BIOGEN IDEC INC.
Form 10-K
February 05, 2013
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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
Form 10-K

þ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2012

or

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission file number: 0-19311

BIOGEN IDEC INC.
(Exact name of registrant as specified in its charter)

Delaware	33-0112644
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

133 Boston Post Road, Weston, Massachusetts 02493
(781) 464-2000
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.0005 par value	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes þ No ¨

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ¨ No þ

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files): Yes þ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer þ	Accelerated filer ¨	Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No þ

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was $34,138,379,832.

As of January 31, 2013, the registrant had 236,312,191 shares of common stock, $0.0005 par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for our 2013 Annual Meeting of Stockholders are incorporated by reference into Part III of this report.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report contains forward-looking statements that are based on our current beliefs and expectations. These forward-looking statements may be accompanied by such words as “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “project,” “target,” “will” and other words and terms of similar meaning. Refe made in particular to forward-looking statements regarding:

- the anticipated amount, timing and accounting of revenues, contingency payments, milestone, royalty and other payments under licensing, collaboration or acquisition agreements, tax positions and contingencies, doubtful accounts, cost of sales, research and development costs, compensation and other expenses, amortization of intangible assets, and foreign currency forward contracts;
- the anticipated regulatory actions relating to and the commercial launch of TECFIDERA (BG-12);
- our plans to develop further risk stratification protocols for TYSABRI and the impact of such protocols;
- anticipated regulatory filings for, regulatory actions relating to, and commercial launch of our long-lasting blood clotting factor candidates;
- additional planned launches and future development costs of FAMPYRA;
- the timing, outcome and impact of proceedings related to: patents and other intellectual property rights; tax audits, assessments and settlements; product liability and other legal proceedings;
- loss to be incurred in connection with Genentech's ongoing arbitration with Hoechst;
- the deferral of TYSABRI revenue in Italy;
- the expected lifetime revenue of AVONEX and amortization recorded in relation to its core technology;
- the costs, timing and therapeutic scope of the development and commercialization of our pipeline products;
- our arrangement with Knopp Neurosciences related to dexpramipexole;
- the timing and impact of U.S. healthcare reform, including the annual fee on prescription drug manufacturers, and other measures worldwide designed to reduce healthcare costs;
- the impact of the deterioration of the credit and economic conditions in certain countries in Europe and our collection of accounts receivable in such countries;
- patent terms, patent term extensions, patent office actions and market exclusivity rights;
- fair value estimates in connection with our acquisitions of Stromedix and other entities;
- lease commitments and purchase obligations;
- our ability to finance our operations and business initiatives and obtain funding for such activities;
- the impact of new laws and accounting standards;
- the availability of our unrepatriated foreign earnings and dividend activity;
- repayment of outstanding debt;
- the timing and expected financial impact of relocating our corporate headquarters from our facility in Weston, Massachusetts to Cambridge, Massachusetts;
- manufacturing capacity;
- the licensure of and plans for our manufacturing facility in Hillerød, Denmark; and
- the drivers for growing our business, including our plans to pursue business development and research opportunities, and competitive conditions.

These forward-looking statements involve risks and uncertainties, including those that are described in the “Risk Factors” section of this report and elsewhere within this report that could cause actual results to differ materially from those reflected in such statements. You should not place undue reliance on these statements. Forward-looking statements speak only as of the date of this report. We do not undertake any obligation to publicly update any forward-looking statements.

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NOTE REGARDING COMPANY AND PRODUCT REFERENCES

Throughout this report, “Biogen Idec,” the “Company,” “we,” “us” and “our” refer to Biogen Idec Inc. and its consolidated subsidiaries. References to “RITUXAN” refer to both RITUXAN (the trade name for rituximab in the U.S., Canada and Japan) and MabThera (the trade name for rituximab outside the U.S., Canada and Japan), and “ANGIOMAX” refers to both ANGIOMAX (the trade name for bivalirudin in the U.S., Canada and Latin America) and ANGIOX (the trade name for bivalirudin in Europe).

NOTE REGARDING TRADEMARKS

AVONEX®, AVONEX PEN® and RITUXAN® are registered trademarks of Biogen Idec. FUMADERM™ and TECFIDERA™ are trademarks of Biogen Idec. TYSABRI® and TOUCH® are registered trademarks of Elan Pharmaceuticals, Inc. The following are trademarks of the respective companies listed: ACTEMRA® — Chugai Seiyaku Kabushiki Kaisha; AUBAGIO® — Sanofi Societe Anonyme France; ANGIOMAX® and ANGIOX® — The Medicines Company; ARZERRA® — Glaxo Group Limited; BENLYSTA® — Human Genome Sciences, Inc.; BETASERON® and BETAFERON® — Bayer Schering Pharma AG; CAMPATH® and LEMTRADA® — Genzyme Corporation; CIMZIA® — UCB Pharma, S.A.; COPAXONE® — Teva Pharmaceutical Industries Limited; ENBREL® — Immunex Corporation; EXTAVIA® and GILENYA® — Novartis AG; FAMPYRA® — Acorda Therapeutics, Inc.; HUMIRA® — AbbVie Biotechnology Ltd.; ORENCIA® — Bristol-Myers Squibb Company; REBIF® — Ares Trading S.A.; REMICADE® — Centocor Ortho Biotech Inc.; SIMPONI® — Johnson & Johnson; and TREANDA® — Cephalon, Inc.

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PART I

Item 1. Business

Overview

Biogen Idec is a global biotechnology company focused on discovering, developing, manufacturing and marketing therapies for the treatment of multiple sclerosis (MS) and other autoimmune disorders, neurodegenerative diseases and hemophilia. We also collaborate on the development and commercialization of RITUXAN and anti-CD20 product candidates for the treatment of non-Hodgkin's lymphoma and other conditions. Summary information about our marketed products is set forth in the table below.

