BRISTOL MYERS SQUIBB CO
Form 10-K
February 12, 2016

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

_____

FORM 10-K

_____

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

For the fiscal year ended December 31, 2015
Commission File Number 1-1136

_____

BRISTOL-MYERS SQUIBB COMPANY
(Exact name of registrant as specified in its charter)

_____

Delaware	22-0790350
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

345 Park Avenue, New York, N.Y. 10154
(Address of principal executive offices)
Telephone: (212) 546-4000

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.10 Par Value	New York Stock Exchange
1.000% Notes due 2025	New York Stock Exchange
1.750% Notes due 2035	New York Stock Exchange

Securities registered pursuant to Section 12(g) of the Act:
Title of each class
$2 Convertible Preferred Stock, $1 Par Value

_____

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes x No ¨
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x
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 x 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 (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) 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 definitions of “large accelerated filer”, “accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer x Accelerated filer ¨ Non-accelerated filer ¨ Smaller reporting company ¨

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

The aggregate market value of the 1,665,867,299 shares of voting common equity held by non-affiliates of the registrant, computed by reference to the closing price as reported on the New York Stock Exchange, as of the last business day of the registrant’s most recently completed second fiscal quarter (June 30, 2015) was approximately $110,846,810,075. Bristol-Myers Squibb has no non-voting common equity. At February 1, 2016, there were 1,669,459,090 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE: Portions of the Proxy Statement for the registrant’s Annual Meeting of Stockholders to be held May 3, 2016, to be filed within 120 days after the conclusion of the registrant's fiscal year ended December 31, 2015, are incorporated by reference into Part III of this Annual Report on Form 10-K.

PART I

Item 1. BUSINESS.

General

Bristol-Myers Squibb Company (which may be referred to as Bristol-Myers Squibb, BMS, the Company, we, our or us) was incorporated under the laws of the State of Delaware in August 1933 under the name Bristol-Myers Company, as successor to a New York business started in 1887. In 1989, Bristol-Myers Company changed its name to Bristol-Myers Squibb Company as a result of a merger. We are engaged in the discovery, development, licensing, manufacturing, marketing, distribution and sale of biopharmaceutical products on a global basis.

We operate in one segment—BioPharmaceuticals. For additional information about business segments, refer to “Item 8. Financial Statements—Note 2. Business Segment Information.”

We compete with other worldwide research-based drug companies, smaller research companies and generic drug manufacturers. Our products are sold worldwide, primarily to wholesalers, retail pharmacies, hospitals, government entities and the medical profession. We manufacture products in the United States (U.S.), Puerto Rico and in six foreign countries.

The percentage of revenues by significant region/country were as follows:

	Year Ended December 31,					
Dollars in Millions	2015		2014		2013	
United States	49	%	49	%	51	%
Europe	21	%	23	%	24	%
Japan	10	%	6	%	5	%
China	4	%	4	%	4	%
Total Revenues	$16,560		$15,879		$16,385	

Acquisitions and Divestitures

We have transitioned BMS into a leading-edge specialty biopharmaceutical company focused exclusively on discovering, developing, and delivering innovative medicines that address serious unmet medical needs. This transition has encompassed all areas of our business and operations. As part of this strategy, we have divested our diabetes and non-pharmaceutical businesses, restructured our alliances to divest certain mature brand products, implemented our acquisition and licensing strategy and executed our productivity transformation initiative. Significant divestitures include the anticipated divestiture of the investigational HIV medicines in the first half of 2016, Erbitux* in North America in 2015, our diabetes business in 2014 and Mead Johnson in 2009. As part of our acquisition and licensing strategy, we acquired Cardioxyl Pharmaceuticals, Inc. (Cardioxyl) and Flexus Biosciences, Inc. (Flexus) in 2015, iPierian, Inc. (iPierian) in 2014, Amylin Pharmaceuticals, Inc. (Amylin) and Inhibitex, Inc. (Inhibitex) in 2012 and Amira Pharmaceuticals, Inc. (Amira) in 2011 and entered into several license and other collaboration arrangements. These transactions have allowed, and continue to allow, us to focus our resources behind growth opportunities which drive the greatest long-term value. From a disease standpoint, we are focused on the following core therapeutic areas: oncology, immuno-oncology, immunoscience, cardiovascular disease, fibrosis and genetically defined diseases.

Products

Our pharmaceutical products include chemically-synthesized drugs, or small molecules, and an increasing portion of products produced from biological processes (typically involving recombinant DNA technology), called “biologics.” Small molecule drugs are typically administered orally, e.g., in the form of a pill or tablet, although other drug delivery mechanisms are used as well. Biologics are typically administered to patients through injections or by infusion. Most of our revenues come from products in the following therapeutic classes: virology, including HIV infection; oncology; immunoscience; cardiovascular; and neuroscience.

In the pharmaceutical industry, the majority of an innovative product's commercial value is usually realized during the period in which the product has market exclusivity. Our business is focused on innovative biopharmaceutical products, and we rely on patent rights and various forms of regulatory protection to maintain the market exclusivity of our products. In the U.S., the European Union (EU) and some other countries, when these patent rights and other forms of exclusivity expire and generic versions of a medicine are approved and marketed, there are often substantial and rapid declines in the sales of the original innovative product. For further discussion of patent rights and regulatory forms of exclusivity, refer to "—Intellectual Property and Product Exclusivity" below. For further discussion of the impact of generic competition on our business, refer to "—Generic Competition" below.

The following chart shows our key products together with the year in which the earliest basic exclusivity loss (patent rights or data exclusivity) occurred or is currently estimated to occur in the U.S., the EU, Japan and China. We also sell our pharmaceutical products in other countries; however, data is not provided on a country-by-country basis because individual country revenues are not significant outside the U.S., the EU, Japan and China. In many instances, the basic exclusivity loss date listed below is the expiration date of the patent that claims the active ingredient of the drug or the method of using the drug for the approved indication, if there is only one approved indication. In some instances, the basic exclusivity loss date listed in the chart is the expiration date of the data exclusivity period. In situations where there is only data exclusivity without patent protection, a competitor could seek regulatory approval by submitting its own clinical trial data to obtain marketing approval prior to the expiration of data exclusivity.

We estimate the market exclusivity period for each of our products for the purpose of business planning only. The length of market exclusivity for any of our products is impossible to predict with certainty because of the complex interaction between patent and regulatory forms of exclusivity and the inherent uncertainties regarding patent litigation. There can be no assurance that a particular product will enjoy market exclusivity for the full period of time that appears in the estimate or that the exclusivity will be limited to the estimate.
The following schedule presents revenues of our key products and estimated basic exclusivity loss in the U.S., EU, Japan and China:

	Total Revenues by Product			Past or Currently Estimated Year of Basic Exclusivity Loss							
Dollars in Millions	2015	2014	2013	U.S.		EU[a]		Japan		China	
Virology											
Baraclude (entecavir)	$1,312	$1,441	$1,527	2014	(b)	2011-2016	(c)	2016		--	
Hepatitis C Franchise[d]	1,603	256	—	2028		2027		2028	(e)	++	
Reyataz (atazanavir sulfate) Franchise	1,139	1,362	1,551	2017		2017-2019	(f)	2019		2017	
Sustiva (efavirenz) Franchise	1,252	1,444	1,614	2017	(g)	2013	(h)	++		++	
Oncology											
Empliciti (elotuzumab)[i]	3	—	—	2026		++		++		++	
Erbitux* (cetuximab)	501	723	696	2016	(j)	++		2016	(k)	++	
Opdivo (nivolumab)	942	6	—	2027	(l)	2026	(l)	2031	(l)	++	
Sprycel (dasatinib)	1,620	1,493	1,280	2020	(m)	^^		2021		2020	
Yervoy (ipilimumab)	1,126	1,308	960	2023	(n)	2021	(o)	2023	(p)	++	
Neuroscience											
Abilify* (aripiprazole)	746	2,020	2,289	2015	(q)	2014	(q)	++		++	
Immunoscience											
Orencia (abatacept)	1,885	1,652	1,444	2019	(r)	2017	(s)	2018	(t)	++	
Cardiovascular											
Eliquis (apixaban)	1,860	774	146	2023	(u)	2022	(v)	2026	(v)	^	

Note: The currently estimated earliest year of basic exclusivity loss includes any statutory extensions of exclusivity that have been granted. In some instances, we may be able to obtain an additional six months exclusivity for a product

based on the pediatric extension. In certain other instances, there may be later-expiring patents that cover particular forms or compositions of the drug, as well as methods of manufacturing or methods of using the drug. Such patents may sometimes result in a favorable market position for our products, but product exclusivity cannot be predicted or assured. Under the U.S. healthcare law enacted in 2010, qualifying biologic products will receive 12 years of data exclusivity before a biosimilar can enter the market, as described in more detail in "—Intellectual Property and Product Exclusivity" below.

* Indicates brand names of products which are trademarks not owned by BMS. Specific trademark ownership information is included in the Exhibit Index.

++ We do not currently market the product in the country or region indicated.

-- There is uncertainty about China's exclusivity laws which has resulted in generic competition in the China market.

^ There is uncertainty about China's exclusivity laws.

^^ In May 2013, Apotex Inc., Actavis Group PTC ehf, Generics [UK] Limited (Mylan) and an unnamed company filed oppositions in the European Patent Office (EPO) seeking revocation of European Patent No. 1169038 (the '038 patent) covering dasatinib, the active ingredient in Sprycel. The '038 patent is scheduled to expire in April 2020 (excluding potential term extensions). On January 20, 2016, the Opposition Division of the EPO revoked the '038 patent. The Company will appeal the EPO's decision to the EPO Board of Appeal. The '038 patent will remain in force pending the outcome of our appeal of the EPO's decision, and we intend to pursue legal options to defend our intellectual property rights from any future infringement. Refer to "Note 22. Legal Proceedings and Contingencies" for more information.

(a) References to the EU throughout this Form 10-K include all member states of the European Union during the year ended December 31, 2015. Basic patent applications have not been filed in all current member states for all of the listed products. In some instances, the date of basic exclusivity loss will be different in various EU member states. For those EU countries where the basic patent was not obtained, there may be data protection available.

Baraclude U.S.: In September 2014, Teva Pharmaceuticals launched a generic version of Baraclude and we have experienced a negative impact on U.S. net product sales of Baraclude beginning in the fourth quarter of 2014. These actions follow a decision in June 2014 by the U.S. Court of Appeals for the Federal Circuit to uphold a
(b) lower court decision invalidating Baraclude's patent in February 2013. In May 2015, the U.S. Supreme Court denied the Company's petition for a writ of certiorari. Accordingly, this case is now concluded. For more information about this patent litigation matter, refer to "Item 8. Financial Statements—Note 22. Legal Proceedings and Contingencies."

(c) Baraclude EU: The composition of matter patent expires in the EU between 2011 and 2016.

(d) Exclusivity period relates to the Daklinza brand.

(e) The composition of matter covering daclatasvir in Japan expires in 2028 including granted patent term extension.

(f) Reyataz EU: Data exclusivity in the EU expired in 2014 and projected market exclusivity expires between 2017 and 2019.

Sustiva U.S.: Exclusivity period relates to the Sustiva brand and does not include exclusivity related to any combination therapy. The composition of matter patent for efavirenz in the U.S. expired in 2013 and the method of use patent for the treatment of HIV infection expired in September 2014. Pediatric exclusivity has been granted,
(g) which provides an additional six month period of exclusivity added to the term of the patents listed in the Orange Book. In October 2014, the Company announced that it has successfully resolved all outstanding U.S. patent litigation relating to efavirenz and that loss of exclusivity in the U.S. for efavirenz is not expected to occur until December 2017.

Sustiva EU: Exclusivity period relates to the Sustiva brand and does not include exclusivity related to any
(h) combination therapy. Market exclusivity for Sustiva expired in November 2013 in countries in the EU. Data exclusivity for Sustiva expired in the EU in 2009.

Empliciti: We have a commercialization agreement with AbbVie Inc. (AbbVie) for Empliciti. For more information about our arrangement with AbbVie, refer to "—Alliances" below and "Item 8. Financial Statements—Note 3. Alliances."
(i) AbbVie owns a patent covering elotuzumab as a composition of matter that expires in 2026 in the U.S. (excluding potential patent term extension) and 2024 in the EU, Japan and China (excluding potential patent term extensions in the EU and Japan).

Erbitux* U.S.: Biologic product approved under a Biologics License Application (BLA). Data exclusivity in the U.S. expires in 2016. There is no patent that specifically claims the composition of matter of cetuximab, the active ingredient in Erbitux*. In 2015, the Company transferred its rights, including full commercialization and
(j) manufacturing responsibilities of Erbitux* in North America to Lilly in return for sales-based royalties. For more information about our arrangement with Lilly, refer to "—Alliances" below and "Item 8. Financial Statements—Note 3. Alliances."

(k) Erbitux* Japan: Exclusivity period is based on regulatory data protection. BMS transferred its co-commercialization rights in Japan to Merck KgaA in 2015 in exchange for sales-based royalties.

Opdivo: We jointly own a patent with Ono Pharmaceutical Co., Ltd. (Ono) covering nivolumab as a composition
(l) of matter that expires in 2027 in the U.S. (excluding potential patent term extension) and 2026 in the EU (excluding potential patent term extensions). The composition of matter patent covering nivolumab in Japan expires in 2031 including granted patent term extension.

Sprycel: A patent term extension has been granted in the U.S. extending the term on the basic composition of matter patent covering dasatinib until June 2020. In 2013, the Company entered into a settlement agreement with
(m) Apotex regarding a patent infringement suit covering the monohydrate form of dasatinib whereby Apotex can launch its generic dasatinib monohydrate abbreviated New Drug Application product in September 2024, or earlier in certain circumstances. In the U.S., orphan drug exclusivity expired in 2013.

Yervoy U.S.: Exclusivity period is based on regulatory data protection. Data exclusivity expires in the U.S. in
(n) 2023. We own a patent covering ipilimumab as a composition of matter that currently expires in 2022 in the U.S. (excluding potential patent term extension).

(o) Yervoy EU: Exclusivity period is based on regulatory data protection. Data exclusivity expires in the EU in 2021. We own a patent covering ipilimumab as a composition of matter that currently expires in 2020 in the EU

(excluding potential patent term extensions).

(p) Yervoy Japan: Exclusivity period is based on regulatory data protection. We own a patent covering ipilimumab as a composition of matter that currently expires in 2020 in Japan (excluding potential patent term extension).

(q) Abilify*: Our commercialization rights of Abilify* terminated in April 2015 in the U.S. and in June 2014 in the EU.

(r) Orencia U.S.: We have a series of patents covering abatacept and its method of use. In the U.S., a patent term extension has been granted for one of the composition of matter patents, extending the term of the U.S. patent to 2019. Data exclusivity expires in the U.S. in 2017 and the method of use patent expires in 2021.

(s) Orencia EU: In the EU, the composition of matter patent covering abatacept expired in 2012. In the majority of the EU countries, we have applied for supplementary protection certificates and also pediatric extension of the supplementary protection certificates for protection until 2017. Most of these protection certificates have been granted. Data exclusivity expires in the EU in 2017 and the method of use patent expires in 2021.

(t) Orencia Japan: Exclusivity period is based on regulatory data protection.

(u) Eliquis U.S.: The composition of matter patent covering apixaban in the U.S. expires in February 2023 (excluding potential patent term extension). In August 2015, we received a Petition for Inter Partes Review of the composition of matter patent covering apixaban filed at the United States Patent and Trademark Office by the Coalition for Affordable Drugs. For more information about this patent litigation matter, refer to “Item 8. Financial Statements—Note 22. Legal Proceedings and Contingencies."

(v) Eliquis EU and Japan: The composition of matter patent covering apixaban in the EU expires in 2022. We have applied for supplementary protection certificates. Some of these supplementary protection certificates have been granted and expire in 2026. Data exclusivity in the EU expires in 2021. The composition of matter covering apixaban in Japan expires in 2026 including granted patent term extension.

Below is a summary of the indication, product partner, if any, and third-party manufacturing arrangements, if any, for each of the above products in the U.S. and, where applicable, the EU and Japan.

Baraclude

Baraclude is a potent and selective inhibitor of hepatitis B virus that was approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic hepatitis B virus infection. Baraclude was discovered and developed internally.

Bulk active entecavir is manufactured by both the company and a third party. The product is then finished in our facilities.

Hepatitis C Franchise

Daklinza (daclatasvir (DCV)) is an oral small molecule NS5A replication complex inhibitor for the treatment of hepatitis C virus infection (HCV) and was approved by the FDA for use with Gilead Sciences, Inc.'s (Gilead) sofosbuvir for genotype 3.

Sunvepra (asunaprevir (ASV)) is an oral small molecule NS3 protease inhibitor for the treatment of HCV and is part of the dual regimen of DCV+ASV in Japan.

We manufacture our bulk requirements of daclatasvir and finish the product in our facilities. We obtain bulk requirements for asunaprevir from a third-party manufacturer and finish the product at a third-party facility.

Reyataz Franchise	Reyataz is a protease inhibitor for the treatment of HIV. The Reyataz Franchise includes Reyataz and combination therapy Evotaz (atazanavir 300 mg and cobicistat 150 mg), a once-daily single tablet two drug regimen combining Reyataz and Gilead's Tybost* (cobicistat) for the treatment of HIV-1 infection in adults.

