BRISTOL MYERS SQUIBB CO
Form 10-K
February 13, 2018

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

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FORM 10-K

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ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2017
Commission File Number 1-1136

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

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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

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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 ¨	Emerging growth company ¨

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ¨

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 1,638,694,099 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, 2017) was approximately $91,308,035,210. Bristol-Myers Squibb has no non-voting common equity. At February 1, 2018, there were 1,632,582,502 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 1, 2018, to be filed within 120 days after the conclusion of the registrant's fiscal year ended December 31, 2017, are incorporated by reference into Part III of this Annual Report on Form 10-K.

BRISTOL-MYERS SQUIBB COMPANY
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DECEMBER 31, 2017

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

PART I
Item 1. BUSINESS.

General

Bristol-Myers Squibb Company 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. Refer to the Summary of Abbreviated Terms at the end of this 2017 Form 10-K for terms used throughout the document.

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 U.S., Puerto Rico and in four foreign countries. Most of our revenues come from products in the following therapeutic classes: oncology; cardiovascular; immunoscience; and virology, including HIV infection.

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

	Year Ended December 31,					
Dollars in Millions	2017		2016		2015	
United States	55	%	55	%	49	%
Europe	24	%	22	%	21	%
Japan	7	%	7	%	10	%
Other	14	%	16	%	20	%
Total Revenues	$20,776		$19,427		$16,560	

Acquisitions and Divestitures

Acquisitions in the last five years include IFM in 2017, Cormorant and Padlock in 2016, Cardioxyl and Flexus in 2015 and iPierian in 2014 and we also entered into several license and other collaboration arrangements. Divestitures in the last five years include our small molecule manufacturing operations in Swords, Ireland in 2017, certain OTC brands and investigational HIV medicines businesses in 2016, Erbitux* in North America and certain mature and other OTC brands businesses in 2015 and our diabetes business in 2014. We also out-licensed our genetically defined disease investigational compounds in 2017. These transactions continue to allow us to focus our resources behind growth opportunities which drive the greatest long-term value.

Products, Intellectual Property and Product Exclusivity

Our pharmaceutical products include chemically-synthesized or small molecule drugs, and products produced from biological processes, 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 intravenous infusion.

Below is a product summary including approved indications. For information about our alliance arrangements for the products below, 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 PD-1 on T and NKT cells. Opdivo has received approvals for several anti-cancer indications including bladder, blood, colon, head and neck, kidney, liver, lung, melanoma and stomach. The Opdivo+Yervoy regimen also is approved in multiple markets for the treatment of melanoma. There are several ongoing potentially registrational studies for Opdivo across other tumor types and disease areas, in monotherapy and in combination with Yervoy and various anti-cancer agents.
Eliquis	Eliquis is an oral Factor Xa inhibitor targeted at stroke prevention in atrial fibrillation and the prevention and treatment of VTE disorders.

Orencia	Orencia, a biological product, is a fusion protein with novel immunosuppressive activity targeted initially at adult patients with moderately to severely active RA and PSA who have had an inadequate response to certain currently available treatments. Orencia is also indicated for certain pediatric patients with moderately to severely active polyarticular juvenile idiopathic arthritis.
Sprycel	Sprycel is a multi-targeted tyrosine kinase inhibitor approved for the first-line treatment of adults with Philadelphia chromosome-positive CML in chronic phase, 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) and the treatment of children with Philadelphia chromosome-positive CML in chronic phase.
Yervoy	Yervoy, a biological product, is a monoclonal antibody for the treatment of adults and pediatric patients with unresectable or metastatic melanoma, as well as the adjuvant treatment of patients with melanoma who have undergone complete resection.
Empliciti	Empliciti, a biological product, is a humanized monoclonal antibody for the treatment of multiple myeloma.
Baraclude	Baraclude is a potent and selective inhibitor of the hepatitis B virus.
Sustiva Franchise	The Sustiva Franchise includes Sustiva, a non-nucleoside reverse transcriptase inhibitor for the treatment of HIV, as well as bulk efavirenz which is included in the combination therapy Atripla*.
Reyataz Franchise	The Reyataz Franchise includes Reyataz, a protease inhibitor for the treatment of HIV, and combination therapy Evotaz combining Reyataz and Gilead's Tybost*.
Hepatitis C Franchise	Daklinza (daclatasvir (DCV)) is an oral small molecule NS5A replication complex inhibitor for the treatment of HCV.

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 and China.

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 data protection exclusivity 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 data protection exclusivity 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 provide a market exclusivity period on a product that expires beyond the patent term.

The U.S., EU and Japan each provide regulatory data protection, a 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. In

certain markets where patent protection and other forms of market exclusivity may have expired, regulatory 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 protection 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. 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 the impact of generic competition on our business, refer to "—Generic Competition".

Specific aspects of the law governing market exclusivity and data regulatory 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 due to regulatory review periods, the innovator may, depending on a number of factors, apply to the government to restore lost patent term by extending 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 product, the company files a NDA. If the medicine is a biological product, a BLA is filed. The type of application filed affects regulatory data protection exclusivity rights.

Chemical products

A competitor seeking to launch a generic substitute of a chemical innovative drug in the U.S. must file an 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 patent protection, certain innovative pharmaceutical products can receive periods of regulatory exclusivity. A 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 studies 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 a NDA can also receive several types of regulatory data protection. An innovative chemical pharmaceutical product is entitled to five years of regulatory data protection in the U.S., during which the FDA cannot approve 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 regulatory 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 studies, may receive three years of regulatory 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 an 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.