			Product Revenues to Biogen Idec (in millions)		
Product	Indications	Development or Marketing Collaborator	2012	2011	2010
AVONEX (1)	Multiple sclerosis	None	$2,913.1	$2,686.6	$2,518.4
TYSABRI (2)	Multiple sclerosis Crohn’s disease	Elan Pharma International	$1,135.9	$1,079.5	$900.2
FAMPYRA (3)	Multiple sclerosis (walking ability)	Acorda Therapeutics	$57.4	$13.6	$—
FUMADERM (4)	Psoriasis	None	$59.7	$54.7	$51.2

			Unconsolidated Joint Business Revenues to Biogen Idec (in millions)		
Product	Indications	Development or Marketing Collaborator	2012	2011	2010
RITUXAN (5)	Non-Hodgkin’s lymphoma Rheumatoid arthritis Chronic lymphocytic leukemia ANCA-associated vasculitis	Genentech (Roche Group)	$1,137.9	$996.6	$1,077.2

(1) AVONEX (interferon beta-1a) is indicated for the treatment of patients with relapsing forms of MS to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations.

(2) TYSABRI (natalizumab) is indicated (1) for the treatment of relapsing forms of MS as a monotherapy to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations and (2) in the U.S. for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn's disease therapies and TNF inhibitors.

(3) FAMPYRA (prolonged-release fampridine tablets) is indicated for the improvement of walking ability in adult patients with MS who have walking disability.

(4) FUMADERM (fumaric acid esters) is only approved in Germany and is indicated for the treatment of adult patients with moderate to severe plaque psoriasis for whom topical therapy is ineffective.

(5) RITUXAN (rituximab) is indicated for the treatment of (1)(a) relapsed or refractory, low-grade or follicular, CD20-positive, B-cell Non-Hodgkin's lymphoma (NHL) as a single agent, (b) previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to RITUXAN in combination with chemotherapy, as a single-agent maintenance therapy, (c) non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent, after first-line CVP chemotherapy, and (d) previously untreated diffuse large B-cell, CD20-positive NHL in combination with CHOP or other anthracycline-based chemotherapy regimens, (2) CD20-positive chronic lymphocytic leukemia in combination with fludarabine and cyclophosphamide, (3) moderately- to severely-active rheumatoid arthritis, in combination with methotrexate, in adult patients who have had an inadequate response to one or more TNF antagonist therapies, and (4) Wegener's Granulomatosis and Microscopic Polyangiitis, in

combination with glucocorticoids, in adult patients.

Additional financial information about our product revenues, other revenues and geographic areas in which we operate is set forth in our consolidated financial statements, in Note 26, Segment Information to our consolidated financial statements, and in Item 6. Selected Consolidated Financial Data included in this report. A discussion of the risks attendant to our international operations is set forth in the “Risk Factors” section of this report.

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We devote significant resources to research and development programs and external business development opportunities, as summarized in the table below:

(In millions)	2012	2011	2010	
Research and development	$1,334.9	$1,219.6	$1,248.6	
Amortization of acquired intangible assets	$202.2	$208.6	$208.9	
Fair value adjustment of contingent consideration	$27.2	$36.1	$—	
Acquired in-process research and development	$—	$—	$245.0	*

* $145.0 million attributed to noncontrolling interests, net of tax.

Additional information about our research and development programs and business development activity during 2012 is set forth below under the subsections entitled “Research and Development Programs” and “Business Development.”

We were formed as a California corporation in 1985 and became a Delaware corporation in 1997. In 2003, we acquired Biogen, Inc. and changed our corporate name from IDEC Pharmaceuticals Corporation to Biogen Idec Inc. Our principal executive offices are located at 133 Boston Post Road, Weston, MA 02493 and our telephone number is (781) 464-2000. Our website address is www.biogenidec.com. We make available free of charge through the Investors section of our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with or furnished to the Securities and Exchange Commission (SEC). We include our website address in this report only as an inactive textual reference and do not intend it to be an active link to our website. The contents of our website are not incorporated into this filing.

Marketed Products

AVONEX

AVONEX is one of the most prescribed treatments for relapsing forms of MS worldwide. MS is a progressive neurological disease in which the body loses the ability to transmit messages along nerve cells, leading to a loss of muscle control, paralysis and, in some cases, death. Patients with active relapsing MS experience an uneven pattern of disease progression characterized by periods of stability that are interrupted by flare-ups of the disease after which the patient returns to a new baseline of functioning. AVONEX is a recombinant form of the interferon beta protein produced in the body in response to viral infection.

2012 Developments

In February 2012, the U.S. Food and Drug Administration (FDA) approved two separate dosing innovations designed to improve the treatment experience for patients receiving once-a-week AVONEX for relapsing forms of MS: AVONEX PEN and a new dose titration regimen. AVONEX PEN is the first intramuscular autoinjector approved for MS and is designed to enhance the self-injection process for patients receiving AVONEX therapy. A new dose titration regimen, facilitated by the AVOSTARTGRIP titration devices, provides patients with the option to gradually increase the dose of AVONEX at treatment initiation to reduce the incidence and severity of flu-like symptoms that patients may experience with therapy. These AVONEX dosing innovations are commercially available in the E.U., U.S. and other countries.

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TYSABRI

TYSABRI has advanced the treatment of MS patients with its established efficacy. TYSABRI is a monoclonal antibody approved in numerous countries as a monotherapy for relapsing MS and is also approved in the U.S. to treat Crohn's disease, an inflammatory disease of the intestines.

TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic infection of the brain by the JC virus that usually leads to death or severe disability. Infection by the JC virus (JCV) is required for the development of PML and patients who are anti-JCV antibody positive have a higher risk of developing PML. Factors that increase the risk of PML are presence of anti-JCV antibodies, prior immunosuppressant use, and longer TYSABRI treatment duration. Patients who have all three risk factors have the highest risk of developing PML. Reports of cases of PML in patients treated with TYSABRI in clinical studies led us to voluntarily suspend the marketing and commercial distribution of TYSABRI in February 2005 until its reintroduction to the market in July 2006. Because of the risk of PML, TYSABRI has a boxed warning and is marketed under risk management or minimization plans approved by regulatory authorities. In the U.S., for example, TYSABRI is marketed under the

TOUCH Prescribing Program, a restricted distribution program designed to assess and minimize the risk of PML, minimize death and disability due to PML, and promote informed benefit-risk decisions regarding TYSABRI use.