We developed atazanavir under a worldwide license from Novartis Pharmaceutical Corporation (Novartis) for which a royalty is paid based on a percentage of net product sales. We are entitled to promote Reyataz for use in combination with Norvir* (ritonavir) under a non-exclusive license agreement with AbbVie, as amended, for which a royalty is paid based on a percentage of net product sales. We have a licensing agreement with Gilead for Evotaz, which was approved in the U.S. in January 2015 and in the EU in July 2015.

We manufacture our bulk requirements for atazanavir and finish the product in our facilities.

Sustiva Franchise	Sustiva is a non-nucleoside reverse transcriptase inhibitor for the treatment of HIV. The Sustiva Franchise includes Sustiva, an antiretroviral drug used in the treatment of HIV, as well as bulk efavirenz which is included in the combination therapy Atripla* (efavirenz 600 mg/ emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg), a once-daily single tablet three-drug regimen combining our Sustiva and Gilead’s Truvada* (emtricitabine and tenofovir disoproxil fumarate). For more information about our arrangement with Gilead, refer to “—Alliances” below and “Item 8. Financial Statements—Note 3. Alliances.”

Rights to market efavirenz in the U.S., Canada, the United Kingdom (UK), France, Germany, Ireland, Italy and Spain are licensed from Merck & Co., Inc. (Merck) for a royalty based on a percentage of revenues. Efavirenz is marketed by another company in Japan.

We obtain our bulk requirements for efavirenz from third parties and produce finished goods in our facilities. We supply our third parties’ bulk efavirenz to Gilead, who is responsible for producing the finished Atripla* product.

Empliciti	Empliciti is a humanized monoclonal antibody which was approved by the FDA as a treatment for multiple myeloma and is part of our alliance with AbbVie. Under the terms of the alliance, we were granted exclusive global rights to co-develop and commercialize Empliciti. In November 2015, the FDA approved Empliciti for the treatment of multiple myeloma as combination therapy with Revlimid* and dexamethasone in patients who have received one to three prior therapies. Revlimid* is a product of Celgene Corporation. In January 2016, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending that Empliciti be granted approval for the treatment of multiple myeloma. We manufacture the bulk requirement for elotuzumab and finish the product in our facilities.
Erbitux*	Erbitux*, a biological product, is an IgG1 monoclonal antibody designed to exclusively target and block the Epidermal Growth Factor Receptor (EGFR), which is expressed on the surface of certain cancer cells in multiple tumor types as well as some normal cells. Erbitux* is approved in combination with irinotecan for the treatment of patients with EGFR-expressing metastatic colorectal cancer (mCRC) who have failed an irinotecan-based regimen and as monotherapy for patients who are intolerant of irinotecan. The FDA approved Erbitux* for use in combination with radiation therapy, for the treatment of locally or regionally advanced squamous cell carcinoma of the head and neck and, as a single agent, for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck for whom prior platinum-based therapy has failed. The FDA also approved Erbitux* for first-line recurrent locoregional or metastatic head and neck cancer in combination with platinum-based chemotherapy with 5-Fluorouracil.

Exclusive distribution rights in North America for cetuximab were granted to the Company by ImClone Systems Incorporated (ImClone), the predecessor company of ImClone LLC, a wholly-owned subsidiary of Eli Lilly and Company (Lilly) and is part of our alliance with Lilly. In October 2015, we transferred our Erbitux* rights in North America to Lilly, including full commercialization and manufacturing responsibilities in return for sales-based royalties. For more information about our arrangement with Lilly, refer to "—Alliances" below and “Item 8. Financial Statements—Note 3. Alliances.”

Opdivo	Opdivo, a biological product, is a fully human monoclonal antibody that binds to the programmed death receptor-1 (PD-1) on T and natural killer T (NKT) cells. In 2015, the FDA approved Opdivo for previously untreated patients with metastatic melanoma, previously treated patients with advanced renal cell carcinoma,

and previously treated non-squamous (NSQ) and squamous (SQ) non-small cell lung cancer (NSCLC). In 2015, Opdivo received approval in the EU for previously treated SQ NSCLC and first-line and previously treated unresectable or metastatic melanoma. The Opdivo+Yervoy (ipilimumab) regimen was also approved by the FDA in 2015 for the treatment of BRAF V600 wild-type unresectable or metastatic melanoma. There are several ongoing potentially registrational trials for Opdivo in head and neck cancer, hodgkin and non-hodgkin lymphoma and bladder cancer, among other tumor types. Refer to "—Alliances" below and “Item 8. Financial Statements—Note 3. Alliances” for further discussion of our arrangement with Ono for Opdivo in Japan, South Korea and Taiwan.

We obtain our bulk requirements for Opdivo from a third party and finish the product in our facilities.

Sprycel

Sprycel is a multi-targeted tyrosine kinase inhibitor approved for the first-line treatment of adults with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase and the treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase chronic myeloid leukemia with resistance or intolerance to prior therapy, including Gleevec* (imatinib mesylate). Gleevec* is a trademark of Novartis.

Sprycel was internally discovered and is part of our alliance with Otsuka Pharmaceutical Co., Ltd. (Otsuka). For more information about our alliance with Otsuka, refer to "—Alliances" below and "Item 8. Financial Statements—Note 3. Alliances."

We manufacture our bulk requirements for dasatinib and finish the product in our facilities.

Yervoy

Yervoy, a biological product, is a monoclonal antibody for the treatment of patients with unresectable or metastatic melanoma. Yervoy was approved in the U.S. and the EU in 2011 and in Japan in 2015. In 2015, the FDA approved Yervoy for the adjuvant treatment of patients with cutaneous melanoma. For more information, about research and development of Yervoy, refer to "—Research and Development" below.

Yervoy was discovered by Medarex and co-developed by the Company and Medarex, which is now our subsidiary. Bulk ipilimumab is manufactured by both the Company and a third party. The product is finished both in our facilities and at a third-party facility.

Abilify*

Abilify* is an atypical antipsychotic agent for adult patients with schizophrenia, bipolar mania disorder and major depressive disorder. Abilify* also has pediatric uses in schizophrenia and bipolar disorder, among others.

BMS's rights to Abilify* expired in the U.S. in April 2015 and in all EU countries in June 2014. For more information about our arrangement with Otsuka, refer to "—Alliances" below and "Item 8. Financial Statements—Note 3. Alliances."

Orencia

Orencia, a biological product, is a fusion protein with novel immunosuppressive activity targeted initially at adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to certain currently available treatments. Orencia is available in both an intravenous and subcutaneous formulation in the U.S., Europe and Japan. Refer to "—Alliances" below and "Item 8. Financial Statements—Note 3. Alliances" for further discussion of our collaborations with Ono for Orencia in Japan.

Bulk abatacept is manufactured by both the Company and a third party. We finish both formulations of the product in our own facilities.

Eliquis

Eliquis is an oral Factor Xa inhibitor targeted at stroke prevention in atrial fibrillation and the prevention and treatment of venous thromboembolic (VTE) disorders. Apixaban was discovered internally and is part of our alliance with Pfizer, Inc. (Pfizer). For more information about our alliance with Pfizer, refer to "Item 8. Financial Statements—Note 3. Alliances."

Apixaban is manufactured by both the Company and a third party. The product is then finished in our facilities.

Research and Development

We invest heavily in research and development (R&D) because we believe it is critical to our long-term competitiveness. We have major R&D facilities in New Jersey, and are expanding our existing California-based research facility and have announced future plans for the opening of a new R&D site in Massachusetts. Research activities at our Connecticut facility will be phased out in the next few years. Research and development is also carried out at various other facilities throughout the world, including in Belgium, the UK, India, Japan and other sites in the U.S. We supplement our internal drug discovery and development programs with alliances and collaborative agreements which help us bring new products into the pipeline. In drug development, we engage the services of physicians, hospitals, medical schools and other research organizations worldwide to conduct clinical trials to establish the safety and effectiveness of new products. Management continues to emphasize leadership, innovation, productivity and quality as strategies for success in our research and development activities.

We concentrate our research and development efforts in the following disease areas with significant unmet medical needs: immuno-oncology, oncology, immunoscience, cardiovascular, fibrotic diseases and genetically defined diseases. We also continue to analyze and may selectively pursue promising leads in other areas. In addition to

discovering and developing new molecular entities, we look for ways to expand the value of existing products through new indications and formulations that can provide additional benefits to patients.

In order for a new drug to reach the market, industry practice and government regulations in the U.S., the EU and most foreign countries provide for the determination of a drug's effectiveness and safety through preclinical tests and controlled clinical evaluation. The clinical development of a potential new drug includes Phase I, Phase II and Phase III clinical trials that have been designed specifically to support a new drug application for a particular indication, assuming the trials are successful.

Phase I clinical trials involve a small number of healthy volunteers or patients suffering from the indicated disease to test for safety and proper dosing. Phase II clinical trials involve a larger patient population to investigate side effects, efficacy, and optimal dosage of the drug candidate. Phase III clinical trials are conducted to confirm Phase II results in a significantly larger patient population over a longer term and to provide reliable and conclusive data regarding the safety and efficacy of a drug candidate.

The R&D process typically takes about fourteen years, with approximately three years often spent in Phase III, or late-stage, development. We consider our R&D programs in Phase III to be our significant R&D programs. These programs include both investigational compounds in Phase III development for initial indications and marketed products that are in Phase III development for additional indications or formulations.

Drug development is time consuming, expensive and risky. On average, only about one in 10,000 chemical compounds discovered by pharmaceutical industry researchers proves to be both medically effective and safe enough to become an approved medicine. Drug candidates can fail at any stage of the process, and even late-stage product candidates sometimes fail to receive regulatory approval. According to the KMR Group, based on industry success rates from 2010-2014, approximately 92% of the compounds that enter Phase I development fail to achieve regulatory approval. The failure rate for compounds that enter Phase II development is approximately 83% and for compounds that enter Phase III development, it is approximately 39%.

Total research and development expenses include the costs of discovery research, preclinical development, early- and late-stage clinical development and drug formulation, as well as post-commercialization and medical support of marketed products, proportionate allocations of enterprise-wide costs, and other appropriate costs. Research and development spending was $5.9 billion in 2015, $4.5 billion in 2014 and $3.7 billion in 2013 and includes payments under third-party collaborations and contracts. At the end of 2015, we employed approximately 8,500 people in R&D activities, including a substantial number of physicians, scientists holding graduate or postgraduate degrees and higher-skilled technical personnel.

We manage our R&D programs on a portfolio basis, investing resources in each stage of research and development from early discovery through late-stage development. We continually evaluate our portfolio of R&D assets to ensure that there is an appropriate balance of early-stage and late-stage programs to support the future growth of the Company. Spending on our late-stage development programs represented approximately 30-45% of our annual R&D expenses in the last three years. No individual investigational compound or marketed product represented 10% or more of our R&D expenses in any of the last three years, except for Opdivo in 2015.

Listed below are the investigational compounds that we have in Phase I, II and III clinical trials. Whether or not any of these or our other investigational compounds ultimately becomes one of our marketed products depends on the results of clinical studies, the competitive landscape of the potential product's market and the manufacturing processes necessary to produce the potential product on a commercial scale, among other factors. There can be no assurance that we will seek regulatory approval of any of these compounds or that, if such approval is sought, it will be obtained. There is also no assurance that a compound that is approved will be commercially successful. At this stage of development, we cannot determine all intellectual property issues or all the patent protection that may, or may not, be available for these investigational compounds. The data is as of January 1, 2016.

Immuno-Oncology	Oncology	Immunoscience	Cardiovascular	Fibrotic Diseases	Genetically Defined Diseases	Virology
Phase I	Phase I	Phase I	Phase I	Phase I	Phase I	
Anti-CSF 1R[a]	Anti-Fucosyl GM1	Anti-CD40	Factor XIa Inhibitors	Galectin-3 Inhibitor[f]	Anti-eTau[j]	
Anti-GITR	Anti-HER2[d]	Anti-CD40L	PAR4 Antagonist	PEG-FGF21	Anti-Myostatin	
Anti-LAG3	BET Inhibitor	BTK Inhibitor				
Lirilumab (Anti-KIR)[b]	Mesothelin-ADC	TYK2 Inhibitor				
Urelumab (Anti-CD137)	Ulocuplumab (Anti-CXCR4)	Anti-PD-L1				
		Phase II	Phase II	Phase II		Phase II
		Lulizumab (Anti-CD28)	IKur Inhibitor	BMS-986020 (LPA1 Antagonist)[g]		BMS-955176 (HIV Maturation Inhibitor)[k]
			Nitroxyl Donor[e]	PEG-FGF21[h]		
				Pentraxin-2[i]		
Phase III						Phase III
Prostvac*[c]						Beclabuvir
						BMS-663068 (HIV Attachment Inhibitor)[k]

(a) Exclusively licensed from Five Prime Therapeutics, Inc.
(b) Exclusively licensed from Innate Pharma S.A.
(c) Obtained through an exclusive option to license from Bavarian Nordic A/S.
(d) Obtained through an exclusive license to acquire F-Star Alpha Ltd.
(e) Obtained through acquisition of Cardioxyl Pharmaceuticals, Inc.
(f) Obtained through an exclusive option to acquire Galecto Biotech AB.
(g) Obtained through the acquisition of Amira Pharmaceuticals, Inc.
Refer to "Item 8. Financial Statements—Note 14. Goodwill and Other Intangible Assets" for additional information.
(h) Exclusively licensed from Ambrx, Inc.
(i) Obtained through an exclusive warrant to acquire Promedior, Inc.
(j) Obtained through acquisition of iPierian, Inc.

(k) Pending sale to ViiV Healthcare.

Additional information on our late-stage investigational compounds that we have in Phase III clinical trials or under regulatory review for at least one potential indication is below. The patent coverage highlighted below includes patent terms and patent term extensions that have been granted.

Beclabuvir	Beclabuvir is an oral small molecule non-nucleoside NS5B inhibitor in regulatory review in Japan for use in combination with DCV and ASV for the treatment of HCV. We own a patent covering Beclabuvir as a composition of matter that expires in 2027 in the U.S.
BMS-663068	BMS-663068 is an investigational compound being studied in HIV-1 which has shown antiviral activity in HIV-1 infected individuals. Attachment inhibitors have a distinct mode of action from other entry inhibitors, which prevent entry of HIV-1 into the host cell following attachment. BMS-663068 is a prodrug which is metabolized to the active basic compound. We hold a patent covering BMS-663068 as a composition of matter that expires in November 2027 in the U.S. BMS-663068 is expected to be sold to ViiV Healthcare in the first half of 2016.
Prostvac*	Prostvac* is Bavarian Nordic's investigational Phase III prostate-specific antigen (PSA)-targeting cancer immunotherapy in development for the treatment of asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. BMS has an exclusive option to license and commercialize Prostvac*.

The following table lists potential additional indications and/or formulations of key marketed products that are in potentially registrational trials or currently under regulatory review:

Key marketed product	Potential indication and/or formulation
Hepatitis C Franchise	Combination with other antivirals for the treatment of HCV
Empliciti	Additional indication in first-line multiple myeloma
Opdivo	Additional indications in melanoma, renal cell carcinoma (RCC), lung cancer, hodgkin and non-hodgkin lymphoma, head and neck cancer, bladder cancer, glioblastoma, hepatocellular carcinoma, gastric cancer, esophageal cancer in monotherapy and/or in combination with Yervoy
Orencia	Additional indications in lupus nephritis, psoriatic arthritis, early RA and auto-injector device
Eliquis	Pediatric VTE treatment

The following key developments are currently expected to occur during 2016 with respect to our significant pipeline programs. The outcome and timing of these expected developments are dependent upon a number of factors including, among other things, the availability of data, the outcome of certain clinical trials, acceptance of presentations at certain medical meetings and/or actions by health authorities. We do not undertake any obligation to publicly update this information, whether as a result of new information, future events, or otherwise.

Hepatitis C Franchise	Data available from clinical trials Potential approvals for additional indications
Empliciti	Potential approval in multiple myeloma in the EU and Japan Data available from Phase III study in first-line multiple myeloma
Opdivo	Potential approval in the EU for NSQ NSCLC, Opdivo+Yervoy combination in melanoma and RCC Data available from potentially registrational clinical trials in hodgkin and non-hodgkin lymphoma, head and neck cancer, bladder cancer, glioblastoma and lung cancer Potential submissions in various tumors based on registrational trials.

Alliances

We enter into alliances with third parties that transfer rights to develop, manufacture, market and/or sell pharmaceutical products that are owned by other parties. These alliances include licensing arrangements, co-development and co-marketing agreements, co-promotion arrangements and joint ventures. When such alliances involve sharing research and development costs, the risk of incurring all research and development expenses for compounds that do not lead to revenue-generating products is reduced. However, profitability on alliance products is generally lower because profits from alliance products are shared with our alliance partners. We actively pursue such arrangements and view alliances as an important complement to our own discovery, development and commercialization activities.

Each of our alliances with third parties who own the rights to manufacture, market and/or sell pharmaceutical products contain customary early termination provisions typically found in agreements of this kind and are generally based on the material breach of the agreement by a party, or bankruptcy (voluntary or involuntary) of a party or product safety

concerns. The amount of notice required for early termination generally ranges from immediately upon notice to 180 days after receipt of notice. Termination immediately upon notice is generally available where the other party files a voluntary bankruptcy petition or if a material safety issue arises with a product such that the medical risk/benefit is incompatible with the welfare of patients to continue to develop or commercialize the product. Termination with a notice period is generally available where an involuntary bankruptcy petition has been filed (and has not been dismissed) or a material breach by a party has occurred (and not been cured). Most of our alliance agreements also permit us to terminate without cause, which is typically exercisable with substantial advance written notice and is sometimes exercisable only after a specified period of time has elapsed after the alliance agreement is signed. Our alliances typically do not otherwise contain provisions that provide the other party the right to terminate the alliance.