Rest of the World

In countries outside of the U.S., the EU and Japan, 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 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.

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 and Japan. 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 and Japan. 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 study 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.

	Total Revenues by Product			Estimated LOE		
Dollars in Millions	2017	2016	2015	U.S.	EU	Japan
Prioritized Brands						
Opdivo (nivolumab) [a]	$4,948	$3,774	$942	2027	2026	2031
Eliquis (apixaban) [b]	4,872	3,343	1,860	2026	2026	2026
Orencia (abatacept) [c]	2,479	2,265	1,885	2019	2017	2018
Sprycel (dasatinib) [d]	2,005	1,824	1,620	2020	^^	2021
Yervoy (ipilimumab) [e]	1,244	1,053	1,126	2025	2025	2025
Empliciti (elotuzumab) [f]	231	150	3	2027	2026	2024
Established Brands						
Baraclude (entecavir)	1,052	1,192	1,312	2014	2011-2016	2016
Sustiva (efavirenz) Franchise [g]	729	1,065	1,252	2017	2013	++
Reyataz (atazanavir sulfate) Franchise [h]	698	912	1,139	2017	2017-2019	2019
Hepatitis C Franchise [i]	406	1,578	1,603	2028	2027	2028

Note: The estimated year of basic LOE in the table above includes granted extensions such as patent term restoration (PTR) and/or six months pediatric extensions only if obtained. There may be other later-expiring patents that cover particular forms, compositions, methods of manufacturing, or methods of using the drug which may result in a favorable market position for our products, but product exclusivity cannot be predicted or assured. Regulatory data protection (RDP) may be obtained as described in more detail in the "—Products, Intellectual Property and Product Exclusivity" section. References to the EU throughout this Form 10-K include all EU member states during the year ended December 31, 2017. Basic patent applications may not have 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.

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

^^ In February 2017, the EPO Board of Appeal revoked the EU composition of matter (COM) patent. In February 2017, the EPO Board of Appeal reversed and remanded an invalidity decision to the use of dasatinib to treat CML, which the EPO's Opposition Division had revoked in October 2012. Refer to "Item 8. Financial Statements—Note 18. Legal Proceedings and Contingencies" for more information.

(a) Opdivo: BMS jointly owns a patent with Ono covering nivolumab as a COM that expires 2027 in the U.S. and 2026 in the EU. PTRs have been filed, and if granted, will expire in 2028 in the U.S. and 2030 in the EU. The COM patent covering nivolumab in Japan expires in 2031 including the granted PTR.

(b) Eliquis: The LOE above is based upon the COM patent and expires in 2026 in the U.S., EU and Japan, including the granted PTR. BMS received Paragraph IV certifications from twenty-five aNDA filers and initiated U.S. Hatch

Waxman patent litigation in April 2017. BMS has settled with several aNDA filers. In EU countries where there is no granted PTR, the COM patent expires in 2022.

(c) Orencia: The COM patent including PTR expires in 2019 in the U.S. and 2017 in the EU. In the U.S. and EU, the method of use patents covering all indications expire in 2021. In Japan, LOE is based on RDP exclusivity, which expires in 2018. Formulation and additional patents directed to abatacept expire in 2026 and beyond. BMS is not aware of an Orencia biosimilar on the market in the U.S., EU or Japan.

(d) Sprycel: In the U.S., the COM patent including PTR expires in June 2020. In 2013, BMS entered into a settlement agreement with Apotex regarding a patent infringement suit covering the monohydrate form of dasatinib whereby Apotex can launch its generic dasatinib monohydrate aNDA product in September 2024, or earlier in certain circumstances. In Japan, the COM patent expires in 2021 and RDP expires in 2019. For information on EU countries, see the above Footnote ^^.

(e) Yervoy: In the U.S. and Japan, the LOE is based on the COM patent which expires in 2025, including the granted PTRs. In the EU, the COM patent expires in 2025 including the PTR which has been granted in most countries; however, in countries in which the PTR has not been granted, the COM patent will expire in 2020. RDP expires in 2023 in the U.S. and 2021 in the EU.

(f) Empliciti: LOE period in the U.S., EU and Japan is based on RDP exclusivity. PTRs have been filed in the U.S., EU and Japan and if granted, will expire in 2029. BMS has a commercialization agreement with AbbVie for Empliciti. AbbVie owns a COM patent covering elotuzumab that expires in 2026 in the U.S. and 2024 in the EU and Japan (excluding potential PTRs). For more information about our arrangement with AbbVie, refer to "—Alliances" below and "Item 8. Financial Statements—Note 3. Alliances."

(g) Sustiva Franchise: Exclusivity period relates to the Sustiva brand and does not include exclusivity related to any combination therapy. In the U.S., the LOE for efavirenz occurred in December 2017.

(h) Reyataz: In the EU, the market exclusivity is projected to expire between 2017 and 2019. The COM patent including PTR expired in 2017 in the U.S. and expires in 2019 in the EU.

(i) Hepatitis C Franchise: Relates to products including daclatasvir, such as the Daklinza brand. In the U.S., the LOE is based on the COM patent expiry and if the pending PTR is granted, the expiry will be 2029. In Europe, the LOE is based on the COM patent expiry in 2027, however, the PTR, which has been granted in many countries, will expire in 2029. In Japan, the COM patent expires in 2028 including the granted PTR.