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U.S. and E.U. regulators continue to monitor and assess on an ongoing basis the criteria for confirming PML diagnosis, the number of PML cases, the incidence of PML in TYSABRI patients, the risk factors for PML, and TYSABRI's benefit-risk profile, which could result in modifications to the approved labels or other restrictions on TYSABRI treatment. We continue to research and develop protocols and therapies that may reduce risk and improve outcomes of PML in patients.

We collaborate with Elan Pharma International, Ltd (Elan) on the development and commercialization of TYSABRI. For information about this collaboration, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

2012 - 2013 Developments

- In January 2013, we and Elan Corporation, plc announced the submission of applications to the FDA and European Medicines Agency (EMA) requesting updates to the TYSABRI product labels. The applications request an expanded indication that would include first-line use for people living with certain relapsing forms of MS who have tested negative for antibodies to the JC virus.

- In January 2012, the FDA approved the inclusion in the U.S. product label for TYSABRI of anti-JCV antibody status as an additional factor in stratifying patients for developing PML. The FDA also approved the inclusion of a table summarizing the estimated incidence of PML according to the duration of TYSABRI treatment, prior immunosuppressant use and anti-JCV antibody status. In addition, the FDA granted Quest Diagnostics a de novo classification petition for the STRATIFY JCV Antibody ELISA testing service, which allows neurologists to determine their MS patients' anti-JCV antibody status.

RITUXAN

RITUXAN is a widely prescribed monoclonal antibody used to treat non-Hodgkin's lymphoma, rheumatoid arthritis, chronic lymphocytic leukemia and two forms of ANCA-associated vasculitis. Non-Hodgkin's lymphoma and chronic lymphocytic leukemia are cancers that affect lymphocytes, which are a type of white blood cell that help to fight infection. Rheumatoid arthritis is a chronic disease that occurs when the immune system mistakenly attacks the body's joints, resulting in inflammation, pain and joint damage. ANCA-associated vasculitis is a rare autoimmune disease that largely affects the small blood vessels of the kidneys, lungs, sinuses, and a variety of other organs.

We collaborate with Genentech, a wholly-owned member of the Roche Group, on the development and commercialization of RITUXAN. For information about this collaboration, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

FAMPYRA

FAMPYRA is the first treatment that addresses the unmet medical need of walking improvement in adult patients with MS who have walking disability. FAMPYRA is a prolonged-release tablet formulation of the drug fampridine. FAMPYRA is commercially available throughout the European Union and in Canada, Australia, New Zealand, Israel and South Korea, and we anticipate making FAMPYRA commercially available in additional markets in 2013.

We have a license from Acorda Therapeutics, Inc. to develop and commercialize FAMPYRA in all markets outside the U.S. For information about this relationship, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

2012 Developments

- The European Commission previously granted a conditional marketing authorization for FAMPYRA in the E.U. in July 2011. A conditional marketing authorization is renewable annually and is granted to a medicinal product with a positive benefit-risk assessment that fulfills an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact that additional data are still required. This marketing authorization was renewed as of July 2012. To meet the conditions of this marketing authorization, we will provide additional data from on-going clinical studies regarding FAMPYRA's benefits and safety in the long term.

FUMADERM

FUMADERM is approved for the treatment of moderate to severe psoriasis in Germany. Psoriasis is a skin disease in which cells build up on the skin surface and form scales and red patches.

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Other Sources of Revenue

Our other sources of revenue consist of royalties we receive from net sales of products related to patents that we licensed (royalty revenues) and revenues from our contract manufacturing, product supply and biosimilar arrangements (corporate partner revenues). Summary information about our other sources of revenue is set forth in the table below:

(In millions)	2012	2011	2010
Royalty revenues	$168.7	$158.5	$137.4
Corporate partner revenues	$43.8	$57.4	$31.7

Our most significant source of royalty revenue is derived from net worldwide sales of ANGIOMAX, which is licensed to The Medicines Company (TMC). TMC markets ANGIOMAX primarily in the U.S. and Europe for use as an anticoagulant in patients undergoing percutaneous coronary intervention. For a description of this royalty arrangement, please read the subsection entitled “Other Revenues - Royalty Revenues” in the “Management's Discussion and Analysis of Financial Condition and Results of Operations” section of this report.

2012 Developments

- In March 2012, the U.S. Patent and Trademark Office granted the extension of the term of the principal U.S. patent that covers ANGIOMAX to December 15, 2014. Under the terms of our royalty arrangement for ANGIOMAX, TMC is obligated to pay us royalties earned, on a country-by-country basis, until the later of (1) twelve years from the date of the first commercial sale of ANGIOMAX in such country or (2) the date upon which the product is no longer covered by a licensed patent in such country. The annual royalty rate is reduced by a specified percentage in any country where the product is no longer covered by a licensed patent and where sales have been reduced to a certain volume-based market share. TMC began selling ANGIOMAX in the U.S. in January 2001.

Research and Development Programs

A commitment to research is fundamental to our mission at Biogen Idec. Our research and development strategy is to discover and develop first-in-class molecules or best-in-class molecules that improve safety or efficacy for unmet medical needs. By applying our expertise in biologics and our growing capabilities in small-molecule drug discovery and development, we target specific medical needs where new or better treatments are needed.

We intend to continue committing significant resources to research and development opportunities and business development activity. As part of our ongoing research and development efforts, we have devoted significant resources to conducting clinical studies to advance the development of new pharmaceutical products and to explore the utility of our existing products in treating disorders beyond those currently approved in their labels. The table below highlights our current research and development programs. Drug development involves a high degree of risk and investment, and the status, timing and scope of our development programs are subject to change. Important factors that could adversely affect our drug development efforts are discussed in the “Risk Factors” section of this report.

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Therapeutic Area	Product Candidate	Targeted Indications	Status
Neurology	TECFIDERA (BG-12)	MS	Marketing applications submitted and under regulatory review
	Peginterferon beta-1a	MS	Expect to submit marketing applications by mid - 2013
	Daclizumab	MS	Phase 3
	TYSABRI	Secondary-progressive MS	Phase 3
	Anti-LINGO	Optic Neuritis	Phase 2
		MS	Phase 1
	BIIB037	Alzheimer’s disease	Phase 1
	ISIS - SMN_{Rx}	Spinal muscular atrophy	Phase 1b/2a
	Neublastin	Neuropathic pain	Phase 1
Hemophilia	Factor IX	Hemophilia B	U.S. BLA submitted and under regulatory review
	Factor VIII	Hemophilia A	Expect to submit U.S. BLA in 1H 2013
Immunology	STX-100	Idiopathic pulmonary fibrosis	Phase 2
	Anti-TWEAK	Lupus nephritis	Phase 2
	Anti-CD40 Ligand	General lupus	Phase 1
Other	GA101	Chronic lymphocytic leukemia	Phase 3
	GA101	Non-Hodgkin’s lymphoma	Phase 3

Late Stage Product Candidates

Additional information about our late stage product candidates is set forth below.