In general, we do not retain any rights to a product brought to an alliance by another party or to the other party's intellectual property after an alliance terminates. The loss of rights to one or more products that are marketed and sold by us pursuant to an alliance could be material to our results of operations and cash flows could be material to our financial condition and liquidity. As is customary in the pharmaceutical industry, the terms of our alliances generally are co-extensive with the exclusivity period and may vary on a country-by-country basis.

Our most significant current alliances for both currently marketed products and investigational compounds are described below. Refer to "Item 8. Financial Statements—Note 3. Alliances" for additional information on our alliance agreements.

Otsuka

We maintain a worldwide commercialization agreement with Otsuka to co-develop and co-promote Abilify*, excluding certain Asian countries. The U.S. portion of the agreement expired in April 2015. The agreement expired in all EU countries in June 2014 and in each other non-U.S. country where we have the exclusive right to sell Abilify*, the agreement expires on the later of April 20, 2015 or loss of exclusivity in any such country. BMS received a share of U.S. net sales of Abilify* based on a tiered structure.

BMS and Otsuka also have an alliance for Sprycel in the U.S., Japan and the EU (the Oncology Territory). In February 2015, the co-promotion agreement with Otsuka was terminated in Japan. Ixempra* (ixabepilone) was included in the above alliance prior to BMS's divestiture of that business in 2015. A fee is paid to Otsuka based on the combined annual net sales of Sprycel and Ixempra* in the Oncology Territory (including post divestiture Ixempra* sales).

Gilead

We have joint ventures with Gilead to develop and commercialize Atripla* in the U.S., Canada and in Europe. The Company and Gilead share responsibility for certain activities related to the commercialization of Atripla* in the U.S., Canada, throughout the EU and certain other European countries. Gilead recognizes 100% of Atripla* revenues in the U.S., Canada and most countries in Europe. Alliance and other revenues recognized for Atripla* include only the bulk efavirenz component of Atripla* which is calculated differently in the EU and the U.S. following the loss of exclusivity of Sustiva in the EU in 2013. The alliance and other revenues are deferred and the related alliance receivable is not recognized until Atripla* is sold to third-party customers.

The collaboration agreement governing the commercialization of Atripla* in the U.S. and Canada will continue until terminated by mutual agreement of the parties or otherwise as described below. In the event of a material breach by one party of the collaboration agreement, the non-breaching party may terminate the agreement only if the breaching party does not cure the material breach and both parties agree that it is both desirable and practicable to withdraw the combination product from the markets where it is commercialized. At such time as one or more generic versions of a party’s component product(s) are launched in the U.S., the other party will have the right to terminate the collaboration agreement and be in control of the joint venture and the commercialization of the combination product, both in the U.S. and Canada; however, for three years the terminated party will continue to receive a percentage of the net product sales-based on the contribution of bulk components to Atripla*, and otherwise retains all rights to its own products.

In Europe, following the 2013 loss of exclusivity of Sustiva and effective January 1, 2014, the percentage of Atripla* net sales in Europe recognized by BMS is equal to the difference between the average net selling prices of Atripla* and Truvada*. This alliance will continue in Europe until either party terminates the arrangement or the last patent expiration occurs for Atripla*, Truvada*, or Sustiva.

In 2011, we entered into a licensing agreement with Gilead to develop and commercialize a fixed-dose combination containing Reyataz and Gilead’s cobicistat, a pharmacoenhancing or “boosting” agent that increases blood levels of certain HIV medicines to potentially allow for one pill once daily dosing. Evotaz was approved by the FDA in January 2015 and the European Commission (EC) in July 2015.

Lilly

BMS had a commercialization agreement with Lilly through Lilly’s subsidiary ImClone for the co-development and promotion of Erbitux* in the U.S., Canada and Japan. In October 2015, BMS transferred its rights to Erbitux* in North America to Lilly in exchange for sales-based royalties. The transferred rights include, but are not limited to, full

commercialization and manufacturing responsibilities.

BMS shared rights to Erbitux* in Japan under an agreement with Lilly and Merck KGaA and received 50% of the pretax profit from Merck KGaA's net sales of Erbitux* in Japan which was further shared equally with Lilly. BMS transferred its co-commercialization rights in Japan to Merck KGaA in 2015 in exchange for sales-based royalties through 2032.

AbbVie

BMS and AbbVie have an alliance for Empliciti. Under the terms of the alliance, BMS was granted exclusive global rights to co-develop and commercialize Empliciti from PDL BioPharma, Inc. (now part of AbbVie). Both parties are co-developing the product and AbbVie funds 20% of global development costs. BMS is solely responsible for supply, distribution and sales and marketing activities within the alliance and is the principal in the end customer product sales. AbbVie shares 30% of all profits and losses in the U.S. and will be paid tiered royalties on net sales of Empliciti outside of the U.S. In addition, AbbVie is entitled to receive milestone payments from BMS if certain regulatory events and sales thresholds are achieved.

AstraZeneca

In February 2014, we sold to AstraZeneca PLC (AstraZeneca) our diabetes business that was comprised of the global alliance with them, including all rights and ownership to Onglyza*, Farxiga*, Bydureon*, Byetta*, Symlin* and Myalept*. We and AstraZeneca terminated our existing alliance agreements in connection with the sale and entered into several new agreements, including a transitional services agreement, a supply agreement and a development agreement. Under the supply agreement, we continue to have some manufacturing responsibilities for Onglyza*, Kombiglyze* and Farxiga*.

Pfizer

The Company and Pfizer are parties to a worldwide co-development and co-commercialization agreement for Eliquis. Pfizer funds between 50% and 60% of all development costs depending on the study. The companies share commercialization expenses and profits and losses equally on a global basis except for in certain countries where Pfizer commercializes Eliquis and pays BMS compensation based on a percentage of net sales.

Ono

BMS is the principal in the end customer product sales and has the exclusive right to develop, manufacture and commercialize Opdivo in all territories worldwide except Japan, South Korea and Taiwan (where Ono was responsible for all development and commercialization prior to the arrangement described below). Ono is entitled to receive royalties following regulatory approvals in all territories excluding the three countries listed above. Royalty rates on net sales are 4% in North America and 15% in all other applicable territories, subject to customary adjustments.

The alliance arrangement was expanded in July 2014 to establish collaboration activities in Japan, South Korea and Taiwan pertaining to Opdivo and several BMS compounds including Yervoy, lirilumab, urelumab and BMS-986016 (anti-LAG3). Both parties have the right and obligation to jointly develop and commercialize the compounds. BMS is responsible for supply of the products. Profits, losses and development costs are shared equally for all combination therapies involving compounds of both parties. Otherwise, sharing is 80% and 20% for activities involving only one of the party’s compounds.

BMS and Ono also have an alliance to co-develop and co-commercialize Orencia in Japan. BMS is responsible for the order fulfillment and distribution of the intravenous formulation and Ono is responsible for the subcutaneous formulation. Both formulations are jointly promoted by both parties with assigned customer accounts and BMS is responsible for the product supply. A co-promotion fee of 60% is paid to the other party when a sale is made to that other party’s assigned customer.

Other Alliances

In May 2013, BMS and Reckitt Benckiser Group plc (Reckitt) started a three-year alliance regarding several over-the-counter-products sold primarily in Mexico and Brazil. Reckitt received the right to sell, distribute and market the products through May 2016. BMS also granted Reckitt an option to acquire the trademarks, inventory and certain other assets exclusively related to the products at the end of the alliance period, including a BMS manufacturing facility located in Mexico, at a price determined primarily based on a multiple of net sales from May 2014 through May 2016. In July 2015, Reckitt notified BMS that it was exercising its option. Substantially all employees at the facility are expected to be transferred to Reckitt. The closing is expected to occur in May 2016.

Other Licensing Arrangements

In addition to the alliances described above, we have other in-licensing and out-licensing arrangements. With respect to in-licenses, we have agreements with Novartis for Reyataz and with Merck for efavirenz, among others. We also own certain compounds out-licensed to third parties for development and commercialization, including those obtained from our acquisitions. We are entitled to receive milestone payments as these compounds move through the regulatory process and royalties based on net product sales, if and when the products are commercialized.

Intellectual Property and Product Exclusivity

We own or license a number of patents in the U.S. and foreign countries primarily covering our products. We have also developed many brand names and trademarks for our products. We consider the overall protection of our patents, trademarks, licenses and other intellectual property rights to be of material value and act to protect these rights from infringement.

In the pharmaceutical industry, the majority of an innovative product's commercial value is usually realized during the period in which the product has market exclusivity. A product's market exclusivity is generally determined by two forms of intellectual property: patent rights held by the innovator company and any regulatory forms of exclusivity to which the innovative drug is entitled.

Patents are a key determinant of market exclusivity for most branded pharmaceuticals. Patents provide the innovator with the right to exclude others from practicing an invention related to the medicine. Patents may cover, among other things, the active ingredient(s), various uses of a drug product, pharmaceutical formulations, drug delivery mechanisms and processes for (or intermediates useful in) the manufacture of products. Protection for individual products extends for varying periods in accordance with the expiration dates of patents in the various countries. The protection afforded, which may also vary from country to country, depends upon the type of patent, its scope of coverage and the availability of meaningful legal remedies in the country.

Market exclusivity is also sometimes influenced by regulatory intellectual property rights. Many developed countries provide certain non-patent incentives for the development of medicines. For example, in the U.S., the EU, Japan, and certain other countries, regulatory intellectual property rights are offered as incentives for research on medicines for rare diseases, or orphan drugs, and on medicines useful in treating pediatric patients. These incentives can extend the market exclusivity period on a product beyond the patent term.

The U.S., EU, Japan and China also each provide for a minimum period of time after the approval of a new drug during which the regulatory agency may not rely upon the innovator's data to approve a competitor's generic copy, or data protection. In some regions such as China, however, it is questionable whether such data protection laws are enforceable. In certain markets where patent protection and other forms of market exclusivity may have expired, data protection can be of particular importance. However, most regulatory forms of exclusivity do not prevent a competitor from gaining regulatory approval prior to the expiration of regulatory data exclusivity on the basis of the competitor's own safety and efficacy data on its drug, even when that drug is identical to that marketed by the innovator.

Specific aspects of the law governing market exclusivity and data protection for pharmaceuticals vary from country to country. The following summarizes key exclusivity rules in markets representing significant sales:

United States

In the U.S., most of our key products are protected by patents with varying terms depending on the type of patent and the filing date. A significant portion of a product's patent life, however, is lost during the time it takes an innovative company to develop and obtain regulatory approval of a new drug. As compensation at least in part for the lost patent term, the innovator may, depending on a number of factors, extend the expiration date of one patent up to a maximum term of five years, provided that the extension cannot cause the patent to be in effect for more than 14 years from the date of drug approval.

A company seeking to market an innovative pharmaceutical in the U.S. must submit a complete set of safety and efficacy data to the FDA. If the innovative pharmaceutical is a chemical, the company files a New Drug Application (NDA). If the medicine is a biological product, a BLA is filed. The type of application filed affects regulatory

exclusivity rights.

Chemical products

A competitor seeking to launch a generic substitute of a chemical innovative drug in the U.S. must file an abbreviated New Drug Application (aNDA) with the FDA. In the aNDA, the generic manufacturer needs to demonstrate only "bioequivalence" between the generic substitute and the approved NDA drug. The aNDA relies upon the safety and efficacy data previously filed by the innovator in its NDA.

An innovator company is required to list certain of its patents covering the medicine with the FDA in what is commonly known as the Orange Book. Absent a successful patent challenge, the FDA cannot approve an aNDA until after the innovator's listed patents expire. However, after the innovator has marketed its product for four years, a generic manufacturer may file an aNDA and allege that one or more of the patents listed in the Orange Book under an innovator's NDA is either invalid or not infringed. This allegation is commonly known as a Paragraph IV certification. The innovator then must decide whether to file a patent infringement suit against the generic manufacturer. From time to time, aNDAs, including Paragraph IV certifications, are filed with respect to certain of our products. We evaluate these aNDAs on a case-by-case basis and, where warranted, file suit against the generic manufacturer to protect our patent rights.

In addition to benefiting from patent protection, certain innovative pharmaceutical products can receive periods of regulatory exclusivity. An NDA that is designated as an orphan drug can receive seven years of exclusivity for the orphan indication. During this time period, neither NDAs nor aNDAs for the same drug product can be approved for the same orphan use. A company may also earn six months of additional exclusivity for a drug where specific clinical trials are conducted at the written request of the FDA to study the use of the medicine to treat pediatric patients, and submission to the FDA is made prior to the loss of basic exclusivity.

Medicines approved under an NDA can also receive several types of regulatory data protection. An innovative chemical pharmaceutical is entitled to five years of regulatory data protection in the U.S., during which competitors cannot file with the FDA for approval of generic substitutes. If an innovator's patent is challenged, as described above, a generic manufacturer may file its aNDA after the fourth year of the five-year data protection period. A pharmaceutical drug product that contains an active ingredient that has been previously approved in an NDA, but is approved in a new formulation, but not for the drug itself, or for a new indication on the basis of new clinical trials, receives three years of data protection for that formulation or indication.

Biologic products

The U.S. healthcare legislation enacted in 2010 created an approval pathway for biosimilar versions of innovative biological products that did not previously exist. Prior to that time, innovative biologics had essentially unlimited regulatory exclusivity. Under the new regulatory mechanism, the FDA can approve products that are similar to (but not generic copies of) innovative biologics on the basis of less extensive data than is required by a full BLA. After an innovator has marketed its product for four years, any manufacturer may file an application for approval of a "biosimilar" version of the innovator product. However, although an application for approval of a biosimilar may be filed four years after approval of the innovator product, qualified innovative biological products will receive 12 years of regulatory exclusivity, meaning that the FDA may not approve a biosimilar version until 12 years after the innovative biological product was first approved by the FDA. The law also provides a mechanism for innovators to enforce the patents that protect innovative biological products and for biosimilar applicants to challenge the patents. Such patent litigation may begin as early as four years after the innovative biological product is first approved by the FDA.

In the U.S., the increased likelihood of generic and biosimilar challenges to innovators' intellectual property has increased the risk of loss of innovators' market exclusivity. First, generic companies have increasingly sought to challenge innovators' basic patents covering major pharmaceutical products. Second, statutory and regulatory provisions in the U.S. limit the ability of an innovator company to prevent generic and biosimilar drugs from being approved and launched while patent litigation is ongoing. As a result of all of these developments, it is not possible to predict the length of market exclusivity for a particular product with certainty based solely on the expiration of the relevant patent(s) or the current forms of regulatory exclusivity.

European Union

Patents on pharmaceutical products are generally enforceable in the EU and, as in the U.S., may be extended to compensate for the patent term lost during the regulatory review process. Such extensions are granted on a country-by-country basis.

The primary route we use to obtain marketing authorization of pharmaceutical products in the EU is through the "centralized procedure." This procedure is compulsory for certain pharmaceutical products, in particular those using biotechnological processes, and is also available for certain new chemical compounds and products. A company seeking to market an innovative pharmaceutical product through the centralized procedure must file a complete set of safety data and efficacy data as part of a MAA with the EMA. After the EMA evaluates the MAA, it provides a

recommendation to the EC and the EC then approves or denies the MAA. It is also possible for new chemical products to obtain marketing authorization in the EU through a "mutual recognition procedure," in which an application is made to a single member state, and if the member state approves the pharmaceutical product under a national procedure, then the applicant may submit that approval to the mutual recognition procedure of some or all other member states.

After obtaining marketing authorization approval, a company must obtain pricing and reimbursement for the pharmaceutical product, which is typically subject to member state law. In certain EU countries, this process can take place simultaneously while the product is marketed but in other EU countries, this process must be completed before the company can market the new product. The pricing and reimbursement procedure can take months and sometimes years to complete.

Throughout the EU, all products for which marketing authorizations have been filed after October/November 2005 are subject to an "8+2+1" regime. Eight years after the innovator has received its first community authorization for a medicinal product, a generic company may file a marketing authorization application for that product with the health authorities. If the marketing authorization application is approved, the generic company may not commercialize the product until after either 10 or 11 years have elapsed from the initial marketing authorization granted to the innovator. The possible extension to 11 years is available if the innovator, during the first eight years of the marketing authorization, obtains an additional indication that is of significant clinical benefit in comparison with existing treatments. For products that were filed prior to October/November 2005, there is a 10-year period of data protection under the centralized procedures and a period of either six or 10 years under the mutual recognition procedure (depending on the member state).

In contrast to the U.S., patents in the EU are not listed with regulatory authorities. Generic versions of pharmaceutical products can be approved after data protection expires, regardless of whether the innovator holds patents covering its drug. Thus, it is possible that an innovator may be seeking to enforce its patents against a generic competitor that is already marketing its product. Also, the European patent system has an opposition procedure in which generic manufacturers may challenge the validity of patents covering innovator products within nine months of grant.

In general, EU law treats chemically-synthesized drugs and biologically-derived drugs the same with respect to intellectual property and data protection. In addition to the relevant legislation and annexes related to biologic medicinal products, the EMA has issued guidelines that outline the additional information to be provided for biosimilar products, also known as generic biologics, in order to review an application for marketing approval.

Japan

In Japan, medicines of new chemical entities are generally afforded eight years of data exclusivity for approved indications and dosage. Patents on pharmaceutical products are enforceable. Generic copies can receive regulatory approval after data exclusivity and patent expirations. As in the U.S., patents in Japan may be extended to compensate for the patent term lost during the regulatory review process.