Research and Development

R&D is critical to our long-term competitiveness. We concentrate our R&D efforts in the following disease areas with significant unmet medical needs: oncology, including IO, immunoscience with priorities in lupus, RA and inflammatory bowel disease, cardiovascular with priority in heart disease and fibrotic disease with priorities in lung (IPF) and liver (NASH). 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 typically includes Phase I, Phase II and Phase III clinical studies that have been designed specifically to support a new drug application for a particular indication, assuming the studies are successful.

Phase I clinical studies involve a small number of healthy volunteers or patients suffering from the indicated disease to test for safety and proper dosing. Phase II clinical studies involve a larger patient population to investigate side effects, efficacy, and optimal dosage of the drug candidate. Phase III clinical studies 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. Although regulatory approval is typically based on the results of Phase III clinical studies, there are times when approval can be granted based on data from earlier studies.

We consider our registrational studies to be our significant R&D programs. These programs may include both investigational compounds in Phases II and III development for initial indications and marketed products that are in development for additional indications or formulations. Expanding our currently marketed products, particularly Opdivo in combination with Yervoy and other agents in both first and second-line therapy with new indications, is a substantial portion of our R&D program strategy.

Drug development is time consuming, expensive and risky. The R&D process typically takes about fourteen years, with approximately two and a half years often spent in Phase III, or late-stage, development. 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 2012-2016, approximately 92% of compounds that enter Phase I development fail to achieve regulatory approval. Compounds that enter Phase II development have a failure rate of approximately 80% while approximately 30% fail Phase III development.

Total R&D 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 licensing and acquiring assets. R&D expenses were $6.4 billion in 2017, $4.9 billion in 2016 and $5.9 billion in 2015 including license and asset acquisition charges of approximately $1.1 billion, $440 million and $1.7 billion in 2017, 2016 and 2015, respectively. At the end of 2017, we employed approximately 7,700 people in R&D and related support 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 R&D 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. Opdivo is the only individual investigational compound or marketed product to represent 10% or more of our R&D expenses in any of the last three years.

As part of our operating model evolution, our R&D geographic footprint will significantly transform to foster speed and innovation in the future. The transformation involves the closing of our Hopewell, New Jersey and Wallingford, Connecticut R&D sites accompanied by additional investment in the expansion and opening of others. For example, we are expanding our Lawrenceville, New Jersey and Redwood City, California sites and plan to open a new R&D facility in Cambridge, Massachusetts in 2018. We supplement our internal drug discovery and development programs with alliances and collaborative agreements which help us bring new molecular agents, capabilities and platforms into our pipeline. Management continues to emphasize leadership, innovation, productivity and quality as strategies for success in our R&D activities.

Listed below are our investigational compounds that we have in clinical studies as well as the approved and potential indications for our marketed products in the related therapeutic area as of January 1, 2018. Whether any of the listed compounds ultimately becomes a marketed product depends on the results of clinical studies, the competitive landscape of the potential product's market, reimbursement decisions by payers 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 which gets 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.

As of February 5, 2018, the following potential registrational study readouts for Opdivo are anticipated through 2019:

Tumor	Study Details	Tumor	Study Details
Non-Small Cell Lung Cancer	CM-227 - Opdivo + Yervoy (1st line) Part 1a	Head and Neck Cancer	CM-651 - Opdivo + Yervoy (1st line)
	CM-227 - Opdivo + Chemo (1st line) Part 2		CM-714 - Opdivo + Yervoy (1st line)
	CM-9LA - Opdivo + Yervoy + Chemo (1st line)		CM-331 - Opdivo (2nd line)
Hepatocellular Carcinoma	CM-459 - Opdivo (1st line)	Small Cell Lung Cancer	CM-451 - Opdivo +/- Yervoy (1st line Maintenance)
Gastric Cancer	CM-649 - Opdivo + Yervoy or Chemo (1st line)	Key	Phase II Phase III

Alliances

We enter into alliances with third parties that transfer rights to develop, manufacture, market and/or sell pharmaceutical products. These alliances include licensing, co-development, co-marketing and 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.

Our alliance arrangements contain customary early termination provisions following material breaches, bankruptcy 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.

We typically do not retain any rights to another party's product or 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 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 these alliance agreements as well as other alliance agreements.

Pfizer

BMS and Pfizer jointly develop and commercialize Eliquis. BMS recognizes net product sales in most markets. Worldwide profits and losses are shared equally except in certain countries where Pfizer commercializes Eliquis and pays BMS a sales-based fee.

Otsuka

BMS and Otsuka jointly promote Sprycel in the U.S. and EU. BMS recognizes net product sales and a sales-based fee is paid to Otsuka.

Ono

BMS has the exclusive right to develop, manufacture and commercialize Opdivo worldwide except Japan, South Korea and Taiwan. BMS recognizes net product sales and pays Ono royalties of 4% in North America and 15% in all other applicable territories excluding the three countries listed above, subject to customary adjustments.

BMS and Ono jointly develop and commercialize Opdivo, Yervoy and several BMS investigational compounds in Japan, South Korea and Taiwan. 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 jointly develop and 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 with assigned customer accounts and BMS is responsible for the product supply. A co-promotion fee of 60% is paid when a sale is made to the other party's assigned customer.