TECFIDERA (BG-12)

In February 2012, we submitted a New Drug Application to the FDA for marketing approval of TECFIDERA, our oral small molecule candidate for the treatment of MS. The regulatory submission was based on TECFIDERA's comprehensive development program, in which TECFIDERA demonstrated significant reductions in MS disease activity coupled with favorable safety and tolerability in the Phase 3 DEFINE and CONFIRM studies. The FDA accepted our application for TECFIDERA and granted us a standard review timeline. In October 2012, we announced that the FDA extended the initial PDUFA date for its review of our application by three months, which is a standard extension period. The extended PDUFA target date is in late March 2013. The FDA has indicated that the extension of the PDUFA date is needed to allow additional time for review of our application. The agency has not asked for additional studies.

In March 2012, we submitted a Marketing Authorisation Application for TECFIDERA to the EMA. The EMA has validated our application for review of TECFIDERA in the E.U. We have submitted additional regulatory applications for TECFIDERA in Australia, Canada and Switzerland.

We acquired TECFIDERA as part of our acquisition of Fumapharm AG in 2006. For more information about this acquisition and associated milestone obligations, please read the subsection entitled “Contractual Obligations and Off-Balance Sheet Arrangements-Contingent Consideration” in the “Management's Discussion and Analysis of Financial Condition and Results of Operations” section of this report.

Peginterferon beta-1a

Peginterferon beta-1a (Peginterferon) is designed to prolong the effects and reduce the dosing frequency of interferon beta-1a. The FDA has granted Peginterferon fast track status, which may result in priority review.

In January 2013, we released the primary efficacy analysis and safety data from our Phase 3 study, ADVANCE. Results support Peginterferon as a potential treatment dosed every two weeks or every four weeks for relapsing-remitting MS. The primary endpoint of ADVANCE, annualized relapse rate at one year, was met for both the two-week and four-week dosing regimens. Results showed that Peginterferon also met the secondary endpoints of risk of 12-week confirmed disability progression, proportion of patients who relapsed and magnetic resonance imaging assessments for both dose regimens. We plan to submit marketing applications for Peginterferon in the U.S. and E.U. by mid - 2013.

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Daclizumab

Daclizumab is a monoclonal antibody that is being tested in relapsing MS. In May 2010, we began patient enrollment in a Phase 3 study of daclizumab in relapsing MS, known as DECIDE, evaluating the efficacy and safety of daclizumab compared to interferon beta-1a (AVONEX). The DECIDE study is designed to have a two year endpoint and is expected to involve approximately 1,800 patients.

In August 2011, we announced positive results from SELECT, a global, registrational Phase 2b study designed to evaluate daclizumab in relapsing MS over one year. Results showed that daclizumab, administered subcutaneously once every four weeks, met primary and key secondary study endpoints, compared to placebo.

We collaborate with AbbVie Biotherapuetics, Inc., a subsidiary of AbbVie, Inc. on the development and commercialization of daclizumab. For information about this collaboration, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

TYSABRI (SPMS)

As part of our efforts with Elan to identify additional applications for TYSABRI, in September 2011 we began patient enrollment in a Phase 3b study of TYSABRI in secondary progressive MS, known as ASCEND. The study is designed to have an endpoint of approximately two years and involve approximately 850 patients. Secondary progressive MS is characterized by a steady progression of nerve damage, symptoms and disability.

Long-Lasting Recombinant Factors VIII and IX

In October 2012, we announced positive top-line results from the Phase 3 study, known as A-LONG, investigating our long-lasting recombinant Factor VIII-Fc fusion protein in hemophilia A, a rare inherited disorder which inhibits blood coagulation. We plan to submit a Biologics License Application to the FDA for our long-lasting Factor VIII product candidate in the first half of 2013.

We submitted a Biologics License Application to the FDA for marketing approval of our long-lasting recombinant Factor IX-Fc fusion protein in hemophilia B, a rare inherited disorder which inhibits blood coagulation, in the fourth quarter of 2012. The regulatory submission was based on the positive top-line results from the Phase 3 study known as B-LONG.

Pediatric data will be required as part of the Marketing Authorization Applications for our long-lasting Factor VIII and IX product candidates that we plan to submit to the EMA, and we have initiated two global pediatric studies of our long-lasting Factor VIII and IX product candidates.

We collaborate with Swedish Orphan Biovitrum AB on the commercialization of long-lasting recombinant Factors VIII and IX. For information about this collaboration, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

GA101

We collaborate with Genentech, Inc., a wholly-owned member of the Roche Group, on the development and commercialization of GA101, a monoclonal antibody. Genentech and Roche are managing the following Phase 3 studies of GA101:

- GOYA: investigating the efficacy and safety of GA101 in combination with CHOP chemotherapy compared to RITUXAN with CHOP chemotherapy in previously untreated patients with CD20-positive diffuse large B-cell lymphoma.
- GALLIUM: investigating the efficacy and safety of GA101 in combination with chemotherapy followed by maintenance with GA101 compared to RITUXAN in combination with chemotherapy followed by maintenance with RITUXAN in previously untreated patients with indolent non-Hodgkin's lymphoma.
- GADOLIN: investigating the efficacy and safety of GA101 plus bendamustine compared with bendamustine alone in patients with RITUXAN-refractory, indolent non-Hodgkin's lymphoma.
- CLL11: investigating the safety and efficacy of GA101 plus chlorambucil, a chemotherapy, compared to RITUXAN plus chlorambucil or chlorambucil alone in previously untreated chronic lymphocytic leukemia patients with co-morbidities.