In general, Japanese law treats chemically-synthesized and biologically-derived drugs the same with respect to intellectual property and market exclusivity.

China

In China, medicines of new chemical entities are generally afforded six years of data exclusivity for approved indications and dosage. There is uncertainty about China’s exclusivity laws which has resulted in generic competition in the China market. Generic copies can receive regulatory approval after data exclusivity and patent expirations. Currently, unlike the U.S., China has no patent term restoration to compensate for the patent term lost during the regulatory process.

In general, Chinese law treats chemically-synthesized and biologically-derived drugs the same with respect to intellectual property and market exclusivity.

Rest of the World

In countries outside of the U.S., the EU, Japan and China, there is a wide variety of legal systems with respect to intellectual property and market exclusivity of pharmaceuticals. Most other developed countries utilize systems similar to either the U.S. or the EU. Among developing countries, some have adopted patent laws and/or regulatory exclusivity laws, while others have not. Some developing countries have formally adopted laws in order to comply with World Trade Organization (WTO) commitments, but have not taken steps to implement these laws in a meaningful way. Enforcement of WTO actions is a long process between governments, and there is no assurance of the outcome. Thus, in assessing the likely future market exclusivity of our innovative drugs in developing countries, we take into account not only formal legal rights but political and other factors as well.

Marketing, Distribution and Customers

We promote the appropriate use of our products directly to healthcare professionals and providers such as doctors, nurse practitioners, physician assistants, pharmacists, technologists, hospitals, Pharmacy Benefit Managers (PBMs) and Managed Care Organizations (MCOs). We also provide information about the appropriate use of our products to consumers in the U.S. through direct-to-consumer print, radio, television, and digital advertising and promotion. In

addition, we sponsor general advertising to educate the public about our innovative medical research and corporate mission. For a discussion of the regulation of promotion and marketing of pharmaceuticals, refer to "—Government Regulation and Price Constraints" below.

Through our field sales and medical organizations, we explain the risks and benefits of the approved uses of our products to medical professionals. We work to gain access for our products on formularies and reimbursement plans (lists of recommended or approved medicines and other products), including Medicare Part D plans, by providing information about the clinical profiles of our products. Our marketing and sales of prescription pharmaceuticals is limited to the approved uses of the particular product, but we continue to develop scientific data and other information about our products and provide such information in response to unsolicited inquiries from doctors, other medical professionals and managed care organizations.

Our operations include several marketing and sales organizations. Each product marketing organization is supported by a sales force, which may be responsible for selling one or more products. We also have marketing organizations that focus on certain classes of customers such as managed care entities or certain types of marketing tools, such as digital or consumer communications. Our sales forces focus on communicating information about new products or new uses, as well as established products, and promotion to physicians is increasingly targeted at physician specialists who treat the patients in need of our medicines.

Our products are sold principally to wholesalers, and to a lesser extent, directly to distributors, retailers, hospitals, clinics, government agencies and pharmacies. Gross revenues to the three largest pharmaceutical wholesalers in the U.S. as a percentage of our global gross revenues were as follows:

	2015	2014	2013
McKesson Corporation	21%	20%	19%
AmerisourceBergen Corporation	16%	17%	15%
Cardinal Health, Inc.	12%	12%	14%

Our U.S. business has Inventory Management Agreements (IMAs) with substantially all of our direct wholesaler and distributor customers that allow us to monitor U.S. wholesaler inventory levels and requires those wholesalers and distributors to maintain inventory levels that are no more than one month of their demand. The IMAs, including those with our three largest wholesalers, expire in December 2017 subject to certain termination provisions.

In a number of defined countries outside of the U.S., we have established a full scale distributor model to make medically necessary drugs available to patients. We continue to own the marketing authorization and trademarks for these products, but have contracted the services of a full-service distributor to provide distribution and logistics; regulatory and pharmacovigilance; and sales, advertising and promotion for certain products. Sales in these distributor-based countries represented approximately 2% of the Company’s total revenues in 2015.

Competition

The markets in which we compete are generally broad based and highly competitive. We compete with other worldwide research-based drug companies, many smaller research companies with more limited therapeutic focus and generic drug manufacturers. Important competitive factors include product efficacy, safety and ease of use, price and demonstrated cost-effectiveness, marketing effectiveness, product labeling, customer service and research and development of new products and processes. Sales of our products can be impacted by new studies that indicate a competitor’s product is safer or more effective for treating a disease or particular form of disease than one of our products. Our revenues also can be impacted by additional labeling requirements relating to safety or convenience that may be imposed on products by the FDA or by similar regulatory agencies in different countries. If competitors introduce new products and processes with therapeutic or cost advantages, our products can be subject to progressive price reductions or decreased volume of sales, or both.

Generic Competition

One of the biggest competitive challenges that we face is from generic pharmaceutical manufacturers. In the U.S. and the EU, the regulatory approval process exempts generics from costly and time-consuming clinical trials to demonstrate their safety and efficacy, allowing generic manufacturers to rely on the safety and efficacy of the innovator product. As a result, generic pharmaceutical manufacturers typically invest far less in research and development than research-based pharmaceutical companies and therefore can price their products significantly lower than branded products. Accordingly, when a branded product loses its market exclusivity, it normally faces intense price competition from generic forms of the product. Upon the expiration or loss of market exclusivity on a product, we can lose the major portion of revenues of that product in a very short period of time.

The rate of revenues decline of a product after the expiration of exclusivity varies by country. In general, the decline in the U.S. market is more rapid than in most other developed countries, though we have observed rapid declines in a number of EU countries as well. Also, the declines in developed countries tend to be more rapid than in developing countries. The rate of revenues decline after the expiration of exclusivity has also historically been influenced by product characteristics. For example, drugs that are used in a large patient population (e.g., those prescribed by key primary care physicians) tend to experience more rapid declines than drugs in specialized areas of medicine (e.g., oncology). Drugs that are more complex to manufacture (e.g., sterile injectable products) usually experience a slower decline than those that are simpler to manufacture.

In certain countries outside the U.S., patent protection is weak or nonexistent and we must compete with generic versions shortly after we launch our innovative products. In addition, generic pharmaceutical companies may introduce a generic product before exclusivity has expired, and before the resolution of any related patent litigation. For more information about market exclusivity, refer to "—Intellectual Property and Product Exclusivity" above.

We believe our long-term competitive position depends upon our success in discovering and developing innovative, cost-effective products that serve unmet medical needs, together with our ability to manufacture products efficiently and to market them effectively in a highly competitive environment.

Managed Care Organizations

The growth of MCOs in the U.S. is also a major factor in the healthcare marketplace. Over half of the U.S. population now participates in some version of managed care. MCOs can include medical insurance companies, medical plan administrators, health-maintenance organizations, Medicare Part D prescription drug plans, alliances of hospitals and physicians and other physician organizations. Those organizations have been consolidating into fewer, larger entities, thus enhancing their purchasing strength and importance to us.

To successfully compete for business with MCOs, we must often demonstrate that our products offer not only medical benefits but also cost advantages as compared with other forms of care. Most new products that we introduce compete with other products already on the market or products that are later developed by competitors. As noted above, generic drugs are exempt from costly and time-consuming clinical trials to demonstrate their safety and efficacy and, as such, often have lower costs than brand-name drugs. MCOs that focus primarily on the immediate cost of drugs often favor generics for this reason. Many governments also encourage the use of generics as alternatives to brand-name drugs in their healthcare programs. Laws in the U.S. generally allow, and in many cases require, pharmacists to substitute generic drugs that have been rated under government procedures to be essentially equivalent to a brand-name drug. The substitution must be made unless the prescribing physician expressly forbids it.

Exclusion of a product from a formulary can lead to its sharply reduced usage in the MCO patient population. Consequently, pharmaceutical companies compete aggressively to have their products included. Where possible, companies compete for inclusion based upon unique features of their products, such as greater efficacy, better patient ease of use or fewer side effects. A lower overall cost of therapy is also an important factor. Products that demonstrate fewer therapeutic advantages must compete for inclusion based primarily on price. We have been generally, although not universally, successful in having our major products included on MCO formularies.

Government Regulation and Price Constraints

The pharmaceutical industry is subject to extensive global regulation by regional, country, state and local agencies. The Federal Food, Drug, and Cosmetic Act (FDC Act), other Federal statutes and regulations, various state statutes and regulations, and laws and regulations of foreign governments govern to varying degrees the testing, approval, production, labeling, distribution, post-market surveillance, advertising, dissemination of information, and promotion of our products. The lengthy process of laboratory and clinical testing, data analysis, manufacturing, development, and regulatory review necessary for required governmental approvals is extremely costly and can significantly delay product introductions in a given market. Promotion, marketing, manufacturing and distribution of pharmaceutical products are extensively regulated in all major world markets. In addition, our operations are subject to complex Federal, state, local, and foreign environmental and occupational safety laws and regulations. We anticipate that the laws and regulations affecting the manufacture and sale of current products and the introduction of new products will continue to require substantial scientific and technical effort, time and expense as well as significant capital investments.

Of particular importance is the FDA in the U.S. It has jurisdiction over virtually all of our activities and imposes requirements covering the testing, safety, effectiveness, manufacturing, labeling, marketing, advertising and post-marketing surveillance of our products. In many cases, the FDA requirements have increased the amount of time and money necessary to develop new products and bring them to market in the U.S.

The FDA mandates that drugs be manufactured, packaged and labeled in conformity with current Good Manufacturing Practices (cGMP) established by the FDA. In complying with cGMP regulations, manufacturers must continue to expend time, money and effort in production, recordkeeping and quality control to ensure that products meet applicable specifications and other requirements to ensure product safety and efficacy. The FDA periodically inspects our drug manufacturing facilities to ensure compliance with applicable cGMP requirements. Failure to comply with the statutory and regulatory requirements subjects us to possible legal or regulatory action, such as suspension of manufacturing, seizure of product or voluntary recall of a product. Adverse experiences with the use of products must be reported to the FDA and could result in the imposition of market restrictions through labeling changes or product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy occur following approval.

The Federal government has extensive enforcement powers over the activities of pharmaceutical manufacturers, including authority to withdraw or delay product approvals, commence actions to seize and prohibit the sale of unapproved or non-complying products, to halt manufacturing operations that are not in compliance with cGMPs, and to impose or seek injunctions, voluntary recalls, civil, monetary and criminal penalties. Such a restriction or prohibition on sales or withdrawal of approval of products marketed by us could materially adversely affect our business, financial condition and results of operations and cash flows.

Marketing authorization for our products is subject to revocation by the applicable governmental agencies. In addition, modifications or enhancements of approved products or changes in manufacturing locations are in many circumstances subject to additional FDA approvals, which may or may not be received and which may be subject to a lengthy application process.

The distribution of pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA) as part of the FDC Act, which regulates such activities at both the Federal and state level. Under the PDMA and its implementing regulations, states are permitted to require registration of manufacturers and distributors who provide pharmaceuticals even if such manufacturers or distributors have no place of business within the state. States are also permitted to adopt regulations limiting the distribution of product samples to licensed practitioners. The PDMA also imposes extensive licensing, personnel recordkeeping, packaging, quantity, labeling, product handling and facility storage and security requirements intended to prevent the sale of pharmaceutical product samples or other product diversions.

Our medicines are priced based on a number of factors, including the value of scientific innovation for patients and society in the context of overall health care spend, economic factors impacting health care systems' ability to provide appropriate and sustainable access and the necessity to sustain our investment in innovation platforms to address serious unmet medical needs. Central to price is the clinical value that this innovation brings to the market, the current landscape of alternative treatment options, the goal of ensuring appropriate patient access to this innovation and sustaining investment in innovative platforms. We continue to explore innovative pricing approaches to ensure that patients have access to our medicines. Enhancing patient access to medicines is a priority for us. We are focused on offering creative tiered pricing, voluntary licensing, reimbursement support and patient assistance programs to optimize access while protecting innovation; advocating for sustainable healthcare policies and infrastructure, leveraging advocacy/payer's input and utilizing partnerships as appropriate; and improving access to care and supportive services for vulnerable patients through partnerships and demonstration projects.

The FDA Amendments Act of 2007 imposed additional obligations on pharmaceutical companies and delegated more enforcement authority to the FDA in the area of drug safety. Key elements of this legislation give the FDA authority to (1) require that companies conduct post-marketing safety studies of drugs, (2) impose certain drug labeling changes relating to safety, (3) mandate risk mitigation measures such as the education of healthcare providers and the restricted distribution of medicines, (4) require companies to publicly disclose data from clinical trials and (5) pre-review television advertisements.

The marketing practices of all U.S. pharmaceutical manufacturers are subject to Federal and state healthcare laws that are used to protect the integrity of government healthcare programs. The Office of Inspector General of the U.S. Department of Health and Human Services (OIG) oversees compliance with applicable Federal laws, in connection with the payment for products by government funded programs (primarily Medicaid and Medicare). These laws include the Federal anti-kickback statute, which criminalizes the offering of something of value to induce the recommendation, order or purchase of products or services reimbursed under a government healthcare program. The OIG has issued a series of Guidances to segments of the healthcare industry, including the 2003 Compliance Program Guidance for Pharmaceutical Manufacturers (the OIG Guidance), which includes a recommendation that pharmaceutical manufacturers, at a minimum, adhere to the PhRMA Code, a voluntary industry code of marketing practices. We subscribe to the PhRMA Code, and have implemented a compliance program to address the requirements set forth in the OIG Guidance and our compliance with the healthcare laws. Failure to comply with these healthcare laws could subject us to administrative and legal proceedings, including actions by Federal and state government agencies. Such actions could result in the imposition of civil and criminal sanctions, which may include fines, penalties and injunctive remedies, the impact of which could materially adversely affect our business, financial condition and results of operations and cash flows.

We are also subject to the jurisdiction of various other Federal and state regulatory and enforcement departments and agencies, such as the Federal Trade Commission, the Department of Justice and the Department of Health and Human Services in the U.S. We are also licensed by the U.S. Drug Enforcement Agency to procure and produce controlled substances. We are, therefore, subject to possible administrative and legal proceedings and actions by these organizations. Such actions may result in the imposition of civil and criminal sanctions, which may include fines, penalties and injunctive or administrative remedies.

Our activities outside the U.S. are also subject to regulatory requirements governing the testing, approval, safety, effectiveness, manufacturing, labeling and marketing of our products. These regulatory requirements vary from country to country. Whether or not FDA approval or approval of the EC has been obtained for a product, approval of the product by comparable regulatory authorities of countries outside of the U.S. or the EU, as the case may be, must be obtained prior to marketing the product in those countries. The approval process may be more or less rigorous from country to country, and the time required for approval may be longer or shorter than that required in the U.S. Approval in one country does not assure that a product will be approved in another country.

In many markets outside the U.S., we operate in an environment of government-mandated, cost-containment programs. Several governments have placed restrictions on physician prescription levels and patient reimbursements, emphasized greater use of generic drugs and/or enacted across-the-board price cuts as methods of cost control. In most EU countries, for example, the government regulates pricing of a new product at launch often through direct price controls, international price comparisons, controlling profits and/or reference pricing. In other markets, such as the UK and Germany, the government does not set pricing restrictions at launch, but pricing freedom

is subsequently limited, such as by the operation of a profit and price control plan in the UK and by the operation of a reference price system in Germany. Companies also face significant delays in market access for new products, mainly in France, Spain, Italy and Belgium, and more than two years can elapse before new medicines become available on some national markets. Additionally, member states of the EU have regularly imposed new or additional cost containment measures for pharmaceuticals such as volume discounts, cost caps, cost sharing for increases in excess of prior year costs for individual products or aggregated market level spending, outcome-based pricing schemes and free products for a portion of the expected therapy period. In recent years, Italy, for example, has imposed mandatory price decreases. The existence of price differentials within the EU due to the different national pricing and reimbursement laws leads to significant parallel trade flows.

The U.S. healthcare industry is subject to various government-imposed regulations authorizing prices or price controls that have and will continue to have an impact on our total revenues. We participate in state government Medicaid programs, as well as certain other qualifying Federal and state government programs whereby discounts and rebates are provided to participating state and local government entities. We also participate in government programs that specify discounts to certain government entities, the most significant of which are the U.S. Department of Defense and the U.S. Department of Veterans Affairs. These entities receive minimum discounts based off a defined “non-federal average manufacturer price” for purchases. As a result of the Patient Protection and Affordable Care Act (HR 3590) and the reconciliation bill containing a package of changes to the healthcare bill, we have experienced and will continue to experience additional financial costs and certain other changes to our business. For example, minimum rebates on our Medicaid drug sales have increased from 15.1 percent to 23.1 percent and Medicaid rebates have also been extended to drugs used in risk-based Medicaid managed care plans. In addition, we extend discounts to certain critical access hospitals, cancer hospitals and other covered entities as required by the expansion of the 340B Drug Pricing Program under the Public Health Service Act.

We are required to provide a 50 percent discount on our brand-name drugs to patients who fall within the Medicare Part D coverage gap, also referred to as the “donut hole” and pay an annual non-tax-deductible fee to the federal government based on an allocation of our market share of branded drug sales to certain government programs including Medicare, Medicaid, Department of Veterans Affairs, Department of Defense and TRICARE.

For further discussion of these rebates and programs, refer to “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations—Total Revenues” and “—Critical Accounting Policies.”