AbbVie

BMS and AbbVie jointly develop Empliciti. AbbVie funds 20% of global development costs. BMS is solely responsible for supply, distribution and sales and marketing activities and recognizes net product sales. AbbVie shares 30% of all profits and losses in the U.S. and is paid tiered royalties outside of the U.S.

Gilead

BMS and Gilead formed a joint venture to develop and commercialize Atripla* in the U.S., Canada and in Europe. BMS recognizes alliance revenue for the bulk efavirenz component of Atripla* upon sales of Atripla* to third-party customers.

In December 2017, Gilead terminated BMS's participation in the U.S. joint venture which included the U.S. and Canada markets following the launch of a generic version of Sustiva in the U.S. BMS will receive a sales based fee from Gilead on net sales of Atripla* in the U.S. in 2018, 2019 and 2020.

Other Licensing Arrangements

We have other in-licensing and out-licensing arrangements without active participation by both parties, including those obtained from our acquisitions. We are typically entitled to receive or obligated to pay contingent milestone payments as well as royalties, if and when the products are commercialized.

Marketing, Distribution and Customers

We promote the appropriate use of our products directly to healthcare professionals and organizations such as doctors, nurse practitioners, physician assistants, pharmacists, technologists, hospitals, PBMs and 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”.

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 potential additional uses of our products and provide such information as scientific exchange at scientific congresses or we share information about our products in other appropriate ways including the development of publications, or in response to unsolicited inquiries from doctors, other medical professionals and MCOs.

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 approved products or uses, as well as approved uses of 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, specialty distributors, and to a lesser extent, directly to distributors, retailers, hospitals, clinics, government agencies and pharmacies. Refer to “Item 8. Financial Statements—Note 2. Business Segment Information” for gross revenues to the three largest pharmaceutical wholesalers in the U.S. as a percentage of our global gross revenues.

Our U.S. business has DSAs with substantially all of our direct wholesaler and distributor customers that allow us to monitor U.S. wholesaler and distributor inventory levels and requires those wholesalers and distributors to maintain inventory levels that are no more than one month of their demand. The DSAs, including those with our three largest wholesalers, expired in December 2017. We have entered into letters of agreement with our three largest wholesalers and specialty distributor affiliates to both extend the current agreements through March 2018 and to enter into final agreements through December 31, 2020 prior to the expiration of the letters of agreement.

Our non-U.S. businesses have significantly more direct customers. Information on available direct customer product level inventory and corresponding out-movement information and the reliability of third-party demand information varies widely. We limit our direct customer sales channel inventory reporting to where we can reliably gather and report inventory levels from our customers.

In a number of countries outside of the U.S., we contract with distributors to support certain products. The services provided by these distributors vary by market, but may include distribution and logistics; regulatory and pharmacovigilance; and/or sales, advertising or promotion. Sales in these distributor-based countries represented approximately 1% of the Company's total revenues in 2017.

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 R&D 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, decreased volume of sales or both.

Advancements in treating cancer with IO therapies continue to evolve at a rapid pace. Our IO products, particularly Opdivo, operate in a highly competitive marketplace. In addition to competing for market share with other IO products in approved indications such as lung cancer and melanoma, we face increased competition from existing competing IO products that receive FDA approval for additional indications and for new IO agents that receive FDA approval and enter the market. Furthermore, as therapies combining different IO products or IO products with existing chemotherapy or targeted therapy treatments are investigated for potential expanded approvals, we anticipate that our IO products will continue to experience intense competition.

Another competitive challenge 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 studies 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 R&D 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 that product's revenue in a very short period of time.

After the expiration of exclusivity, the rate of revenues decline of a product 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 “—Products, Intellectual Property and Product Exclusivity”.

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

Pricing, Price Constraints and Market Access

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 creative platforms. We continue to explore new 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. We are also monitoring new state laws, such as laws that have recently been enacted in California, Vermont, Nevada and New York that are focused on drug

pricing transparency and/or limiting state spending on drugs. These laws could create new constraints on our ability to set prices and/or impact our market access in certain states.

The growth of MCOs, such as Optum (UHC), Silver Scripts (CVS) and Express Scripts (ESI) 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 studies 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.

In many markets outside the U.S., we operate in an environment of government-mandated, cost-containment programs. In these markets, a significant portion of funding for healthcare services and the determination of pricing and reimbursement for pharmaceutical products are subject to government control. As a result, our products may face restricted access by both public and private payers and may be subject to assessments of comparative value and effectiveness against competitive products. 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 Germany, the government does not set pricing restrictions at launch, but pricing freedom is subsequently limited. Companies may also face significant delays in market access for new products, mainly in France, Spain, Italy and Belgium, and more than a year 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.

Government Regulation

The pharmaceutical industry is subject to extensive global regulations by regional, country, state and local agencies. The Federal Food, Drug, and Cosmetic Act, other Federal statutes and regulations, various state statutes and regulations (including newly enacted state laws regulating drug price transparency and drug spending), 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.

The FDA is of particular importance 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 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 may be subject to a lengthy application process.

The distribution of pharmaceutical products is subject to the PDMA as part of the Federal Food, Drug, and Cosmetic 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.

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 safety related drug labeling changes, (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 studies 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 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, 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 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.

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 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% to 23.1% 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% 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. The amount of the annual fee imposed on pharmaceutical manufacturers as a whole was $4.0 billion in 2017. The 2018 fee is $4.1 billion, and will then decrease to $2.8 billion in 2019 and thereafter.

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 or EC approval 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.