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In January 2013, the Roche Group announced that stage 1 of the CLL11 study met its primary endpoint with an improvement in progression-free survival (PFS): GA101 plus chlorambucil significantly reduced the risk of disease worsening or death compared to chlorambucil alone. The CLL11 study includes two separate stages. Stage 1 evaluated GA101 plus chlorambucil compared to chlorambucil alone and included a pre-planned PFS futility analysis comparing GA101 plus chlorambucil to RITUXAN plus chlorambucil. The goal of the futility analysis was to evaluate the likelihood that the study would meet its pre-specified endpoint criteria during stage 2 analysis: improved efficacy (PFS) in the direct comparison of GA101 plus chlorambucil versus RITUXAN plus chlorambucil. The independent Data and Safety Monitoring Board assessment concluded that stage 2 of the study should continue until its final analysis.

For information about our collaboration with Genentech, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

Former Registrational Program

At the end of December 2012, we learned that a Phase 3 trial investigating dexpramipexole in people with amyotrophic lateral sclerosis (ALS) did not meet its primary endpoint, a joint rank analysis of function and survival, and no efficacy was seen in the individual components of function or survival. The trial also failed to show efficacy in its key secondary endpoints. Based on these results, we have discontinued development of dexpramipexole in ALS. Dexpramipexole was being developed pursuant to a license agreement with Knopp Neurosciences, Inc. For more information about this relationship, please read Note 20, Investments in Variable Interest Entities to our consolidated financial statements included in this report.

Business Development

In December 2012, we entered into an arrangement with Eisai, Inc. to lease a portion of their facility in Research Triangle Park, North Carolina (RTP) to manufacture our and Eisai's oral solid dose products and for Eisai to provide us with vial-filling services for biologic therapies and packaging services for oral solid dose products. For additional information about this transaction, please read Note 12, Property, Plant and Equipment to our consolidated financial statements included in this report.

In December, June and January 2012, we entered into three separate exclusive, worldwide option and collaboration agreements with Isis Pharmaceuticals, Inc. (Isis) under which both companies will develop and commercialize antisense therapeutics for up to three gene targets, Isis' product candidates for the treatment of myotonic dystrophy type 1 (DM1) and the treatment of spinal muscular atrophy (SMA), respectively. For additional information about these transactions, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

In March 2012, we acquired Stromedix, Inc., a privately held biotechnology company involved in the discovery of antibodies designed to treat fibrosis disorders. Stromedix' lead candidate, STX-100, is in a Phase 2 study for idiopathic pulmonary fibrosis, a disease in which lung tissue becomes scarred over time. There is no FDA-approved treatment for idiopathic pulmonary fibrosis at this time. For additional information about this transaction, please read Note 2, Acquisitions to our consolidated financial statements included in this report.

In February 2012, we finalized an agreement with Samsung Biologics that established an entity, Samsung Bioepis, to develop, manufacture and market biosimilar pharmaceuticals. For additional information about this transaction, please read Note 21, Collaborative and Other Relationships to our consolidated financial statements included in this report.

Patents and Other Proprietary Rights

Patents are important to developing and protecting our competitive position. We regularly seek patent protection in the U.S. and in selected countries outside the U.S. for inventions originating from our research and development efforts. In addition, we license rights to various patents and patent applications, generally, in return for the payment of royalties to the patent owner. U.S. patents, as well as most foreign patents, are generally effective for 20 years from the date the earliest (priority) application was filed; however, U.S. patents that issue on applications filed before June 8, 1995 may be effective until 17 years from the issue date, if that is later than the 20 year date. In some cases, the patent term may be extended to recapture a portion of the term lost during FDA regulatory review or because of U.S. Patent and Trademark Office (USPTO) delays in prosecuting the application. The duration of foreign patents varies similarly, in accordance with local law.

Regulatory data protection also can provide meaningful protection for our products. Regulatory data protection provides to the holder of a drug or biologic marketing authorization, for a set period of time, the exclusive use of the proprietary pre-clinical and clinical data that it compiled at significant cost and submitted to the applicable regulatory authority to obtain approval of its product. After the set period of time, third parties are then permitted to rely upon the data to obtain approval of their abbreviated applications to market generic drugs and biosimilars. Although the World Trade Organization's agreement on

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trade-related aspects of intellectual property rights (TRIPS) requires signatory countries to provide regulatory data protection to innovative pharmaceutical products, implementation and enforcement varies widely from country to country.

We also rely upon other forms of unpatented confidential information to remain competitive. We protect such information principally through confidentiality agreements with our employees, consultants, outside scientific collaborators, scientists whose research we sponsor and other advisers. In the case of our employees, these agreements also provide, in compliance with relevant law, that inventions and other intellectual property conceived by such employees during their employment shall be our exclusive property.

Our trademarks, including RITUXAN and AVONEX, are important to us and are generally covered by trademark applications or registrations in the USPTO and the patent or trademark offices of other countries. We also use trademarks licensed from third parties, such as the mark TYSABRI which we license from Elan. Trademark protection varies in accordance with local law, and continues in some countries as long as the mark is used and in other countries as long as the mark is registered. Trademark registrations generally are for fixed but renewable terms.

A discussion of certain risks and uncertainties that may affect our patent position and proprietary rights is set forth in the “Risk Factors” section of this report.

Additional information about the patents and other proprietary rights covering our marketed products and several of our late-stage product candidates is set forth below.

AVONEX and Pegylated Beta Interferon

Our U.S. patent No. 7,588,755, granted in September 2009, claims the use of recombinant beta interferon for immunomodulation or treating a viral condition, viral disease, cancers or tumors. This patent, which expires in September 2026, covers, among other things, the treatment of MS with our product AVONEX, as well as the treatment of MS with pegylated beta interferon. A discussion of legal proceedings related to this patent is set forth in Note 22, Litigation to our consolidated financial statements included in this report.

We have non-exclusive rights under certain third-party patents and patent applications to manufacture, use and sell AVONEX, including a patent owned by the Japanese Foundation for Cancer Research, which expires in 2013 in the U.S. Additionally, we and third parties own pending U.S. patent applications related to recombinant interferon-beta protein and nucleic acid. These applications, which fall outside of the GATT amendments to the U.S. patent statute, are not published by the USPTO and, if they mature into granted patents, may be entitled to a term of seventeen years from the grant date. There are two pending interference proceedings in the USPTO involving such third party applications, and additional interferences could be declared in the future. We do not know which, if any, such applications will mature into patents with claims relevant to our AVONEX product or to pegylated beta interferon.