Sources and Availability of Raw Materials

In general, we purchase our raw materials and supplies required for the production of our products in the open market. For some products, we purchase our raw materials and supplies from one source (the only source available to us) or a single source (the only approved source among many available to us), thereby requiring us to obtain such raw materials and supplies from that particular source. We attempt, if possible, to mitigate our raw material supply risks, through inventory management and alternative sourcing strategies. For further discussion of sourcing, refer to “—Manufacturing and Quality Assurance” below and discussions of particular products.

Manufacturing and Quality Assurance

We operate and manage our manufacturing network in a manner that permits us to improve efficiency while maintaining flexibility to reallocate manufacturing capacity. Pharmaceutical production processes are complex, highly regulated and vary widely from product to product. Given that shifting or adding manufacturing capacity can be a lengthy process requiring significant capital and other expenditures as well as regulatory approvals, we maintain and operate our flexible manufacturing network, consisting of internal and external resources that minimize unnecessary product transfers and inefficient uses of manufacturing capacity. For further discussion of the regulatory impact on our

manufacturing, refer to "—Government Regulation and Price Constraints" above.

Our pharmaceutical manufacturing facilities are located in the U.S., Puerto Rico, France, Italy, Ireland, Japan, Mexico and China and require significant ongoing capital investment for both maintenance and compliance with increasing regulatory requirements. In addition, as our product line changes over the next several years, we expect to continue modification of our existing manufacturing network to meet complex processing standards that may be required for newly introduced products, including biologics. Biologics manufacturing involves more complex processes than those of traditional pharmaceutical operations. The FDA approved our large scale multi-product bulk biologics manufacturing facility in Devens, Massachusetts in May 2012 and we continue to make capital investments in this facility. We are building a new large-scale biologics manufacturing facility in Cruiserath, Ireland.

We rely on third parties to manufacture or supply us with all or a portion of the active ingredients necessary for us to manufacture various products, including Baraclude, the Sustiva Franchise, Yervoy, Opdivo, Reyataz, Orencia and Eliquis. Beginning in October 2015, following the transfer of our rights to Erbitux* in North America to Lilly, Lilly assumed manufacturing responsibilities for Erbitux*. To maintain a stable supply of these products, we take a variety of actions including inventory management and maintenance of additional quantities of materials, when possible, designed to provide for a reasonable level of these ingredients to be held by the third-party supplier, us or both, so that our manufacturing operations are not interrupted. As an additional protection, in some cases, we take steps to maintain an

approved back-up source where available. For example, we will rely on the capacity of our Devens, Massachusetts facility and the capacity available at our third-party contract manufacturers to manufacture Orencia.

If we or any third-party manufacturer that we rely on for existing or future products is unable to maintain a stable supply of products, operate at sufficient capacity to meet our order requirements, comply with government regulations for manufacturing pharmaceuticals or meet the complex processing requirements for biologics, our business performance and prospects could be negatively impacted. Additionally, if we or any of our third-party suppliers were to experience extended plant shutdowns or substantial unplanned increases in demand or suspension of manufacturing for regulatory reasons, we could experience an interruption in supply of certain products or product shortages until production could be resumed or expanded.

In connection with divestitures, licensing arrangements or distribution agreements of certain of our products, or in certain other circumstances, we have entered into agreements under which we have agreed to supply such products to third parties. In addition to liabilities that could arise from our failure to supply such products under the agreements, these arrangements could require us to invest in facilities for the production of non-strategic products, result in additional regulatory filings and obligations or cause an interruption in the manufacturing of our own products.

Our success depends in great measure upon customer confidence in the quality of our products and in the integrity of the data that support their safety and effectiveness. Product quality arises from a total commitment to quality in all parts of our operations, including research and development, purchasing, facilities planning, manufacturing, and distribution. We maintain quality-assurance procedures relating to the quality and integrity of technical information and production processes.

Control of production processes involves detailed specifications for ingredients, equipment and facilities, manufacturing methods, processes, packaging materials and labeling. We perform tests at various stages of production processes and on the final product to ensure that the product meets regulatory requirements and our standards. These tests may involve chemical and physical chemical analyses, microbiological testing, or a combination of these along with other analyses. Quality control is provided by business unit/site quality assurance groups that monitor existing manufacturing procedures and systems used by us, our subsidiaries and third-party suppliers.

Environmental Regulation

Our facilities and operations are subject to extensive U.S. and foreign laws and regulations relating to environmental protection and human health and safety, including those governing discharges of pollutants into the air and water; the use, management and disposal of hazardous, radioactive and biological materials and wastes; and the cleanup of contamination. Pollution controls and permits are required for many of our operations, and these permits are subject to modification, renewal or revocation by the issuing authorities.

Our environment, health and safety group monitors our operations around the world, providing us with an overview of regulatory requirements and overseeing the implementation of our standards for compliance. We also incur operating and capital costs for such matters on an ongoing basis. We expended approximately $18 million in 2015, $18 million in 2014 and $19 million in 2013 on capital projects undertaken specifically to meet environmental requirements. In addition, we invested in projects that reduce resource use of energy and water. Although we believe that we are in substantial compliance with applicable environmental, health and safety requirements and the permits required for our operations, we nevertheless could incur additional costs, including civil or criminal fines or penalties, clean-up costs, or third-party claims for property damage or personal injury, for violations or liabilities under these laws.

Many of our current and former facilities have been in operation for many years, and over time, we and other operators of those facilities have generated, used, stored or disposed of substances or wastes that are considered

hazardous under Federal, state and/or foreign environmental laws, including the U.S. Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). As a result, the soil and groundwater at or under certain of these facilities is or may be contaminated, and we may be required to make significant expenditures to investigate, control and remediate such contamination, and in some cases to provide compensation and/or restoration for damages to natural resources. Currently, we are involved in investigation and remediation at 17 current or former facilities. We have also been identified as a "potentially responsible party" (PRP) under applicable laws for environmental conditions at approximately 21 former waste disposal or reprocessing facilities operated by third parties at which investigation and/or remediation activities are ongoing.

We may face liability under CERCLA and other Federal, state and foreign laws for the entire cost of investigation or remediation of contaminated sites, or for natural resource damages, regardless of fault or ownership at the time of the disposal or release. In addition, at certain sites we bear remediation responsibility pursuant to contractual obligations. Generally, at third-party operator sites involving multiple PRPs, liability has been or is expected to be apportioned based on the nature and amount of hazardous substances disposed of by each party at the site and the number of financially viable PRPs. For additional information about these matters, refer to "Item 8. Financial Statements—Note 22. Legal Proceedings and Contingencies."

Employees

As of December 31, 2015, we employed approximately 25,000 people.

Foreign Operations

We have significant operations outside the U.S. They are conducted both through our subsidiaries and through distributors.

For further discussion of our total revenues by geographic area refer to “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations—Total Revenues.”

International operations are subject to certain risks, which are inherent in conducting business abroad, including, but not limited to, currency fluctuations, possible nationalization or expropriation, price and exchange controls, counterfeit products, limitations on foreign participation in local enterprises and other restrictive governmental actions. Our international businesses are also subject to government-imposed constraints, including laws on pricing or reimbursement for use of products.

Depending on the direction of change relative to the U.S. dollar, foreign currency values can increase or decrease the reported dollar value of our net assets and results of operations. The change in foreign exchange rates had a net unfavorable impact on the growth rate of revenues in 2015. While we cannot predict with certainty future changes in foreign exchange rates or the effect they will have on the growth rate of revenues, we attempt to mitigate their impact through operational means and by using various financial instruments. Refer to the discussions under “Item 7A. Quantitative and Qualitative Disclosures About Market Risk” and “Item 8. Financial Statements—Note 10. Financial Instruments and Fair Value Measurements.”

Bristol-Myers Squibb Website

Our internet website address is www.bms.com. On our website, we make available, free of charge, our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the U.S. Securities and Exchange Commission (SEC).

Information relating to corporate governance at Bristol-Myers Squibb, including our Principles of Integrity, Code of Ethics for Senior Financial Officers, Code of Business Conduct and Ethics for Directors, (collectively, the “Codes”), Corporate Governance Guidelines, and information concerning our Executive Committee, Board of Directors, including Board Committees and Committee charters, and transactions in Bristol-Myers Squibb securities by directors and executive officers, is available on our website under the “Investors—Corporate Governance” caption and in print to any stockholder upon request. Any waivers to the Codes by directors or executive officers and any material amendment to the Code of Business Conduct and Ethics for Directors and Code of Ethics for Senior Financial Officers will be posted promptly on our website. Information relating to stockholder services, including our Dividend Reinvestment Plan and direct deposit of dividends, is available on our website under the “Investors—Stockholder Services” caption. In addition, information about our Sustainability programs is available on our website under the "Responsibility" caption.

We incorporate by reference certain information from parts of our proxy statement for the 2015 Annual Meeting of Stockholders. The SEC allows us to disclose important information by referring to it in that manner. Please refer to such information. Our proxy statement for the 2016 Annual Meeting of Stockholders and 2015 Annual Report will be available on our website under the “Investors—SEC Filings” caption on or about March 21, 2016.

Item 1A. RISK FACTORS.

Any of the factors described below could significantly and negatively affect our business, prospects, financial condition, operating results, or credit ratings, which could cause the trading price of our common stock to decline.

Additional risks and uncertainties not presently known to us, or risks that we currently consider immaterial, could also impair our operations or financial condition.

We face intense competition from other manufacturers, including for both innovative medicines and lower-priced generic products.

BMS is dependent on the market access, uptake and expansion for marketed brands, new product introductions, new indications, product extensions and co-promotional activities with alliance partners, to deliver future growth. Competition is keen and includes (i) lower-priced generics and increasingly aggressive generic commercialization tactics, (ii) lower prices for other companies' products, real or perceived superior efficacy (benefit) or safety (risk) profiles, or other differentiating factors, (iii) technological advances and patents attained by our competitors, (iv) clinical study results from our products or a competitor’s products that affect the value proposition for our products, (v) business combinations among our competitors and major third-party payers, and (vi) competing interests for external partnerships to develop and bring new products to markets.

We could lose market exclusivity of a product earlier than expected.

In the pharmaceutical and biotechnology industries, the majority of an innovative product’s commercial value is realized during its market exclusivity period. In the U.S. and in some other countries, when market exclusivity expires and generic versions are approved and marketed or when biosimilars are introduced (even if only for a competing product), there are usually very substantial and rapid declines in a product’s revenues.

Market exclusivity for our products is based upon patent rights and certain regulatory forms of exclusivity. The scope of our patent rights varies from country to country and may also be dependent on the availability of meaningful legal remedies in a country. The failure to obtain patent and other intellectual property rights, or limitations on the use or loss of such rights, could be material to us. In some countries, including certain EU member states, basic patent protections for our products may not exist because certain countries did not historically offer the right to obtain specific types of patents and/or we (or our licensors) did not file in those countries. In addition, the patent environment can be unpredictable and the validity and enforceability of patents cannot be predicted with certainty. Absent relevant patent protection for a product, once the data exclusivity period expires, generic versions can be approved and marketed.

Generic and biosimilar product manufacturers as well as other groups seeking financial gain are also increasingly seeking to challenge patents before they expire, and we could face earlier-than-expected competition for any products at any time. Patents covering our key products have been and are likely to continue to be subject to patent litigation. In some cases, manufacturers may seek regulatory approval by submitting their own clinical trial data to obtain marketing approval or choose to launch a generic product “at risk” before the expiration of the applicable patent(s) and/or before the final resolution of related patent litigation. There is no assurance that a particular product will enjoy market exclusivity for the full time period that appears in the estimates disclosed in this Form 10-K. In addition, some countries, such as India, are allowing competitors to manufacture and sell competing generic products, which negatively impacts the protections afforded the Company. Lower-priced biosimilars for BMS biologic products or competing biologics could negatively impact our volumes and prices.

Increased pricing pressure and other restrictions in the U.S. and abroad from managed care organizations, institutional purchasers, and government agencies and programs, among others, could negatively affect our revenues and profit margins.

Our products continue to be subject to increasing pressures across the portfolio from market access, pricing and discounting and other restrictions in the U.S., the EU and other regions around the world, including from (i) rules and practices of managed care organizations and institutional and governmental purchasers; (ii) judicial decisions and changes in laws and regulations for federal healthcare programs such as Medicare and Medicaid as well as U.S. healthcare reform, and other government actions and inquiries; (iii) the potential impact of changes to pharmaceutical reimbursement, and increased pricing pressure from Medicare Part D formularies, Medicare Part B reimbursement rates as well as commercial formularies in general; (iv) reimbursement delays; (v) government price erosion mechanisms across Europe and in other countries, resulting in deflation for pharmaceutical product pricing; (vi) collection delays in government-funded public hospitals outside the U.S. (vii) the impact on pricing from parallel trade across borders; (viii) other developments in technology and/or industry practices that could impact the reimbursement policies and practices of third-party payers; and (ix) inhibited market access due to real or perceived differences in value propositions for our products compared to competing products.

Third-party royalties represent a significant percentage of our pretax income and operating cash flow.

We have entered into several arrangements which entitle us to potential royalties from third parties for out-licensed intellectual property, commercialization rights and sales-based contingent proceeds related to the divestiture of businesses. In many of these arrangements we have minimal, if any, continuing involvement that contribute to the financial success of those activities. Royalties have continued to represent a significant percentage of our pretax income, including royalties related to our Sanofi alliance, out-licensed intellectual property and contingent proceeds resulting from the divestiture of the diabetes and Erbitux* businesses. Pretax income generated from royalties were approximately $675 million in 2015. Our pretax income could be adversely affected if the royalty streams decline in future periods.

Failure to execute our business strategy could adversely impact our growth and profitability.

We may not be able to consistently maintain a rich pipeline, through internal R&D programs or transactions with third parties, to support future revenue growth. Competition among pharmaceutical companies for acquisition and product licensing opportunities is intense, and we may not be able to locate suitable acquisition targets or licensing partners at reasonable prices, or successfully execute such transactions. We also may not be able to successfully realize the expected efficiencies and effectiveness from changes in our structure and operations to further our diversified specialty biopharmaceuticals strategy. If we are unable to support and grow our marketed products, successfully execute the launches of newly approved products, advance our late-stage pipeline, manage change and transformational issues, and manage our costs effectively, our operating results and financial condition could be negatively impacted.

Failure to attract and retain highly qualified personnel could affect our ability to successfully develop and commercialize products.

Our success is largely dependent on our continued ability to attract and retain highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical research and development, governmental regulation and commercialization. Competition for qualified personnel in the biopharmaceutical field is intense. We cannot be sure that we will be able to attract and retain quality personnel or that the costs of doing so will not materially increase.

The public announcement of data from our clinical studies, or those of our competitors, or news of any developments related to our, or our competitors', immuno-oncology products or late-stage compounds may cause significant volatility in our stock price. If the development of any of our key immuno-oncology compounds, whether alone or as part of a combination therapy, is delayed or discontinued, our stock price could decline significantly.
We are focusing our efforts and resources in certain disease areas. With our more focused portfolio, investors are placing heightened scrutiny on some of our products or late-stage compounds. In particular, Opdivo is an important asset in our immuno-oncology portfolio. During 2015, we announced multiple regulatory milestones for Opdivo, a fully human monoclonal antibody that was approved as an anticancer treatment in non-small cell lung cancer, renal cell cancer and melanoma, and being investigated for other tumor types, alone or in combination with other approved cancer products such as Yervoy. In 2016, we expect to receive further news from ongoing clinical trials and health authorities.

The announcement of data from our clinical studies, or those of our competitors, or news of any developments related to our, or our competitors', immuno-oncology products or late-stage compounds, such as Opdivo, may cause significant volatility in our stock price. Furthermore, the announcement of any negative or unexpected data or the discontinuation of development of any of our key immuno-oncology compounds, whether alone or as part of a combination therapy, any delay in our anticipated timelines for filing for regulatory approval, or a significant advancement of a competitor, will likely cause our stock price to decline significantly. There is no assurance that data from our clinical studies will support a filing for regulatory approval or even if approved, that any of our key immuno-oncology compounds will become commercially successful for all approved indications.

We may experience difficulties or delays in the development and commercialization of new products.
Compounds or products may appear promising in development but fail to reach market within the expected or optimal timeframe, or at all. In addition, product extensions or additional indications may not be approved. Developing and commercializing new compounds and products include inherent risks and uncertainties, including (i) due to efficacy and safety concerns, delayed or denied regulatory approvals, delays or challenges with producing products on a commercial scale or excessive costs to manufacture them; (ii) failure to enter into or implement optimal alliances for the development and/or commercialization of new products; (iii) failure to maintain a consistent scope and variety of promising late-stage products; (iv) failure of one or more of our products to achieve or maintain commercial viability, (v) changes in regulatory approval processes may cause delays or denials of new product approvals.

Regulatory approval delays are especially common when a product is expected to have a Risk Evaluation and Mitigation Strategy, as required by the FDA to address significant risk/benefit issues. The inability to bring a product to market or a significant delay in the expected approval and related launch date of a new product could negatively impact our revenues and earnings. In addition, if certain acquired pipeline programs (including in-process research and development (IPR&D)) are canceled or we believe their commercial prospects have been reduced, we may recognize material non-cash impairment charges for those programs. For example, in 2015, we recognized a $160 million IPRD impairment charge for an LPA1 antagonist and in 2014, we recognized a $310 million IPRD impairment charge for peginterferon lambda. Finally, losing key molecules and intermediaries or our compound library through a natural or man-made disaster or act of sabotage could negatively impact the product development cycle.