For further discussion of these rebates and programs, refer to "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—GTN Adjustments" 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 significant pharmaceutical manufacturing facilities are located in the U.S., Puerto Rico, France and Italy and require significant ongoing capital investment for both maintenance and compliance with increasing regulatory requirements. In addition, as our product portfolio 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 in the startup phase of our new large-scale biologics manufacturing facility in Cruiserath, Ireland, which is expected to be operational in 2019.

We rely on third parties to manufacture or supply us with all or a portion of the active product ingredient or drug substance necessary for us to manufacture various products, such as Opdivo, Sprycel, Yervoy, Eliquis, Orencia, Baraclude, Reyataz and the Sustiva Franchise, and we continue to shift towards using third party manufactures for supply of our established brands. 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. Certain supply arrangements extend over multiple years with minimum purchase obligations determined using expected near or long-term demand requirements. As an additional protection, in some cases, we take steps to maintain an approved back-up source where available. For example, we have the capability to

manufacture Opdivo internally and also have arrangements with third-party manufacturers to meet demand.

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 records to demonstrate the quality and integrity of technical information and production processes.

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

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, which were not material for 2017, 2016 and 2015. 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 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 16 current or former facilities. We have also been identified as a PRP under applicable laws for environmental conditions at approximately 20 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 18. Legal Proceedings and Contingencies.”

Employees

We have approximately 23,700 employees as of December 31, 2017.

Foreign Operations

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

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.

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 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 2017 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 2018 Annual Meeting of Stockholders and 2017 Annual Report will be available on our website under the “Investors—SEC Filings” caption on or about March 22, 2018.

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.

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', IO products or late-stage compounds may cause significant volatility in our stock price and depending on the data, may result in an adverse impact on our business, financial condition or results of operation. If the development of any of our key IO compounds, whether alone or as part of a combination therapy, is delayed or discontinued or a clinical study does not meet one or more of its primary endpoints, our stock price could decline significantly and there may be an adverse impact on our business, financial condition or results of operations. We are focusing our efforts and resources in disease areas of high unmet need. With our more focused portfolio, investors are placing heightened scrutiny on some of our products or late-stage compounds. In particular, Opdivo is the backbone of our IO portfolio. During 2017, we announced multiple regulatory milestones for Opdivo, including the early stoppage of certain clinical studies for meeting their endpoints and label expansions for new indications. We have, however, also experienced setbacks and may continue to do so as there are further developments in our clinical studies. In 2018, we expect to receive further data from ongoing clinical studies including CheckMate-227, a combination study in the first-line lung cancer setting and decisions from health authorities regarding potential label expansions.

The announcement of data from our clinical studies, or those of our competitors, or news of any developments related to our, or our competitors', IO products or late-stage compounds, such as Opdivo, may cause significant volatility in our stock price and depending on the news, may result in an adverse impact on our business, financial condition or results of operation. Furthermore, the announcement of any negative or unexpected data or the discontinuation of development of any of our key IO 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, may cause our stock price to decline significantly and may have an adverse impact on our business, financial condition or results of operations. There is no assurance that data from our clinical studies will support filings for regulatory approval, or that our key IO compounds may prove to be effective or as effective as other competing compounds, or even if approved, that any of our key IO compounds will become commercially successful for all approved indications.

We depend on several key products for most of our revenues, cash flows and earnings.
We derive a majority of our revenue and earnings from several key products. Our six prioritized brands comprised approximately 75% of revenues in 2017. Growth products such as Opdivo and Eliquis represented, and are expected to increasingly represent, a significant part of our revenue, earnings and cash flows. A reduction in revenue from any of these products could adversely impact our earnings and cash flows. Also, if one of our major products were to become subject to issues such as loss of patent protection, significant changes in demand, formulary access changes, material product liability, unexpected side effects, regulatory proceedings, negative publicity or a significant advancement of competing products, we may incur an adverse impact on our business, financial condition, results of operation or trading price of our stock.

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. Furthermore, products or indications approved under the U.S. FDA's Accelerated Approval Program may be contingent upon verification and description of clinical benefit in confirmatory studies and such studies may not be successful. For example, when we announced we would not pursue an accelerated regulatory pathway for the combination of

Opdivo+Yervoy in lung cancer and when we reported negative results from CheckMate-026, we experienced negative impacts on our stock price in 2016. 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; and (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 are canceled or we believe their commercial prospects have been reduced, we may recognize material non-cash impairment charges for those programs. 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.

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) new competitive products entering the market, particularly in IO, (iii) lower prices for other companies' products, real or perceived superior efficacy (benefit) or safety (risk) profiles or other differentiating factors, (iv) technological advances and patents attained by our competitors, (v) clinical study results from our products or a competitor’s products that affect the value proposition for our products, (vi) business combinations among our competitors and major third-party payers and (vii) competing interests for external partnerships to develop and bring new products to markets. If we are unable to compete successfully against our competitors' products in the marketplace, this could have a material negative impact on our revenues and earnings.

Litigation claiming infringement of intellectual property may adversely affect our future revenues and operating earnings.
Third parties may claim that we infringe upon their intellectual property. Resolving an intellectual property infringement claim can be costly and time consuming and may require us to enter into license agreements, which may not be available on commercially reasonable terms. A successful claim of patent or other intellectual property infringement could subject us to significant damages or an injunction preventing the manufacture, sale, or use of the affected product or products. Any of these events could have a material adverse effect on our profitability and financial condition.