Additional protection for our pegylated beta interferon is provided by patents and patent applications with expiration dates in 2021 in the U.S. and 2019 in the E.U., with the potential for patent term extension. We also expect our pegylated beta interferon to be granted regulatory exclusivity until 2026 in the U.S. and 2024 in the E.U.

TYSABRI

We and our collaborator, Elan, have patents and patent applications covering TYSABRI in the U.S. and other countries. These patents and patent applications cover TYSABRI and related manufacturing methods, as well as various methods of treatment using the product. In the U.S., the principal patents covering the product and use of the product to treat MS generally expire between 2015 and 2020. Additional U.S. patents and applications covering other indications, including treatment of inflammatory bowel disease, and methods of manufacturing, generally expire between 2012 and 2020. In the rest of world, patents on the product and methods of manufacturing the product generally expire between 2015 and 2020, subject to any supplemental protection (i.e., patent term extension) certificates that may be obtained. In the rest of world, patents and patent applications covering methods of treatment using TYSABRI generally expire between 2012 and 2020.

RITUXAN and Anti-CD20 Antibodies

We have several U.S. patents and patent applications, and numerous corresponding foreign counterparts, directed to anti-CD20 antibody technology, including RITUXAN. The principal patents with claims to RITUXAN or its uses expire in the U.S. between 2015 and 2018 and in the rest of the world in 2013, subject to any available patent term extensions. In addition, we and our collaborator, Genentech, have filed numerous patent applications directed to

anti-CD20 antibodies and their uses to treat various diseases. These pending patent applications have the potential of issuing as patents in the U.S. and in the rest of world with claims to anti-CD20 antibody molecules for periods beyond those stated above for RITUXAN. In 2008, a European patent of ours claiming the treatment with anti-CD20 antibodies of certain auto-immune indications, including RA, was revoked by the European Patent Office. We are appealing that decision.

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Genentech, our collaborator on RITUXAN, has secured an exclusive license to five U.S. patents and counterpart U.S. and foreign patent applications assigned to Xoma Corporation that relate to chimeric antibodies against the CD20 antigen. These patents expire between 2007 and 2014. We, along with Genentech, share the cost of any royalties due to Xoma in our co-promotion territory on sales of RITUXAN.

FAMPYRA

We have an exclusive license under two European granted patents, several pending European patent applications and numerous corresponding non-U.S. counterpart applications related to FAMPYRA. European patent EP0484186B1 claims pharmaceutical formulations containing aminopyridines including fampridine. This patent expired in November 2011 but is subject to pending and granted supplemental protection (i.e., patent term extension) certificates which, if granted, will extend the patent term to 2016 on a country-by-country basis. European patent EP1732548B1, which claims sustained-release aminopyridine compositions for increasing walking speed in patients with MS, expires in 2025 but is subject to pending and granted supplemental protection certificates which, if granted, will extend the patent term to 2026 on a country-by-country basis. In addition to these patent rights, FAMPYRA is covered by regulatory data protection in Europe until 2021.

TECFIDERA

We have several U.S. patents and patent applications, and a number of corresponding foreign counterparts, related to TECFIDERA. The principal U.S. patents are U.S. 6,509,376, having claims to formulations of dimethyl fumarate (the active ingredient of TECFIDERA) for use in the treatment of autoimmune diseases including MS, and U.S. 7,320,999 having claims to a method of treating MS using dimethyl fumarate. U.S. 6,509,376 and U.S. 7,320,999, expire in 2019 and 2020, respectively, subject to any available patent term extension following product approval. We also own a patent application, recently determined to be allowable by the USPTO, that covers the dosing regimen (240 mg of dimethyl fumarate administered twice a day) stated on our label under current review at the FDA. Once granted, this patent will expire in 2028. The granted European patent, EP 1131065, is directed to formulations of dimethyl fumarate and to uses thereof for treating autoimmune diseases, including MS. EP 1131065 expires in 2019, subject to any potential supplemental patent certificates that may be available. The E.U. counterpart to our recently allowed dosing regimen application is pending at the European Patent Office. Our pending patent applications, if granted, would expire as late as 2033, subject to any potential patent term adjustments or extensions that may be available.

In addition to patent protection, TECFIDERA is entitled to regulatory data protection in both the U.S. and the E.U. In the U.S., TECFIDERA is entitled to the 5 year data exclusivity given to new chemical entities. In the E.U. there are a number of ways to obtain data exclusivity and the EMA has informed us that TECFIDERA is, in principle, eligible for 8 years data exclusivity plus 2 years market exclusivity through the European centralized filing pathway. In both the US and the EU, the period of data exclusivity runs from the date of approval of the marketing application.

Long-Lasting Recombinant Factors VIII and IX

We have several U.S. patents and patent applications, and a number of corresponding foreign counterparts, related to our long-lasting recombinant Factor VIII and Factor IX product candidates and their use, including U.S. patents nos. U.S. 7,404,956; U.S. 8,329,182; U.S. 7,348,004; and U.S. 7,862,820. These patents will expire in 2024 - 2025, and some may be entitled to additional patent term pursuant to the patent term adjustment or patent term extension provisions of the U.S. patent laws. A related European patent, EP 1624891, expires in 2024 and may be entitled to additional patent term in at least some countries. Additionally, pending patent applications, if granted, would provide additional patent protection through 2033.

Sales, Marketing and Distribution

We focus our sales and marketing efforts on specialist physicians in private practice or at major medical centers. We use customary pharmaceutical company practices to market our products and to educate physicians, such as sales representatives calling on individual physicians, advertisements, professional symposia, direct mail, public relations and other methods. We provide customer service and other related programs for our products, such as disease and product-specific websites, insurance research services and order, delivery and fulfillment services. We have also established programs in the U.S. which provide qualified uninsured or underinsured patients with marketed products at no or reduced charge, based on specific eligibility criteria. Additional information about our sales, marketing and distribution efforts for our marketed products is set forth below.

