Horsham, PA

II. Standard Drugs

Arcapta Neohaler (indacaterol inhalation powder)	7/1/11	For long term, once-daily maintenance bronchodilator treatment of airflow obstruction in people with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and/or emphysema.			✓		Novartis Pharmaceuticals Corp., East Hanover, NJ
Ardovax (Adenovirus Type 4 and Type 7 Vaccine, Live, Oral)	3/16/11	For active immunization for the prevention of febrile acute respiratory disease caused by Adenovirus Type 4 and Type 7. Adenovirus Type 4 and Type 7 Vaccine, Live, Oral is approved for use in military populations 17 through 50 years of age.		✓	✓		Teva Women's Health, Inc., Horsham, PA

II. Standard Drugs (continued)

Drug Name	Approval Date	Indication	Orphan Drug	Approved First in U.S.	PDUFA Date Met	Approved 1st Cycle	Sponsor
Brilinta (ticagrelor)	7/20/11	To reduce cardiovascular death and heart attack in patients with acute coronary syndromes (ACS).			✓		AstraZeneca, Wilmington, DE
Daliresp (roflumilast)	2/28/11	To decrease the frequency of flare-ups (exacerbations) or worsening of symptoms from severe chronic obstructive pulmonary disease (COPD).			✓		Forest Pharmaceuticals St. Louis, MO
Edarbi azilsartan medoxomil)	2/25/11	For treatment of high blood pressure (hypertension) in adults.		✓	✓	✓	Takeda Pharmaceuticals North America, Deerfield, IL
Edurant (rilpivirine)	5/20/11	For treatment of HIV-1 infection in adults who have never taken HIV therapy.		✓	✓	✓	Tibotec Therapeutics, a division of Centocor Ortho Biotech Inc., Raritan, NJ
Egrifta (tesamorelin acetate)	11/10/10	For reduction of excess abdominal fat in HIV-infected patients with lipodystrophy.		✓		✓	Theratechnologies Inc., Montreal, Canada Marketed in US by EMD Serono, Inc., Rockland, MA
Gadavist (gadobutrol)	3/14/11	Contrast agent to help detect lesions in patients undergoing magnetic resonance imaging (MRI) of the central nervous system			✓	✓	Bayer Pharmaceuticals Wayne, NJ
Horizant (gabapentin enacarbil)	4/6/11	For once-daily treatment for moderate-to-severe restless legs syndrome (RLS).		✓	✓		GlaxoSmithKline, Research Triangle Park, NC and Xenoport, Santa Clara, CA
Latuda (lurasidone hydrochloride)	10/28/10	For treatment of schizophrenia in adults.		✓	✓	✓	Sunovian Pharm, Inc., Fort Lee, NJ
LaViv (Azficel-T)	6/21/11	For improvement of the appearance of moderate to severe nasolabial fold wrinkles in adults.		✓	✓		Fibrocell Technologies, Inc., Exton, PA

II. Standard Drugs (continued)

Drug Name	Approval Date	Indication	Orphan Drug	Approved First in U.S.	PDUFA Date Met	Approved 1st Cycle	Sponsor
Natroba (spinosad)	1/18/11	For treatment of head lice infestation in patients ages 4 years and older.		✓	✓		ParaPRO, LLC, Carmel, IN
Nulojix (belatacept)	6/15/11	To prevent organ rejection in adult patients who have had a kidney transplant, in combination with other immunosuppressants.	✓	✓	✓		Bristol-Meyers Squibb, Princeton, NJ
Potiga (ezogabine)	6/10/11	For use as an add-on medication to treat seizures associated with epilepsy in adults.			✓		Developed by Valeant Pharmaceuticals North America, Durham, NC Marketed by GlaxoSmithKline, Research Triangle Park, NC.
Spherusol (Coccidioides immitis Spherule-Derived Skin Test Antigen)	7/29/11	For detection of delayed type hypersensitivity to C. immitis in individuals, 18-64 years of age, with a history of pulmonary coccidioidomycosis.	✓	✓	✓		Allermed Laboratories, Inc., San Diego, CA
Teflaro (ceftaroline fosamil)	10/29/10	For treatment of acute bacterial skin and skin structure infections and community acquired bacterial pneumonia.		✓	✓	✓	Cerexa, Inc., Oakland, CA
Tradjenta (linagliptin)	5/2/11	For use as an adjunct to diet and exercise to improve glycemic (blood sugar) control in adults with type 2 diabetes.		✓	✓	✓	Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT and Eli Lilly Co., Indianapolis, IN
Viibryd (vilazodone hydrochloride)	1/21/11	For treatment of major depressive disorder in adults.		✓	✓	✓	PGxHealth, New Haven, CT
Xarelto (rivaroxaban)	7/1/11	To reduce the risk of blood clots, deep vein thrombosis (DVT), and pulmonary embolism (PE) following knee or hip replacement surgery.			✓		Janssen Pharmaceuticals, Inc., a member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Raritan, NJ.