Adverse outcomes in other 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, (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 (ix) tax liabilities resulting from assessments from tax authorities.

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. For example, in February 2017 one of the EU patents for Sprycel was revoked by the Opposition Division of the EPO. We may experience a decline in European revenues upon the entry of generics into the market. Refer to "Item 8. Financial Statements—Note 18. Legal Proceedings and Contingencies" for further information. In some cases, manufacturers may seek regulatory approval by submitting their own clinical study 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 or that we assume when we provide our financial guidance. 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 MCOs, 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 MCOs and institutional and governmental purchasers; (ii) judicial decisions and changes in laws and regulations for federal healthcare programs such as Medicare and Medicaid, and other government actions and inquiries at both the federal and state level such as laws that have recently been enacted in California, Vermont, Nevada and New York that are focused on drug pricing transparency and/or limiting state spending on drugs; (iii) the potential impact of changes to pharmaceutical reimbursement, and increased pricing pressure from Medicare Part D formularies, Medicare Part B reimbursement rates to physicians 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 or failures to pay 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.

We are subject to a variety of U.S. and international laws and regulations.
We are currently subject to a number of government laws and regulations and in the future, could become subject to new government laws and regulations. The costs of compliance with such laws and regulations, or the negative results of non-compliance, could adversely affect our business, our operating results and the financial condition of our Company; these include (i) additional healthcare reform initiatives in the U.S. or in other countries, including additional mandatory discounts or fees; (ii) new laws, regulations and judicial or other governmental decisions affecting pricing, drug reimbursement, receivable payments, and access or marketing within or across jurisdictions; (iii) changes in intellectual property law; (iv) changes in accounting standards; (v) new and increasing data privacy regulations and enforcement, particularly in the European Union and the U.S.; (vi) emerging and new global regulatory requirements for reporting payments and other value transfers to healthcare professionals; and (vii) the potential impact of importation restrictions, legislative and/or other regulatory changes.

Changes to tax regulations could negatively impact our earnings.
We are subject to income taxes in the U.S. and various other countries globally. In particular, although the passage of the Tax Cut and Jobs Act of 2017 reduced the U.S. tax rate to 21%, our future earnings could be negatively impacted by changes in tax legislation including changing tax rates and tax base such as limiting, phasing-out or eliminating deductions or tax credits, taxing certain excess income from intellectual property, changing rules for earnings repatriations and changing other tax laws in the U.S. or other countries. In addition, the one-time deemed repatriation tax of approximately $2.6 billion will be payable over the next eight years.

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 the divestiture of our Erbitux* and diabetes businesses (including the transfer of certain future royalty rights pertaining to Amylin, Onglyza* and Farxiga* product sales), our Sanofi alliance, out-licensed intellectual property and the Merck patent infringement settlement. Pretax income generated from royalties were approximately $1.2 billion in 2017 and is expected to increase in 2018. Our pretax income could be adversely affected if the royalty streams decline in future periods.

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The failure of third parties to meet their contractual, regulatory, and other obligations could adversely affect our business.

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, IT and other business unit and functional services, and meet their contractual, regulatory and other obligations. Using these third parties poses a number of risks, such as: (i) they may not perform to our standards or legal requirements, for example, in relation to the outsourcing of significant clinical development activities for innovative medicines to some contract research organizations; (ii) they may not produce reliable results; (iii) they may not perform in a timely manner; (iv) they may not maintain confidentiality of our proprietary information; (v) they may incur a significant cyberattack or business disruption; (vi) disputes may arise with respect to ownership of rights to technology developed with our partners; and (vii) disagreements could cause delays in, or termination of, the research, development or commercialization of the product or result in litigation or arbitration. Moreover, 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 our 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, UK 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.

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

Our strategy is focused on delivering innovative, transformational medicines to patients. If we are unable to successfully execute on this strategy, this could negatively impact our future results of operations and market capitalization. In connection with this strategy, we are in the process of evolving our operating model to focus on investment in commercial opportunities against key brands and markets, accelerate the pipeline, streamline operations and realign manufacturing capabilities that broaden biologics capabilities, among other things. Our ability to successfully execute our operating model evolution could impact our results. If we are not able to achieve the cost savings we expect, this could negatively impact our operating margin and earnings results. In addition, we may be unable to consistently maintain an adequate 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. 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 from our operating model evolution 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 R&D, 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.

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.

An essential component of our strategy has been business development activities seeking to source innovation externally to supplement our own discovery and development efforts. As such, we have acquired, or in-licensed, a

number of assets and we expect to 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 low 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. For example we discontinued the development of FS102 which was in Phase I development for the treatment of breast and gastric cancer, and consequently did not exercise our option to purchase F-Star Alpha. As a result, we recorded an IPRD charge of $75 million. 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; and (iii) tax considerations.

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 cGMP 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 and with required quality; (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 disasters, acts of war or terrorism or other external factors over which we have no control impacting one or more of our facilities or at a critical supplier. For example, our new biologics manufacturing facility in Cruiserath, Ireland is expected to be operational in 2019. A delay in the planned opening of the site could impact the supply of our products or require us to obtain product supply from third parties at a significant cost.

Our manufacturing and commercial operations in Puerto Rico were impacted by the recent hurricanes. Our two manufacturing sites sustained some damage but are currently operating at reduced capacity. We continue to work to restore to normal operations. Disruption in our ability to operate our Puerto Rico manufacturing facilities (whether due to problems with the facility itself, the infrastructure and services available on the island, the unavailability of raw materials or supplies from vendors, the unavailability of key staff or otherwise) could materially and adversely affect our ability to supply our products and affect our product sales.