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AVONEX

We continue to focus our marketing and sales activities on maximizing the potential of AVONEX in the U.S. and the rest of world in the face of increased competition. The principal markets for AVONEX are the U.S., Germany, France, Italy and the United Kingdom. In the U.S., Canada, Brazil, Argentina, Australia, Japan and most of the major countries of the E.U., we market and sell AVONEX through our own sales forces and marketing groups and distribute AVONEX principally through wholesale distributors of pharmaceutical products, mail order specialty distributors or shipping service providers. In other countries, we sell AVONEX to distribution partners who are then responsible for most marketing and distribution activities.

TYSABRI

The principal markets for TYSABRI are the U.S., the United Kingdom, France, Germany, Italy and Spain.

In the U.S., we are principally responsible for marketing TYSABRI for MS and use our own sales force and marketing group for this. Elan is responsible for TYSABRI distribution in the U.S. and uses a third party distributor to ship TYSABRI directly to customers.

In the rest of world, we are responsible for TYSABRI marketing and distribution and we use a combination of our own sales force and marketing group and third party service providers.

RITUXAN

The Roche Group and its sub-licensees market and sell RITUXAN worldwide. We collaborate with Genentech, a wholly-owned member of the Roche Group, on the development and commercialization of RITUXAN, but Genentech maintains sole responsibility for the U.S. sales and marketing efforts related to RITUXAN. RITUXAN is generally sold to wholesalers, specialty distributors and directly to hospital pharmacies.

FAMPYRA

We market and sell FAMPYRA outside the U.S. through our own sales forces and marketing groups. Our development and commercialization rights do not include the U.S. market.

FUMADERM

FUMADERM is marketed only in Germany, through our own sales force and marketing group.

Competition

Competition in the biotechnology and pharmaceutical industries is intense and comes from many and varied sources, including specialized biotechnology firms and large pharmaceutical companies. Many of our competitors are working to develop products similar to those we are developing or already market and have considerable experience in undertaking clinical trials and in obtaining regulatory approval to market pharmaceutical products. Certain of these companies have substantially greater financial, marketing and research and development resources than we do.

We believe that competition and leadership in the industry is based on managerial and technological superiority and establishing patent and other proprietary positions through research and development. The achievement of a leadership position also depends largely upon our ability to identify and exploit commercially the products resulting from research and the availability of adequate financial resources to fund facilities, equipment, personnel, clinical testing, manufacturing and marketing. Another key aspect of remaining competitive within the industry is recruiting and retaining qualified scientists and technicians. We believe that we have been successful in attracting skilled and experienced scientific personnel.

Competition among products approved for sale may be based, among other things, on patent position, product efficacy, safety, convenience, reliability, availability and price. In addition, early entry of a new pharmaceutical product into the market may have important advantages in gaining product acceptance and market share. Accordingly, the relative speed with which we can develop products, complete the testing and approval process and supply commercial quantities of products will have an important impact on our competitive position.

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We may face increased competitive pressures as a result of the emergence of biosimilars. In the U.S., most of our marketed products, including AVONEX, TYSABRI and RITUXAN, are licensed under the Public Health Service Act (PHSA) as biological products. In March 2010, U.S. healthcare reform legislation amended the PHSA to authorize the FDA to approve biological products, known as biosimilars or follow-on biologics, that are shown to be highly similar to previously approved biological products based upon potentially abbreviated data packages. The approval pathway for biosimilars does, however, grant a biologics manufacturer a 12 year period of exclusivity from the date of approval of its biological product before biosimilar competition can be introduced. Biosimilars legislation has also been in place in the E.U. since 2003. In December 2012, guidelines issued by the EMA for approving biosimilars of marketed monoclonal antibody products became effective. If a biosimilar version of one of our products were approved, it could reduce our sales of that product.

Additional information about the competition that our marketed products face is set forth below.

AVONEX AND TYSABRI

Each of AVONEX and TYSABRI competes with the following products:

- COPAXONE (glatiramer acetate), which is marketed by Teva Pharmaceutical Industries Ltd. COPAXONE generated worldwide revenues of approximately $3.9 billion in 2011.
- REBIF (interferon-beta-1a), which is marketed by Merck (and co-promoted with Pfizer Inc. in the U.S.). REBIF generated worldwide revenues of approximately $2.2 billion in 2011.
- BETASERON/BETAFERON (interferon-beta-1b), which is marketed by the Bayer Group. BETASERON/BETAFERON generated worldwide revenues of approximately $1.4 billion in 2011.
- EXTAVIA (interferon-beta-1b), which is marketed by Novartis AG. EXTAVIA generated worldwide revenues of approximately $154.0 million in 2011.
- GILENYA (fingolimod), which is marketed by Novartis AG. GILENYA generated worldwide revenues of approximately $494.0 million in 2011.
- AUBAGIO (teriflunomide), which is marketed by Sanofi-Aventis. AUBAGIO was approved in the U.S. in September 2012.

Along with us, a number of companies are working to develop additional treatments for MS that may in the future compete with AVONEX, TYSABRI or both. For example, a marketing application for LEMTRADA (alemtuzumab) (developed by Sanofi-Aventis) has been filed as a potential treatment for MS. In addition, the commercialization of certain of our own pipeline product candidates, such as TECFIDERA, may also negatively impact future sales of AVONEX, TYSABRI or both.

FAMPYRA

FAMPYRA is indicated as a treatment to improve walking in adult patients with MS who have walking disability and is the first treatment that addresses this unmet medical need with demonstrated efficacy in people with all types of MS. The product benefits from exclusivity rights that prohibit generic versions from being manufactured. However, the exclusivity rights are set to expire in 2017, which is the earliest predictable date that a generic version may be available. There are no commercially available generic versions of FAMPYRA.

FUMADERM

FUMADERM competes with several different types of therapies in the psoriasis market within Germany, including oral systemics such as methotrexate and cyclosporine.

RITUXAN IN ONCOLOGY

RITUXAN competes with several different types of therapies in the oncology market, including:

- TREANDA (bendamustine HCL) (marketed by Cephalon), which is indicated for patients with indolent B-cell NHL that has progressed within 6 months of treatment with RITUXAN and for CLL.
- ARZERRA (ofatumumab) (marketed by GenMab in collaboration with GlaxoSmithKline), which is indicated for refractory CLL patients to both alemtuzumab and fludarabine.