Any businesses or assets we acquire in the future may underperform, and we may not be able to successfully integrate them into our existing business.
We may continue to support our pipeline with compounds or products obtained through licensing and acquisitions. Future revenues, profits and cash flows of an acquired company’s products, technologies and pipeline candidates, may not materialize due to lower product uptake, delayed or missed pipeline opportunities, the inability to capture expected synergies, increased competition, safety concerns, regulatory issues, supply chain problems or other factors beyond our control. Substantial difficulties, costs and delays could result from integrating our acquisitions, including for

(i) R&D, manufacturing, distribution, sales, marketing, promotion and information technology activities; (ii) policies, procedures, processes, controls and compliance; (iii) company cultures; (iv) compensation structures and other human resource activities; and (v) tax considerations.

We depend on several key products for most of our revenues, cash flows and earnings.
We have historically derived a majority of our revenue and earnings from several key products and while we are not as heavily dependent on one or two products as in past years, our dependence on the profitability of certain products is likely to continue. For instance, in 2015, Orencia, Eliquis, Sprycel and the Hepatitis C Franchise each represented approximately 10% or greater of consolidated revenues. We expect that growth products such as Opdivo and Eliquis will become an increasingly important part of our revenue base. A reduction in revenues from one or more of these products could significantly negatively impact our revenues, cash flows and earnings.

We could experience difficulties and delays in the manufacturing, distribution and sale of our products.
Our product supply and related patient access could be negatively impacted by, among other things: (i) product seizures or recalls or forced closings of manufacturing plants; (ii) our failure, or the failure of any of our suppliers, to comply with Current Good Manufacturing Practices and other applicable regulations or quality assurance guidelines that could lead to manufacturing shutdowns, product shortages or delays in product manufacturing;
(iii) manufacturing, quality assurance/quality control, supply problems or governmental approval delays; (iv) the failure of a sole source or single source supplier to provide us with the necessary raw materials, supplies or finished

goods within a reasonable timeframe; (v) the failure of a third-party manufacturer to supply us with bulk active or finished product on time; (vi) construction or regulatory approval delays for new facilities or the expansion of existing facilities, including those intended to support future demand for our biologics products, such as Opdivo; (vii) the failure to meet new and emerging regulations requiring products to be tracked throughout the distribution channels using unique identifiers to verify their authenticity in the supply chain; (viii) other manufacturing or distribution issues, including limits to manufacturing capacity and changes in the types of products produced, such as biologics, physical limitations or other business interruptions and (ix) disruption in supply chain continuity including from natural or man-made disasters at one of our facilities or at a critical supplier.

Changes in U.S. or foreign laws and regulations may negatively affect our revenues and profit margins.
We could become subject to new government laws and regulations, which could negatively affect our business, our operating results and the financial condition of our Company, such as (i) additional healthcare reform initiatives in the U.S. or in other countries, including additional mandatory discounts or fees; (ii) increasing tax revenues in the U.S. or other countries as a means to reduce debt by changing tax rates; limiting, phasing-out or eliminating deductions or tax credits; modifying tax collection processes; taxing certain tax havens; taxing certain excess income from intellectual property; changing rules for earnings repatriations; and changing other tax laws; (iii) new laws, regulations and judicial or other governmental decisions affecting pricing, drug reimbursement, receivable payments, and access or marketing within or across jurisdictions; (iv) changes in intellectual property law; (v) changes in accounting standards; (vi) increasing data privacy regulations and enforcement; (vii) emerging and new global regulatory requirements for reporting payments and other value transfers to healthcare professionals, and (viii) the potential impact of importation restrictions, legislative and/or other regulatory changes.

Product labeling changes for our marketed products could result in a negative impact on revenues and profit margins.
We or regulatory authorities may need to change the labeling for any pharmaceutical product, including after a product has been marketed for several years. These changes are often the result of additional data from post-marketing studies, head-to-head trials, adverse events reports, studies that identify biomarkers (objective characteristics that can indicate a particular response to a product or therapy) or other studies or post-marketing experience that produce important additional information about a product. New information added to a product's label can affect its risk-benefit profile, leading to potential recalls, withdrawals, or declining revenue, as well as product liability claims. Sometimes additional information from these studies identifies a portion of the patient population that may be non-responsive to a medicine or would be at higher risk of adverse reactions and labeling changes based on such studies may limit the patient population. The studies providing such additional information may be sponsored by us, but they could also be sponsored by competitors, insurance companies, government institutions, managed care organizations, scientists, investigators, or other interested parties. While additional safety and efficacy information from such studies assist us and healthcare providers in identifying the best patient population for each product, it can also negatively impact our revenues due to inventory returns and a more limited patient population going forward. Additionally, certain study results, especially from head-to-head trials, could affect a product's formulary listing, which could also adversely affect revenues.

Adverse outcomes in legal matters could negatively affect our business.
Current or future lawsuits, claims, proceedings and government investigations could preclude or delay the commercialization of our products or could adversely affect our operations, profitability, liquidity or financial condition, after any possible insurance recoveries, where available. Such legal matters include (i) intellectual property disputes; (ii) adverse decisions in litigation, including product liability and commercial cases; (iii) anti-bribery regulations, such as the U.S. Foreign Corrupt Practice Act or UK Bribery Act, including compliance with ongoing reporting obligations to the government resulting from any settlements such as the civil settlement reached by the Company with the SEC in October 2015, (iv) recalls or withdrawals of pharmaceutical products or forced closings of manufacturing plants; (v) the failure to fulfill obligations under supply contracts with the government and other customers; (vi) product pricing and promotional matters; (vii) lawsuits and claims asserting, or investigations into,

violations of securities, antitrust, Federal and state pricing, consumer protection, data privacy and other laws; (viii) environmental, health, safety and sustainability matters; and (iv) tax liabilities.

We depend on third parties to meet their contractual, regulatory, and other obligations.
We rely on suppliers, vendors, outsourcing partners, alliance partners and other third parties to research, develop, manufacture, commercialize, co-promote and sell our products, manage certain marketing, selling, human resource, finance, information technology and other business unit and functional services, and meet their contractual, regulatory, and other obligations. Some third parties are located in markets subject to political and social risk, corruption, infrastructure problems and natural disasters, in addition to country specific privacy and data security risk given current legal and regulatory environments. The failure of any critical third party to meet its obligations, including for future royalty and milestone payments; adequately deploy business continuity plans in the event of a crisis; and/or satisfactorily resolve significant disagreements with us or address other factors, could have a material adverse impact on the Company’s operations and results. In addition, if these third parties violate, or are alleged to have violated, any laws or regulations, including the local pharmaceutical code, U.S. Foreign Corrupt Practice Act, U.K. Bribery Act and other similar laws and regulations, during the performance of their obligations for us, it is possible that we could suffer financial and reputational harm or other negative outcomes, including possible legal consequences.

The illegal distribution and sale by third parties of counterfeit versions of our products or stolen products could have a negative impact on our reputation and business.
Third parties may illegally distribute and sell counterfeit versions of our products, which do not meet our rigorous manufacturing and testing standards. A patient who receives a counterfeit drug may be at risk for a number of dangerous health consequences. Our reputation and business could suffer harm as a result of counterfeit drugs sold under our brand name. In addition, thefts of inventory at warehouses, plants or while in-transit, which are then not properly stored and are later sold through unauthorized channels, could adversely impact patient safety, our reputation and our business.

We are increasingly dependent on information technology and our systems and infrastructure face certain risks, including from cyber security and data leakage.
A significant breakdown, invasion, corruption, destruction or interruption of critical information technology systems or infrastructure, by our workforce, others with authorized access to our systems, or unauthorized persons could negatively impact operations. The ever-increasing use and evolution of technology, including cloud-based computing, creates opportunities for the unintentional dissemination or intentional destruction of confidential information stored in our systems, in non-encrypted portable media or storage devices. We could also experience a business interruption, theft of confidential information, or reputational damage from industrial espionage attacks, malware or other cyber-attacks, which may compromise our system infrastructure or lead to data leakage, either internally or at our third-party providers. Although the aggregate impact on our operations and financial condition has not been material to date, we have been the target of events of this nature and expect them to continue and possibly increase in frequency. We have invested in industry appropriate protections and monitoring practices of our data and information technology to reduce these risks and continue to monitor our systems on an ongoing basis for any current or potential threats. There can be no assurance, however, that our efforts will prevent breakdowns or breaches to our or our third-party providers' databases or systems that could adversely affect our business.

Social media platforms present risks and challenges.
The inappropriate and/or unauthorized use of certain media vehicles could cause brand damage or information leakage or could lead to legal implications, including from the improper collection and/or dissemination of personally identifiable information from employees, patients, healthcare professionals or other stakeholders. In addition, negative or inaccurate posts or comments about us on any social networking website could damage our reputation, brand image and goodwill. Further, the disclosure of non-public Company-sensitive information by our workforce or others through external media channels could lead to information loss. Identifying new points of entry as social media continues to expand presents new challenges.

Adverse changes in U.S., global, regional or local economic conditions could adversely affect our profitability.
Global economic risks pose significant challenges to a company's growth and profitability and are difficult to mitigate. The world's major economies hold historically-high debt levels and many are experiencing slow growth and high unemployment rates. Several risks lie ahead, including the management of the U.S. debt and the European sovereign debt. We have significant operations in Europe, including for manufacturing. We have exposure to customer credit risks in Europe, South America and other markets including from government-guaranteed hospital receivables in markets where payments are not received on time. In addition, future pension plan funding requirements continue to be sensitive to global economic conditions and the related impact on equity markets. We are also exposed to other commercial risks and economic factors over which we do not have any control, which could pose significant challenges to our underlying profitability.

Changes in foreign currency exchange, interest and tax rates could have a material adverse effect on our operating results and liquidity.
We have significant operations outside of the U.S. generating approximately 51% of our revenues in 2015. As such, our revenues, earnings and cash flow are exposed to risk from a strengthening U.S. dollar against the euro, Japanese

yen, Chinese renminbi, Canadian dollar and South Korean won, among others, which can be difficult to mitigate. Derivative financial instruments are used to hedge certain, but not all, underlying economic exposures. All of the financial instruments used, including derivatives, are subject to counterparty credit risk. In addition, the results of our operations could be negatively impacted by any member country exiting the eurozone monetary union or EU. We are also exposed to changes in interest rates. Our ability to access money markets and/or capital markets could be impeded if adverse liquidity market conditions occur. Debt ratings would be pressured if financial and clinical expectations are not met.

Item 1B. UNRESOLVED STAFF COMMENTS.

None.

Item 2. PROPERTIES.

Our principal executive offices are located at 345 Park Avenue, New York, NY, where we lease approximately 81,000 square feet of floor space. We own or lease approximately 182 properties in 49 countries.

We manufacture products at 10 worldwide locations, all of which are owned by us. Our manufacturing locations and aggregate square feet of floor space by geographic area were as follows at December 31, 2015:

	Number of Locations	Square Feet
United States	4	2,190,000
Europe	3	1,296,000
Rest of the World	3	514,000
Total	10	4,000,000

Portions of these manufacturing locations and the other properties owned or leased by us in the U.S. and elsewhere are used for research and development, administration, storage and distribution. For further information about our properties, refer to “Item 1. Business—Manufacturing and Quality Assurance."

Item 3. LEGAL PROCEEDINGS.

Information pertaining to legal proceedings can be found in “Item 8. Financial Statements—Note 22. Legal Proceedings and Contingencies” and is incorporated by reference herein.

Item 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART IA

Executive Officers of the Registrant

Listed below is information on our executive officers as of February 12, 2016. Executive officers are elected by the Board of Directors for an initial term, which continues until the first Board meeting following the next Annual Meeting of Stockholders, and thereafter, are elected for a one-year term or until their successors have been elected. All executive officers serve at the pleasure of the Board of Directors.

Name and Current Position	Age	Employment History for the Past 5 Years
Giovanni Caforio, M.D. Chief Executive Officer and Director Member of the Leadership Team	51	2010 to 2011 – Senior Vice President, Oncology and Immunology, Global Commercialization 2011 to 2013 – President, U.S. Pharmaceuticals 2013 to 2014 – Executive Vice President and Chief Commercial Officer 2014 to 2015 – Chief Operating Officer and Director of the Company 2015 to present – Chief Executive Officer and Director of the Company
Charles Bancroft Executive Vice President and Chief Financial Officer Member of the Leadership Team	56	2010 to 2011 – Chief Financial Officer of the Company 2011 to present – Executive Vice President and Chief Financial Officer of the Company
Emmanuel Blin Senior Vice President and Head of Commercialization, Policy and Operations Member of the Leadership Team	46	2010 to 2013 – President & General Manager, Japan 2013 to 2015 – President, Global Commercialization 2015 to present – Senior Vice President, Head of Commercialization, Policy and Operations
Joseph C. Caldarella Senior Vice President and Corporate Controller	60	2010 to present – Senior Vice President and Corporate Controller
Francis Cuss, MB BChir, FRCP Executive Vice President and Chief Scientific Officer Member of the Leadership Team	61	2010 to 2013 – Senior Vice President, Research 2013 to present – Executive Vice President and Chief Scientific Officer
John E. Elicker Senior Vice President, Public Affairs and Investor Relations Member of the Leadership Team	56	2010 to 2012 – Senior Vice President, Investor Relations 2012 to present – Senior Vice President, Public Affairs and Investor Relations
Murdo Gordon Senior Vice President and Head of Worldwide Markets Member of the Leadership Team	49	2010 to 2011 – Senior Vice President, Access 2011 to 2013 – Senior Vice President, Oncology and Immunology 2013 to 2015 – President, U.S. Pharmaceuticals 2015 to present – Senior Vice President, Head of Worldwide Markets
Ann Powell Judge Senior Vice President, Global Human Resources Member of the Leadership Team	50	2009 to 2013 – Chief Human Resources Officer, Shire Pharmaceuticals 2013 to present – Senior Vice President, Global Human Resources
Sandra Leung Executive Vice President and General Counsel Member of the Leadership Team	55	2007 to 2014 – General Counsel and Corporate Secretary 2014 to 2015 – Executive Vice President, General Counsel and Corporate Secretary 2015 to present – Executive Vice President and General Counsel
Anne Nielsen Senior Vice President and Chief Compliance and Ethics Officer	55	2009 to 2013 – Vice President and Associate General Counsel 2013 to 2013 – Senior Vice President and Deputy General Counsel 2013 to present – Senior Vice President and Chief Compliance and

Member of the Leadership Team		Ethics Officer
Louis S. Schmukler President, Global Manufacturing and Supply Member of the Leadership Team	60	2009 to 2011 – Senior Vice President, Specialty/Biotechnology Operating Unit, Pfizer 2011 to present – President, Global Manufacturing and Supply
Paul von Autenried Senior Vice President, Enterprise Services and Chief Information Officer Member of the Leadership Team	54	2007 to 2011 – Vice President and Chief Information Officer 2011 to 2012 – Senior Vice President and Chief Information Officer 2012 to present – Senior Vice President, Enterprise Services and Chief Information Officer

PART II

Item 5. MARKET FOR THE REGISTRANT'S COMMON STOCK AND OTHER STOCKHOLDER MATTERS.

Market Prices

Bristol-Myers Squibb common stock is traded on the New York Stock Exchange (NYSE) (Symbol: BMY). A quarterly summary of the high and low market prices is presented below:

	2015		2014	
	High	Low	High	Low
Common:				
First Quarter	$68.47	$58.48	$56.61	$48.54
Second Quarter	69.15	63.00	52.19	46.59
Third Quarter	70.06	57.30	51.96	47.86
Fourth Quarter	70.71	59.88	61.30	48.92

Holders of Common Stock

The number of record holders of common stock at December 31, 2015 was 45,942.

The number of record holders is based upon the actual number of holders registered on our books at such date and does not include holders of shares in "street names" or persons, partnerships, associations, corporations or other entities identified in security position listings maintained by depository trust companies.

Dividends

Our Board of Directors declared the following quarterly dividends per share, which were paid in the periods indicated below:

	Common		Preferred	
	2015	2014	2015	2014
First Quarter	$0.37	$0.36	$0.50	$0.50
Second Quarter	0.37	0.36	0.50	0.50
Third Quarter	0.37	0.36	0.50	0.50
Fourth Quarter	0.37	0.36	0.50	0.50
	$1.48	$1.44	$2.00	$2.00

In December 2015, our Board of Directors declared a quarterly dividend of $0.38 per share on our common stock which was paid on February 1, 2016 to shareholders of record as of January 4, 2016. The Board of Directors also declared a quarterly dividend of $0.50 per share on our preferred stock, payable on March 1, 2016 to shareholders of record as of February 5, 2016.

UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

The following table summarizes the surrenders of our equity securities during the 12 month period ended December 31, 2015:

Period	Total Number of Shares Purchased[a]	Average Price Paid per Share[a]	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs[b]	Approximate Dollar Value of Shares that May Yet Be Purchased Under the Plans or Programs[b]
Dollars in Millions, Except Per Share Data				
January 1 to 31, 2015	33,737	$ 59.51	—	$ 1,368
February 1 to 28, 2015	9,178	$ 60.50	—	$ 1,368
March 1 to 31, 2015	1,825,224	$ 63.41	—	$ 1,368
Three months ended March 31, 2015	1,868,139		—	
April 1 to 30, 2015	19,294	$ 63.42	—	$ 1,368
May 1 to 31, 2015	14,672	$ 64.93	—	$ 1,368
June 1 to 30, 2015	10,387	$ 66.17	—	$ 1,368
Three months ended June 30, 2015	44,353		—	
July 1 to 31, 2015	13,256	$ 67.47	—	$ 1,368
August 1 to 31, 2015	8,553	$ 65.69	—	$ 1,368
September 1 to 30, 2015	5,444	$ 60.08	—	$ 1,368
Three months ended September 30, 2015	27,253		—	
October 1 to 31, 2015	11,137	$ 60.48	—	$ 1,368
November 1 to 30, 2015	17,550	$ 64.53	—	$ 1,368
December 1 to 31, 2015	18,582	$ 67.52	—	$ 1,368
Three months ended December 31, 2015	47,269		—	
Twelve months ended December 31, 2015	1,987,014		—	

(a) Reflects the shares of common stock surrendered to the Company to satisfy tax withholding obligations in connection with the vesting of awards under our long-term incentive program.