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 studies, 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 studies, could affect a product's formulary listing, which could also adversely affect revenues.

The illegal distribution and sale by third parties of counterfeit or unregistered versions of our products or stolen products could have a negative impact on our revenues, earnings, 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. 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. In addition, diversion of products from their authorized market into other channels may result in reduced revenues and negatively affect our profitability.

We are dependent on information technology and our systems and infrastructure face certain risks, including from cybersecurity breaches and data leakage.

We rely extensively on IT systems, networks and services, including internet sites, data hosting and processing facilities and tools, physical security systems and other hardware, software and technical applications and platforms, some of which are managed, hosted provided and/or used for third-parties or their vendors, to assist in conducting our business. 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, or our third-party providers', systems, 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 as cybersecurity threats have been rapidly evolving in sophistication and becoming more prevalent in the industry. We have invested in industry appropriate protections and monitoring practices of our data and IT to reduce these risks and continue to monitor our systems on an ongoing basis for any current or potential threats. We maintain cyber insurance, however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. There can be no assurance that our continuing efforts will prevent breakdowns or breaches to our or our third-party providers’ databases or systems that could adversely affect our business.

Adverse changes in U.S., global, regional, local economic and political conditions could adversely affect our profitability.

Global economic and political risks pose significant challenges to a company’s growth and profitability and are difficult to mitigate. We generated approximately 45% of our revenues outside of the U.S. in 2017. As such, our revenues, earnings and cash flow are exposed to risk from a strengthening U.S. dollar. 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. We have significant operations in Europe, including for manufacturing and distribution. The results of our operations could be negatively impacted by any member country exiting the eurozone monetary union or EU, including the planned exit of the UK from the EU. Of note, the exit of the UK from the EU may have an impact on our research, commercial and general business operations in the UK and the EU. In addition, future pension plan funding requirements continue to be sensitive to global economic conditions and the related impact on equity markets. Additionally, disruptions in the credit markets or a downgrade of our current credit rating could increase our future borrowing costs and impair our ability to access capital and credit markets on terms commercially acceptable to us, which could adversely affect our liquidity and capital resources or significantly increase our cost of capital. Finally, our business, operations may be adversely affected by political volatility, conflicts or crises in individual countries or regions, including terrorist activities or war.

There can be no guarantee that we will pay dividends or repurchase stock.

The declaration, amount and timing of any dividends fall within the discretion of our Board of Directors. The Board's decision will depend on many factors, including our financial condition, earnings, capital requirements, debt service obligations, industry practice, legal requirements, regulatory constraints and other factors that our Board of Directors may deem relevant. A reduction or elimination of our dividend payments or dividend program could adversely affect our stock price. In addition, we could, at any time, decide not to buy back any more shares in the market, which could also adversely affect our stock price.

Increased use of social media platforms present risks and challenges.

We are increasing our use of social media to communicate Company news and events. 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.

Item 1B. UNRESOLVED STAFF COMMENTS.

None.

Item 2. PROPERTIES.

Our principal executive offices are located at 345 Park Avenue, New York, NY. We own or lease manufacturing, R&D, administration, storage and distribution facilities at approximately 160 sites worldwide. We believe our manufacturing properties, in combination with our third-party manufacturers, provide adequate production capacity for our current operations. For further information about our manufacturing properties, refer to “Item 1. Business—Manufacturing and Quality Assurance."

Our significant manufacturing and R&D locations by geographic area were as follows at December 31, 2017:

	Manufacturing	R&D
United States	4	5
Europe	2	2
Total	6	7

Item 3. LEGAL PROCEEDINGS.

Information pertaining to legal proceedings can be found in “Item 8. Financial Statements—Note 18. 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 13, 2018. 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. Executive officers serve at the discretion of the Board of Directors.

Name and Current Position	Age	Employment History for the Past 5 Years
Giovanni Caforio, M.D. Chairman of the Board and Chief Executive Officer Member of the Leadership Team	53	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 2017 – Chief Executive Officer and Director of the Company 2017 to present – Chairman of the Board and Chief Executive Officer
Charles A. Bancroft Chief Financial Officer and Executive Vice President, Global Business Operations Member of the Leadership Team	58	2011 to 2016 - Chief Financial Officer and Executive Vice President, Global Services 2016 to present - Chief Financial Officer and Executive Vice President, Global Business Operations
Joseph C. Caldarella Senior Vice President and Corporate Controller	62	2010 to present – Senior Vice President and Corporate Controller
John E. Elicker Senior Vice President, Corporate Affairs and Investor Relations Member of the Leadership Team	58	2012 to 2017 – Senior Vice President, Public Affairs and Investor Relations 2017 to present – Senior Vice President, Corporate Affairs and Investor Relations
Murdo Gordon Executive Vice President, Chief Commercial Officer Member of the Leadership Team	51	2011 to 2013 – Senior Vice President, Oncology and Immunology 2013 to 2015 – President, U.S. Pharmaceuticals 2015 to 2016 – Senior Vice President, Head of Worldwide Markets 2016 to present – Executive Vice President, Chief Commercial Officer
Ann Powell Judge Senior Vice President, Chief Human Resources Officer Member of the Leadership Team	52	2009 to 2013 – Chief Human Resources Officer, Shire Pharmaceuticals 2013 to 2016 – Senior Vice President, Global Human Resources 2016 to present – Senior Vice President, Chief Human Resources Officer
Sandra Leung Executive Vice President, General Counsel Member of the Leadership Team	57	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, General Counsel
Thomas J. Lynch., M.D. Executive Vice President and Chief Scientific Officer Member of the Leadership Team	57	2017 to present – Executive Vice President and Chief Scientific Officer