We are also aware of other anti-CD20 molecules in development, including our own product candidate GA101, that, if successfully developed and registered, may compete with RITUXAN in the oncology market.

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RITUXAN IN RHEUMATOID ARTHRITIS (RA)

RITUXAN competes with several different types of therapies in the RA market, including:

- traditional therapies for RA, including disease-modifying anti-rheumatic drugs such as steroids, methotrexate and cyclosporine, and pain relievers such as acetaminophen.
- TNF inhibitors, such as REMICADE (infliximab) and SIMPONI (golimumab) (marketed by Johnson & Johnson), HUMIRA (adalimumab) (marketed by AbbVie, Inc.), ENBREL (etanercept) (marketed by Amgen, Inc. and Pfizer) and CIMZIA (certolizumab pegol) (marketed by UCB, S.A.).
- ORENCIA (abatacept) (marketed by Bristol-Myers Squibb Company).
- ACTEMRA (tocilizumab) (marketed by the Roche Group).

We are also aware of other products in development that, if successfully developed and registered, may compete with RITUXAN in the RA market.

Regulatory

Our current and contemplated activities and the products and processes that will result from such activities are subject to substantial government regulation.

Regulation of Pharmaceuticals

Product Approval and Post-Approval Regulation in the United States

Before new pharmaceutical products may be sold in the U.S., preclinical studies and clinical trials of the products must be conducted and the results submitted to the FDA for approval. With limited exceptions, the FDA requires companies to register both pre-approval and post-approval clinical trials and disclose clinical trial results in public databases. Failure to register a trial or disclose study results within the required time periods could result in penalties, including civil monetary penalties. Clinical trial programs must establish efficacy, determine an appropriate dose and dosing regimen, and define the conditions for safe use. This is a high-risk process that requires stepwise clinical studies in which the candidate product must successfully meet predetermined endpoints. The results of the preclinical and clinical testing of a product are then submitted to the FDA in the form of a Biologics License Application (BLA) or a New Drug Application (NDA). In response to a BLA or NDA, the FDA may grant marketing approval, request additional information or deny the application if it determines the application does not provide an adequate basis for approval.

The receipt of regulatory approval often takes a number of years, involves the expenditure of substantial resources and depends on a number of factors, including the severity of the disease in question, the availability of alternative treatments, potential safety signals observed in preclinical or clinical tests, and the risks and benefits of the product as demonstrated in clinical trials. The FDA has substantial discretion in the product approval process, and it is impossible to predict with any certainty whether and when the FDA will grant marketing approval. The agency may on occasion require the sponsor of a BLA or NDA to conduct additional clinical studies or to provide other scientific or technical information about the product, and these additional requirements may lead to unanticipated delay or expense. Furthermore, even if a product is approved, the approval may be subject to limitations based on the FDA's interpretation of the existing pre-clinical or clinical data.

The FDA has developed four distinct approaches intended to make therapeutically important drugs available as rapidly as possible, especially when the drugs are the first available treatment or have advantages over existing treatments: accelerated approval, fast track, breakthrough therapy, and priority review.

The FDA may grant “accelerated approval” status to products that treat serious or life-threatening illnesses and that provide meaningful therapeutic benefits to patients over existing treatments. Under this pathway, the FDA may approve a product based on surrogate endpoints, or clinical endpoints other than survival or irreversible morbidity. When approval is based on surrogate endpoints or clinical endpoints other than survival or morbidity, the sponsor will be required to conduct additional post-approval clinical studies to verify and describe clinical benefit. Under the agency's accelerated approval regulations, if the FDA concludes that a drug that has been shown to be effective can be safely used only if distribution or use is restricted, it may require certain post-marketing restrictions as necessary to assure safe use. In addition, for products approved under accelerated approval, sponsors may be required to submit all copies of their promotional materials, including advertisements, to the FDA at least thirty days prior to initial dissemination. The FDA may withdraw approval under accelerated approval after a hearing if, for instance,

post-marketing studies fail to verify any clinical benefit, it becomes clear that restrictions on the distribution of the product are inadequate to ensure its safe use, or if a sponsor fails to comply with the conditions of the accelerated approval.

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In addition, the FDA may grant “fast track” status to products that treat serious diseases or conditions and fill an unmet medical need. Fast track is a process designed to expedite the review of such products by providing, among other things, more frequent meetings with the FDA to discuss the product's development plan, more frequent written correspondence from the FDA about trial design, eligibility for accelerated approval, and rolling review, which allows submission of individually completed sections of a NDA or BLA for FDA review before the entire filing is completed. Fast track status does not ensure that a product will be developed more quickly or receive FDA approval.

The FDA may also grant “breakthrough therapy” status to drugs designed to treat, alone or in combination with another drug or drugs, a serious or life-threatening disease or condition and for which preliminary evidence suggests a substantial improvement over existing therapies. Such drugs need not address an unmet need, but are nevertheless eligible for expedited review if they offer the potential for an improvement. Breakthrough therapy status entitles the sponsor to earlier and more frequent meetings with the FDA regarding the development of nonclinical and clinical data and permits the FDA to offer product development or regulatory advice for the purpose of shortening the time to product approval. Breakthrough therapy status does not guarantee that a product will be developed or reviewed more quickly and does not ensure FDA approval.

Finally, the FDA may grant “priority review” status to products that offer major advances in treatment or provide a treatment where no adequate therapy exists. Priority review is intended to reduce the time it takes for the FDA to review a NDA or BLA, with the goal for completing a priority review being six months (compared to ten months under standard review).

Regardless of the approval pathway employed, the FDA may require a sponsor to conduct additional post-marketing studies as a condition of approval to provide data on safety and effectiveness. If a sponsor fails to conduct the required studies, the agency may withdraw its approval. In addition, regardless of the approval pathway, if the FDA concludes that a drug that has been shown to be effective can be safely used only if distribution or use is restricted, it can mandate post-marketing restrictions as necessary to assure safe use. In such a case, the sponsor may be required to establish rigorous systems to assure use of the product under safe conditions. These systems are usually referred to as Risk Evaluation and Mitigation Strategies (REMS). The FDA can impose fi