(b) In May 2010, the Board of Directors authorized the repurchase of up to $3.0 billion of common stock. In June 2012, the Board of Directors increased its authorization for the repurchase of common stock by an additional $3.0 billion. The repurchase program does not have an expiration date and we may consider future repurchases.

Item 6. SELECTED FINANCIAL DATA.

Five Year Financial Summary

Amounts in Millions, except per share data	2015	2014	2013	2012	2011
Income Statement Data:[a]					
Total Revenues	$16,560	$15,879	$16,385	$17,621	$21,244
Continuing Operations:					
Net Earnings	1,631	2,029	2,580	2,501	5,260
Net Earnings Attributable to:					
Noncontrolling Interest	66	25	17	541	1,551
BMS	1,565	2,004	2,563	1,960	3,709
Net Earnings per Common Share Attributable to BMS:					
Basic	$0.94	$1.21	$1.56	$1.17	$2.18
Diluted	$0.93	$1.20	$1.54	$1.16	$2.16
Average common shares outstanding:					
Basic	1,667	1,657	1,644	1,670	1,700
Diluted	1,679	1,670	1,662	1,688	1,717
Cash dividends paid on BMS common and preferred stock	$2,477	$2,398	$2,309	$2,286	$2,254
Cash dividends declared per common share	$1.49	$1.45	$1.41	$1.37	$1.33
Financial Position Data at December 31:					
Cash and cash equivalents	$2,385	$5,571	$3,586	$1,656	$5,776
Marketable securities[b]	6,545	6,272	4,686	4,696	5,866
Total Assets	31,748	33,749	38,592	35,897	32,970
Long-term debt[b]	6,550	7,242	7,981	7,232	5,376
Equity	14,424	14,983	15,236	13,638	15,867

(a) For a discussion of items that affected the comparability of results for the years 2015, 2014 and 2013, refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Non-GAAP Financial Measures."

(b) Includes current and non-current portion.

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

EXECUTIVE SUMMARY

Bristol-Myers Squibb Company (which may be referred to as Bristol-Myers Squibb, BMS, the Company, we, our or us) is a global specialty biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases.

Our revenues increased by 4% in 2015 as a result of recently launched products such as our Hepatitis C Franchise (including previously deferred revenue in France) and Opdivo (nivolumab) and continued sales growth in Eliquis (apixaban). These impacts were partially offset by the changes in foreign currency rates, expiration of our U.S. and European Union (EU) commercialization rights to Abilify* (aripiprazole), competitive pressures resulting from exclusivity losses and other factors for Baraclude (entecavir), Reyataz (atazanavir sulfate) and Sustiva (efavirenz) in certain markets and the expiration/transfer of certain licensing and royalty rights.

The decrease in GAAP earnings per share (EPS) from $1.20 in 2014 to $0.93 in 2015 was due to higher research and development expenses as a result of upfront payments for licensing and asset acquisitions of investigational compounds. The tax impact of specified items contributed to the changes in the effective tax rate, including the non-tax-deductible research and development charges for the acquisitions of Flexus Biosciences, Inc. (Flexus) and Cardioxyl Pharmaceuticals, Inc. (Cardioxyl). After adjusting for specified items, the increase in non-GAAP EPS from $1.85 in 2014 to $2.01 in 2015 was primarily due to higher revenues.

Highlights

The following table summarizes our financial information:

	Year Ended December 31,		
Dollars in Millions, except per share data	2015	2014	2013
Total Revenues	$16,560	$15,879	$16,385
Total Expenses	14,483	13,498	13,494
Earnings before Income Taxes	2,077	2,381	2,891
Provision for Income Taxes	446	352	311
Effective tax rate	21.5 %	14.8 %	10.8 %
Net Earnings Attributable to BMS			
GAAP	1,565	2,004	2,563
Non-GAAP	3,378	3,085	3,019
Diluted Earnings Per Share			
GAAP	0.93	1.20	1.54
Non-GAAP	2.01	1.85	1.82
Cash, Cash Equivalents and Marketable Securities	8,930	11,843	8,272

Our non-GAAP financial measures, including non-GAAP earnings and related EPS information, are adjusted to exclude specified items which represent certain costs, expenses, gains and losses and other items impacting the comparability of financial results. For a detailed listing of all specified items and further information and reconciliations of non-GAAP financial measures refer to "—Non-GAAP Financial Measures."

Significant Product and Pipeline Approvals

We received over 100 approvals for new medicines and additional indications and formulations of currently marketed medicines including over 20 in major markets (the U.S., EU and Japan). The following is a summary of some of the more significant approvals received in 2015.

Product	Date	Approvals
Opdivo	December 2015	Japanese Ministry of Health, Labour and Welfare manufacturing and marketing approval for patients with unresectable, advanced or recurrent non-small cell lung cancer (NSCLC), received by Ono Pharmaceutical Co., Ltd. (Ono).
	November 2015	U.S. Food and Drug Administration (FDA) approval as a single agent for the treatment of previously untreated patients with BRAF V600 wild-type unresectable or metastatic melanoma
	November 2015	FDA approval for the treatment of previously treated patients with advanced (metastatic) renal cell carcinoma (RCC)
	October 2015	FDA approval for the treatment of previously treated patients with non-squamous (NSQ) NSCLC
	July 2015	EU approval for the treatment of locally advanced or metastatic squamous (SQ) NSCLC after prior chemotherapy
	June 2015	EU approval for the treatment of both first-line and previously treated unresectable or metastatic melanoma patients, regardless of BRAF status
	March 2015	FDA approval for the treatment of patients with advanced SQ NSCLC with progression on or after platinum-based chemotherapy
Opdivo+ Yervoy (ipilimumab)	September 2015	FDA approval for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma
Yervoy	October 2015	FDA approval for the adjuvant treatment of patients with cutaneous melanoma
	July 2015	Japanese Ministry of Health, Labour and Welfare approval for first and second line treatment for unresectable malignant melanoma
Empliciti (elotuzumab)	November 2015	FDA approval for the treatment of multiple myeloma as combination therapy with Revlimid* and dexamethasone in patients who have received one to three prior therapies
Hepatitis C Portfolio - Daklinza (daclatasvir)	July 2015	FDA approval for use with sofosbuvir for the treatment of patients with chronic hepatitis C virus (HCV) genotype 3

Refer to "—Product and Pipeline Developments" for all of the developments in our marketed products and late-stage pipeline in 2015.

Strategy

We have transitioned to a specialty biopharmaceutical company, with a strategy designed to leverage both the reach and resources of a major pharmaceutical company as well as the entrepreneurial spirit and agility of a biotech firm. We are focused on discovering, developing and delivering innovative medicines that address serious unmet medical needs. Our four strategic priorities are to drive business performance, maintain our leadership in immuno-oncology, maintain a diversified portfolio both within and outside of immuno-oncology, and continue our disciplined approach to capital allocation, with business development as a top priority.

We are developing new medicines in the following core therapeutic areas: oncology, immuno-oncology, immunoscience, cardiovascular diseases, fibrosis and genetically defined diseases. We are pioneering innovative medicines in the area of immuno-oncology which unlock the body’s own immune system to battle cancer. Yervoy, our

first immuno-oncology agent, was introduced in 2011 for the treatment of metastatic melanoma. During 2015, we announced several significant clinical and regulatory milestones in the U.S. and EU for Opdivo, a programmed death receptor-1 (PD-1) immune checkpoint inhibitor. Within 12 months of Opdivo's first approval in the U.S. for metastatic melanoma in late December 2014, we worked with unprecedented speed with the FDA and received five additional U.S. approvals for indications across three different tumor types, transforming cancer care in advanced NSCLC, melanoma and RCC. As of the end of 2015, Opdivo was approved in 43 countries. We continue to invest significantly in our deep pipeline of innovative medicines covering a broad array of cancers and have entered into several collaboration agreements to research and develop Opdivo and other approved or investigational oncology agents in combination regimens. Additionally in 2015, we enhanced our portfolio by acquiring rights to novel assets across several therapeutic areas including cardiovascular diseases and fibrosis.

We are evolving our commercial model and growing our marketed product portfolio in a manner consistent with our overall strategy. In oncology, we are building on the rapid commercial acceptance of Opdivo, which had revenues of approximately $900 million, and the continued success of Yervoy and Sprycel (dasatinib). Beyond oncology, we remain strongly committed to Orencia (abatacept) and Eliquis, each with revenues of approximately $1.9 billion in 2015. In 2015, we received U.S. approval for Daklinza for use with sofosbuvir for

the treatment of patients with chronic HCV genotype 3. We also continue to support key brands in our virology franchise such as Reyataz, Baraclude and the Sustiva Franchise.

In December 2015, we announced the divestiture of our pipeline of investigational human immunodeficiency virus (HIV) medicines to ViiV Healthcare, a global specialist company exclusively dedicated to finding new medicines for people living with HIV. This transaction will allow us to focus on therapeutic areas which are a priority and will drive the greatest long-term value to us.

Looking ahead, we will continue to implement our biopharma strategy by driving the growth of key brands, executing new product launches, investing in our diverse and innovative pipeline, including through business development, focusing on prioritized markets, increasing investments in our biologics manufacturing capabilities and maintaining a culture of continuous improvement.

Acquisition and Licensing Arrangements
Acquisition and licensing transactions allow us to focus our resources behind our growth opportunities that drive the greatest long-term value. We are focused on the following core therapeutic areas: oncology, immuno-oncology, immunoscience, cardiovascular diseases, fibrosis and genetically defined diseases. Significant transactions entered into in 2015 are summarized below:

Kyorin Pharmaceutical Co., Ltd. (Kyorin)
In December 2015, BMS and Kyorin entered into an exclusive worldwide license agreement granting BMS the right to develop, manufacture and commercialize Kyorin's FPR2 agonist program. Kyorin will have an option to collaborate with BMS in the development and commercialization in Japan.

Cardioxyl
In December 2015, BMS acquired all of the outstanding shares of Cardioxyl, a privately held biotechnology company focused on the discovery and development of novel therapeutic agents for cardiovascular disease. The acquisition provided BMS with full rights to CXL-1427, a nitroxyl prodrug in Phase II development for acute decompensated heart failure.

Five Prime Therapeutics, Inc. (Five Prime)
In November 2015, BMS and Five Prime entered into an exclusive worldwide licensing and collaboration agreement for the development and commercialization of Five Prime’s colony stimulating factor 1 receptor (CSF1R) antibody program, including FPA008 currently in Phase I development for immunology and oncology indications. BMS will be responsible for the development, manufacturing and commercialization of FPA008, subject to Five Prime’s option to conduct certain studies at its cost to develop FPA008 in pigmented vilonodular synovitis (PVNS) and in combination with its own internal oncology pipeline assets. Five Prime also retained an option to co-promote in the U.S. The agreement replaces a previous clinical collaboration agreement between the two parties.

Promedior, Inc. (Promedior)
In September 2015, the Company purchased a warrant that gives BMS the exclusive right to acquire Promedior and gain worldwide rights to its lead asset, PRM-151, a recombinant form of human pentraxin-2 protein in Phase II development for the treatment of idiopathic pulmonary fibrosis (IPF) and myelofibrosis (MF). PRM-151 has been granted Fast Track designation in the U.S. and Orphan designation in the U.S. and Europe for the treatment of MF. In addition, PRM-151 has been granted Orphan Designation in the U.S. and Europe for the treatment of IPF.

uniQure N.V. (uniQure)
In May 2015, the Company entered into a collaboration and license agreement with uniQure granting BMS an exclusive license to uniQure’s gene therapy technology platform for specific collaboration targets. The potential gene

therapy products for such collaboration targets developed with uniQure’s platform may be developed for any disease, although the parties intend to focus initially on cardiovascular diseases. The collaboration includes uniQure’s proprietary gene therapy program for congestive heart failure that is intended to restore the heart’s ability to synthesize S100A1, a calcium sensor and master regulator of heart function, and thereby improve clinical outcomes for patients with reduced ejection fraction. In total, the companies may collaborate on 10 targets, including S100A1. BMS will be solely responsible for global commercialization of all products from the collaboration. In August 2015, the Company selected three additional collaboration targets.

In 2015, the Company acquired 2.4 million shares of uniQure in two separate tranches, or 9.9% of uniQure's outstanding shares immediately following the second of the two acquisitions. The Company also has been granted two warrants under which the Company has the right to purchase additional shares that, together with the shares currently owned by BMS, would equal 19.9% of uniQure's oustanding shares immediately after such issuance. The exercise of each warrant is conditioned upon the designation by BMS of a certain number of additional collaboration targets and the payment by BMS to uniQure of related fees under the collaboration and license agreement.

Flexus
In April 2015, the Company acquired all of the outstanding shares of Flexus, a privately held biotechnology company focused on discovering and developing novel anti-cancer therapeutics. The acquisition provided BMS with full rights to F001287, a preclinical small molecule IDO1-inhibitor targeted immunotherapy with potential to be used in combination with BMS's immuno-oncology portfolio. In addition, the transaction included Flexus's IDO/TDO discovery program which includes its IDO-selective, IDO/TDO dual and TDO-selective compounds.

Novo Nordisk A/S (Novo Nordisk)
In March 2015, the Company acquired an exclusive global license from Novo Nordisk to a discovery biologics research program focused on modulating the innate immune system as a therapy for autoimmune diseases.

Bavarian Nordic A/S (Bavarian Nordic)
In March 2015, the Company acquired an exclusive option to globally license and commercialize Prostvac*, Bavarian Nordic’s investigational Phase III prostate-specific antigen-targeting cancer immunotherapy in development for the treatment of asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer.

Rigel Pharmaceuticals, Inc. (Rigel)
In February 2015, the Company executed an agreement with Rigel for the discovery, development and global commercialization of cancer immunotherapies based on Rigel’s extensive portfolio of small molecule TGF beta receptor kinase inhibitors. The collaboration will focus on developing a new class of therapeutics aimed at increasing the immune system’s activity against various cancers either as monotherapy or in combination with immune checkpoint inhibitors, including Opdivo and Yervoy.

California Institute for Biomedical Research (Calibr)
In January 2015, the Company entered into a worldwide research collaboration with Calibr to develop novel small molecule anti-fibrotic therapies, and an exclusive global license agreement that allows the Company to develop, manufacture and commercialize Calibr's preclinical compounds resulting from the collaboration.

RESULTS OF OPERATIONS

Total Revenues
The composition of the changes in revenues was as follows:

	Year Ended December 31, Total Revenues			2015 vs. 2014 Analysis of % Change		2014 vs. 2013 Analysis of % Change	
Dollars in Millions	2015	2014	2013	Total Change	Foreign Exchange[b]	Total Change	Foreign Exchange[b]
United States	$8,188	$7,716	$8,318	6 %	—	(7)%	—
Europe	3,491	3,592	3,930	(3)%	(17)%	(9)%	—
Rest of the World	4,142	3,459	3,295	20 %	(13)%	5 %	(5)%
Other[a]	739	1,112	842	(34)%	N/A	32 %	N/A
Total	$16,560	$15,879	$16,385	4 %	(7)%	(3)%	(1)%

(a) Other revenues include royalties and alliance-related revenues for products not sold by our regional commercial organizations.

(b) Foreign exchange impacts were derived by applying the prior period average currency rates to the current period sales.

The increase in U.S. revenues in 2015 resulted from the launch of Opdivo and Daklinza and higher demand for Eliquis and Sprycel partially offset by the expiration of commercialization rights to Abilify* and the transfer of Erbitux* in North America. Average U.S. net selling prices increased by approximately 3%. Refer to "—Product Sales Discussion"

below for additional information.

The decrease in U.S. revenues in 2014 resulted from the diabetes business divestiture in February 2014 partially offset by higher demand for Eliquis, Yervoy and Sprycel and higher average net selling prices of approximately 3%.

The decrease in Europe revenues in 2015 resulted from unfavorable foreign exchange and the expiration of commercialization rights to Abilify* in the EU in June 2014 partially offset by the launch of Daklinza in certain EU countries in the third quarter of 2014 and higher demand for Eliquis. Revenues were also impacted by approximately $170 million of Daklinza net product sales for amounts previously deferred in 2014 until final pricing was obtained in France which occurred in 2015. Revenues continue to be negatively impacted in many European countries as healthcare payers, including government agencies, continued to reduce healthcare costs through actions that directly or indirectly impose additional price reductions.

The decrease in Europe revenues in 2014 resulted from the expiration of EU commercialization rights to Abilify* in June 2014, the diabetes business divestiture and the loss of exclusivity of Sustiva in November 2013 partially offset by higher demand for Eliquis, Yervoy and Orencia and the launch of Daklinza in certain EU countries in the third quarter of 2014.

The increase in Rest of the World revenues in 2015 resulted from the launch of the Daklinza and Sunvepra dual regimen in Japan in the third quarter of 2014 and higher demand for Eliquis, partially offset by unfavorable foreign exchange (primarily in Japan).

The increase in Rest of the World revenues in 2014 resulted from higher demand for key products, particularly Eliquis, Yervoy, Sprycel and the launch of the Daklinza and Sunvepra dual regimen in Japan in the third quarter of 2014 partially offset by the diabetes business divestiture and unfavorable foreign exchange (primarily in Japan).

The decrease in Other revenues in 2015 resulted from the expiration/transfer of certain licensing and royalty rights. The increase in Other revenues in 2014 resulted from higher royalties, mature brand and over-the-counter product alliances and diabetes product supply sales in 2014. Refer to "Item 8. Financial Statements—Note 3. Alliances" for further discussion of the alliances.

No single country outside the U.S. contributed more than 10% of total revenues in 2015, 2014 or 2013 except for Japan which contributed 10% of total revenues in 2015.

We recognize revenue net of gross-to-net adjustments that are further described in "—Critical Accounting Policies". Our share of certain Abilify* and Atripla* revenues is reflected net of all gross-to-net adjustments in alliance and other revenues. Although not presented as a gross-to-net adjustment in the below tables, our share of Abilify* and Atripla* gross-to-net adjustments were approximately $1.1 billion in 2015, $1.6 billion in 2014 and $1.3 billion in 2013. These gross-to-net adjustments decreased in 2015 due to the expiration of our U.S. commercialization rights to Abilify* in April 2015.

The activities and ending reserve balances for each significant category of gross-to-net adjustments were as follows:

Dollars in Millions	Charge-Backs and Cash Discounts	Medicaid and Medicare Rebates	Sales Returns	Other Rebates, Discounts and Adjustments	Total
Balance at January 1, 2014	$ 49	$286	$279	$324	$938
Provision related to sale made in:					
Current period	755	574	94	776	2,199
Prior period	—	(23)	(33)	(10)	(66)
Returns and payments	(748)	(570)	(105)	(711)	(2,134)
Foreign currency translation and other	—	—	(3)	(27)	(30)
Balance at December 31, 2014	$ 56	$267	$232	$352	$907
Provision related to sale made in:					
Current period	1,043	878	109	1,206	3,236
Prior period	—	(19)	(73)	(23)	(115)
Returns and payments	(1,002)	(688)	(85)	(782)	(2,557)
Foreign currency translation and other	—	(4)	(2)	(44)	(50)
Balance at December 31, 2015	$ 97	$434	$181	$709	$1,421

The reconciliation of gross product sales to net product sales (which excludes alliance and other revenues) by each significant category of gross-to-net adjustments was as follows:

	Year Ended December 31,		
Dollars in Millions	2015	2014	2013
Gross product sales	$17,166	$13,793	$14,391
Gross-to-Net Adjustments			
Charge-backs and cash discounts	(1,043)	(755)	(717)
Medicaid and Medicare rebates	(859)	(551)	(490)
Sales returns	(36)	(61)	(62)
Other rebates, discounts and adjustments	(1,183)	(766)	(818)
Total Gross-to-Net Adjustments	(3,121)	(2,133)	(2,087)
Net product sales	$14,045	$11,660	$12,304

Gross-to-net adjustment rates are primarily a function of changes in revenue mix and contractual and legislative discounts and rebates. Gross-to-net adjustments increased in 2015 and 2014 due to:

- Charge-backs and cash discounts increased in 2015 primarily due to higher product sales in the U.S., particularly regarding Eliquis and Opdivo.
- Medicaid and Medicare rebates increased in 2015 primarily due to higher product sales and rebate rates in the U.S., particularly Medicare for Eliquis. Medicaid and Medicare rebates increased in 2014 primarily due to higher Medicare sales and rebate rates for Eliquis, and higher Medicaid rebates on virology products due to price increase limitations, partially offset by the diabetes business divestiture in February 2014.
- The U.S. sales return reserve for Plavix* was reduced by $63 million in 2015, $30 million in 2014 and $22 million in 2013 after considering several factors including actual return experience and estimated inventory levels in the distribution channels. In accordance with Company policy, these products are eligible to be returned between six months prior to and twelve months after product expiration. The U.S. sales return reserve for Plavix* was not material at December 31, 2015.
- Other rebates, discounts and adjustments increased in 2015 primarily due to additional rebates and discounts for Daklinza (including approximately $180 million upon obtaining final pricing in France for amounts deferred through March 31, 2015) and Eliquis.

Product Revenues

	Year Ended December 31,			% Change		% Change Attributable to Foreign Exchange	
Dollars in Millions	2015	2014	2013	2015 vs. 2014	2014 vs. 2013	2015 vs. 2014	2014 vs. 2013
Virology							
Baraclude (entecavir)	$1,312	$1,441	$1,527	(9)%	(6)%	(7)%	(2)%
U.S.	135	215	289	(37)%	(26)%	—	—
Non-U.S.	1,177	1,226	1,238	(4)%	(1)%	(9)%	(2)%
Hepatitis C Franchise (daclatasvir and asunaprevir)	1,603	256	—	**	N/A	N/A	N/A
U.S.	323	—	—	N/A	N/A	—	—
Non-U.S.	1,280	256	—	**	N/A	N/A	N/A
Reyataz (atazanavir sulfate) Franchise	1,139	1,362	1,551	(16)%	(12)%	(5)%	(1)%
U.S.	591	689	769	(14)%	(10)%	—	—
Non-U.S.	548	673	782	(19)%	(14)%	(11)%	(3)%
Sustiva (efavirenz) Franchise	1,252	1,444	1,614	(13)%	(11)%	—	—
U.S.	1,041	1,118	1,092	(7)%	2%	—	—
Non-U.S.	211	326	522	(35)%	(38)%	(1)%	—
Oncology							
Empliciti (elotuzumab)	3	—	—	N/A	N/A	N/A	N/A
U.S.	3	—	—	N/A	N/A	—	—
Erbitux* (cetuximab)	501	723	696	(31)%	4%	—	N/A
U.S.	487	682	682	(29)%	—	—	—
Non-U.S.	14	41	14	(66)%	**	(3)%	N/A
Opdivo (nivolumab)	942	6	—	**	N/A	N/A	N/A
U.S.	823	1	—	**	N/A	—	—
Non-U.S.	119	5	—	**	N/A	N/A	N/A
Sprycel (dasatinib)	1,620	1,493	1,280	9%	17%	(8)%	(2)%
U.S.	829	671	541	24%	24%	—	—
Non-U.S.	791	822	739	(4)%	11%	(16)%	(5)%
Yervoy (ipilimumab)	1,126	1,308	960	(14)%	36%	(7)%	(2)%
U.S.	602	709	577	(15)%	23%	—	—
Non-U.S.	524	599	383	(13)%	56%	(16)%	(4)%
Neuroscience							
Abilify* (aripiprazole)	746	2,020	2,289	(63)%	(12)%	(1)%	—
U.S.	600	1,572	1,519	(62)%	3%	—	—
Non-U.S.	146	448	770	(67)%	(42)%	(4)%	—

Immunoscience										
Orencia (abatacept)	1,885	1,652	1,444	14	%	14	%	(6	)%	(2	)%
U.S.	1,271	1,064	954	19	%	12	%	—		—	
Non-U.S.	614	588	490	4	%	20	%	(18	)%	(6	)%
Cardiovascular											
Eliquis (apixaban)	1,860	774	146	**		**		N/A		N/A	
U.S.	1,023	404	97	**		**		—		—	
Non-U.S.	837	370	49	**		**		N/A		N/A	
Mature Products and All Other	2,571	3,400	4,878	(24	)%	(30	)%	(6	)%	(1	)%
U.S.	460	591	1,798	(22	)%	(67	)%	—		—	
Non-U.S.	2,111	2,809	3,080	(25	)%	(9	)%	(7	)%	(2	)%

** Change in excess of 100%

Baraclude — an oral antiviral agent for the treatment of chronic hepatitis B.

- U.S. revenues decreased in both periods following the loss of exclusivity in September 2014.
- International revenues decreased in 2015 due to unfavorable foreign exchange partially offset by higher demand in certain countries.

Hepatitis C Franchise — Includes Daklinza - an NS5A replication complex inhibitor (revenues of $1,315 million in 2015 and $201 million in 2014) and Sunvepra (asunaprevir) - an NS3 protease inhibitor (revenues of $288 million in 2015 and $55 million in 2014).

- Daklinza was launched in the U.S. in July 2015. Additional competition is expected in the U.S. during 2016.
- Daklinza was launched in Germany and certain other EU countries in the third quarter of 2014 and subsequently approved in other international markets during 2015. The Daklinza and Sunvepra dual regimen was launched in Japan in the third quarter of 2014. International revenues also include $170 million of previously deferred revenue in France recognized in 2015. International revenues are expected to significantly decline in 2016 due to increased competition primarily in Japan.

Reyataz Franchise — a protease inhibitor for the treatment of the HIV, which includes Reyataz and is also included in the combination therapy, Evotaz (atazanavir 300 mg and cobicistat 150 mg).

- U.S. revenues decreased in both periods due to lower demand resulting from increased competition.
- International revenues decreased in both periods due to unfavorable foreign exchange and lower demand resulting from increased competition.

Sustiva Franchise — a non-nucleoside reverse transcriptase inhibitor for the treatment of HIV, which includes Sustiva, an antiretroviral drug, and bulk efavirenz, which is also included in the combination therapy, Atripla*.

- U.S. revenues decreased in 2015 due to lower demand resulting from increased competition partially offset by higher average net selling prices. U.S. revenues increased in 2014 due to higher average net selling prices partially offset by lower demand.
- International revenues decreased in both periods due to Sustiva's loss of exclusivity in Europe in November 2013, which continues to negatively impact demand, average net selling prices and Atripla* revenue sharing.

Empliciti - a humanized monoclonal antibody for the treatment of multiple myeloma.

- Empliciti was launched in the U.S. in December 2015.

Erbitux* — a monoclonal antibody designed to exclusively target and block the Epidermal Growth Factor Receptor, which is expressed on the surface of certain cancer cells in multiple tumor types as well as normal cells and is currently indicated for use in the treatment of patients with certain types of metastatic colorectal cancer and squamous cell carcinoma of the head and neck.

- U.S. revenues decreased in 2015 due to BMS transferring its rights to Erbitux* in North America to Eli Lilly and Company (Lilly) in October 2015. Refer to "Item 8. Financial Statements—Note 3. Alliances" for further discussion.

Opdivo — a fully human monoclonal antibody that binds to the programmed death receptor-1 (PD-1) on T and natural killer T (NKT) cells that has been approved and continues to be investigated as an anti-cancer treatment.

- U.S. revenues increased in 2015 due to the launch of Opdivo in December 2014 for the treatment of unresectable melanoma and subsequent approvals for additional indications in 2015, including in NSQ and SQ NSCLC and RCC, as well as the rapid commercial acceptance of Opdivo throughout the year. Refer to "—Significant Product and Pipeline Highlights" for further discussion on the additional Opdivo approvals in 2015.
- Opdivo was launched in Japan in September 2014 and was subsequently approved in the EU in June 2015 for the treatment of unresectable melanoma and in July 2015 for the treatment of advanced SQ NSCLC. Opdivo also was approved in other international markets in 2015.

Sprycel — an oral inhibitor of multiple tyrosine kinases indicated for the first-line treatment of adults with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase and the treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase chronic myeloid leukemia with resistance or intolerance to prior therapy, including Gleevec* (imatinib meslylate).

- U.S. revenues increased in both periods primarily due to higher demand.
- International revenues decreased in 2015 due to unfavorable foreign exchange partially offset by higher demand. International revenues increased in 2014 primarily due to higher demand partially offset by unfavorable foreign

exchange.

Yervoy — a monoclonal antibody for the treatment of patients with unresectable or metastatic melanoma.

- U.S. revenues decreased in 2015 due to lower demand resulting from the introduction of other immuno-oncology products being used to treat patients with melanoma, including Opdivo. U.S. revenues increased in 2014 due to higher demand.
- International revenues decreased in 2015 due to unfavorable foreign exchange. International revenues increased in 2014 due to higher demand.

Abilify* — an antipsychotic agent for the treatment of schizophrenia, bipolar mania disorder and major depressive disorder.

- U.S. revenues decreased in 2015 due to the expiration of our commercialization rights in April 2015. U.S. revenues increased in 2014 primarily due to higher average net selling prices partially offset by the reduction in our share of Abilify* revenues. BMS's share of Abilify* revenue was 50% in 2015, 33% in 2014 and 34% in 2013.
- International revenues decreased in both periods following the expiration of our EU commercialization rights in June 2014 and Otsuka Pharmaceutical Co., Ltd. becoming the principal for the end customer sales in certain markets.

Orencia — a fusion protein indicated for adult patients with moderate to severe active rheumatoid arthritis (RA) and is also indicated for reducing signs and symptoms in certain pediatric patients with moderately to severely active polyarticular juvenile idiopathic arthritis.

- U.S. revenues increased in both periods due to higher average net selling prices and demand.
- International revenues increased in both periods primarily due to higher demand for the subcutaneous formulation partially offset by unfavorable foreign exchange.

Eliquis — an oral Factor Xa inhibitor, targeted at stroke prevention in nonvalvular atrial fibrillation (NVAF) and the prevention and treatment of venous thromboembolic (VTE) disorders.

- U.S. and international revenues increased in both periods due to higher demand following the 2013 launches in most major markets for the reduction of the risk of stroke and systemic embolism for patients with NVAF and the treatment of VTE in 2014 in the U.S. and in 2015 in the EU. International revenues were also impacted by unfavorable foreign exchange.

Mature Products and All Other — includes all other products, including those which have lost exclusivity in major markets, the diabetes alliance products, over-the-counter brands and royalty revenue.

- U.S. revenues decreased in both periods primarily due to the diabetes business divestiture in February 2014.
- International revenues decreased in 2015 due to the expiration/transfer of certain licensing and royalty rights, the diabetes business divestiture in February 2014, unfavorable foreign exchange and continued generic erosion.
- International revenues decreased in 2014 due to the diabetes business divestiture and the continued generic erosion of other products partially offset by higher alliance revenues.

Estimated End-User Demand

Pursuant to the U.S. Securities and Exchange Commission (SEC) Consent Order described below under “—SEC Consent Order”, we monitor the level of inventory on hand in the U.S. wholesaler distribution channel and outside of the U.S. in the direct customer distribution channel. We are obligated to disclose products with levels of inventory in excess of one month on hand or expected demand, subject to a de minimis exception. Estimated levels of inventory in the distribution channel in excess of one month on hand for the following products were not material to our results of operations as of the dates indicated. No U.S. products had estimated levels of inventory in the distribution channel in excess of one month on hand at December 31, 2015. Below are international products that had estimated levels of inventory in the distribution channel in excess of one month on hand at September 30, 2015.

Dafalgan, an analgesic product sold principally in Europe, had 1.1 months of inventory on hand internationally at direct customers compared to 1.2 months of inventory on hand at June 30, 2015. The level of inventory on hand was primarily due to the ordering patterns of pharmacists in France.

Efferalgan, an analgesic product sold principally in Europe, had 1.4 months of inventory on hand internationally at direct customers at September 30, 2015 and June 30, 2015. The level of inventory on hand was primarily due to the ordering patterns of pharmacists in France and changes to our distribution model for over-the-counter products in Greece.

Fervex, a cold and flu product, had 2.9 months of inventory on hand at direct customers compared to 3.1 months of inventory on hand at June 30, 2015. The level of inventory on hand was primarily in Russia and France to support product seasonality.

Donormyl, a prescription sleeping aid, had 6.4 months of inventory on hand at direct customers compared to 4.8 months of inventory on hand at June 30, 2015. The level of inventory on hand was primarily in Russia and due to lower than expected demand from competitor pricing.

In the U.S., we generally determine our months on hand estimates using inventory levels of product on hand and the amount of out-movement provided by our three largest wholesalers, which account for approximately 95% of total gross sales of U.S. products. Factors that may influence our estimates include generic competition, seasonality of products, wholesaler purchases in light of increases in wholesaler list prices, new product launches, new warehouse openings by wholesalers and new customer stockings by wholesalers. In addition, these estimates are calculated using third-party data, which may be impacted by their recordkeeping processes.

For our businesses outside of the U.S., we have significantly more direct customers. Limited information on direct customer product level inventory and corresponding out-movement information and the reliability of third-party demand information, where available, varies widely. When direct customer product level inventory, ultimate patient/consumer demand or out-movement data does not exist or is otherwise not available, we have developed a variety of other methodologies to estimate such data, including using such factors as historical sales made to direct customers and third-party market research data related to prescription trends and end-user demand. Accordingly, we rely on a variety of methods to estimate direct customer product level inventory and to calculate months on hand. Factors that may affect our estimates include generic competition, seasonality of products, direct customer purchases in light of price increases, new product launches, new warehouse openings by direct customers, new customer stockings by direct customers and expected direct customer purchases for governmental bidding situations. As such, all of the information required to estimate months on hand in the direct customer distribution channel for non-U.S. business for the year ended December 31, 2015 is not available prior to the filing of this annual report on Form 10-K. We will disclose any product with levels of inventory in excess of one month on hand or expected demand, subject to a de minimis exception, in the next quarterly report on Form 10-Q.

Expenses

				% Change	
Dollar in Millions	2015	2014	2013	2015 vs. 2014	2014 vs. 2013
Cost of products sold	$3,909	$3,932	$4,619	(1)%	(15)%
Marketing, selling and administrative	4,841	4,822	4,939		