Louis S. Schmukler Senior Vice President & President, Global Product Development and Supply Member of the Leadership Team	62	2011 to 2017 – President, Global Product Development and Supply 2017 to present – Senior Vice President & President, Global Product Development and Supply
Paul von Autenried Senior Vice President, Chief Information Officer Member of the Leadership Team	56	2012 to 2016 – Senior Vice President, Enterprise Services and Chief Information Officer 2016 to present – Senior Vice President, 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 (Symbol: BMY). A quarterly summary of the high and low closing market price is presented below:

	2017		2016	
	High	Low	High	Low
Common:				
First Quarter	$60.13	$46.82	$68.35	$58.87
Second Quarter	57.33	51.66	74.29	64.91
Third Quarter	63.74	54.24	76.77	53.87
Fourth Quarter	65.35	59.94	59.61	49.23

Holders of Common Stock

The number of record holders of common stock at December 31, 2017 was 41,402.

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	
	2017	2016	2017	2016
First Quarter	$0.39	$0.38	$0.50	$0.50
Second Quarter	0.39	0.38	0.50	0.50
Third Quarter	0.39	0.38	0.50	0.50
Fourth Quarter	0.39	0.38	0.50	0.50
	$1.56	$1.52	$2.00	$2.00

In December 2017, our Board of Directors declared a quarterly dividend of $0.40 per share on our common stock which was paid on February 1, 2018 to shareholders of record as of January 5, 2018. The Board of Directors also declared a quarterly dividend of $0.50 per share on our preferred stock, payable on March 1, 2018 to shareholders of record as of February 6, 2018.

UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

The following table summarizes the surrenders of our equity securities during the three months ended December 31, 2017:

Period	Total Number of Shares Purchased[a]	Average Price Paid per Share[a]	Total Number of Shares Purchased as Part of Publicly Announced Programs[b]	Approximate Dollar Value of Shares that May Yet Be Purchased Under the Programs[b]
Dollars in Millions, Except Per Share Data				
October 1 to 31, 2017	1,498,834	$ 63.02	1,491,785	$ 1,818

November 1 to 30, 2017	1,444,201	$ 61.85	1,434,937	$ 1,729
December 1 to 31, 2017	1,121,513	$ 62.11	1,099,102	$ 1,661
Three months ended December 31, 2017	4,064,548		4,025,824	

(a) Includes shares repurchased as part of publicly announced programs and 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 and in June 2012 increased its authorization for the repurchase of common stock by an additional $3.0 billion. In October 2016, the Board of Directors approved a new share repurchase program authorizing the repurchase of an additional $3.0 billion of common stock. The stock repurchase program does not have an expiration date.

Item 6. SELECTED FINANCIAL DATA.

Five Year Financial Summary

Amounts in Millions, except per share data	2017	2016	2015	2014	2013
Income Statement Data:[a]					
Total Revenues	$20,776	$19,427	$16,560	$15,879	$16,385
Net Earnings	975	4,507	1,631	2,029	2,580
Net Earnings/(Loss) Attributable to:					
Noncontrolling Interest	(32)	50	66	25	17
BMS	1,007	4,457	1,565	2,004	2,563
Net Earnings per Common Share Attributable to BMS:					
Basic	$0.61	$2.67	$0.94	$1.21	$1.56
Diluted	$0.61	$2.65	$0.93	$1.20	$1.54
Average common shares outstanding:					
Basic	1,645	1,671	1,667	1,657	1,644
Diluted	1,652	1,680	1,679	1,670	1,662
Cash dividends paid on BMS common and preferred stock	$2,577	$2,547	$2,477	$2,398	$2,309
Cash dividends declared per common share	$1.57	$1.53	$1.49	$1.45	$1.41
Financial Position Data at December 31:					
Cash and cash equivalents	$5,421	$4,237	$2,385	$5,571	$3,586
Marketable securities[b]	3,871	4,832	6,545	6,272	4,686
Total Assets	33,551	33,707	31,748	33,749	38,592
Long-term debt[b]	6,975	6,465	6,550	7,242	7,981
Equity	11,847	16,347	14,424	14,983	15,236

(a) For a discussion of items that affected the comparability of results for the years 2017, 2016 and 2015, 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 is a global specialty biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. Refer to the Summary of Abbreviated Terms at the end of this 2017 Form 10-K for terms used throughout the document.

In 2017, we received 15 approvals for new medicines and additional indications and formulations of currently marketed medicines in major markets (the U.S., EU, Japan and China) including multiple regulatory milestone achievements for Opdivo. We are committed to investigating Opdivo alone and in combination with Yervoy and other anti-cancer agents for a wide array of tumor types, including broad programs in lung, head & neck, liver, kidney, bladder and gastric. We continue to believe that the breadth and depth of our IO portfolio positions us well for the future. We have 17 new IO compounds in clinical development and studies across more than 35 different tumor types. In addition, we advanced certain other non-IO R&D programs in our pipeline, including FGF21 for the treatment of NASH and TYK-2 inhibitor for the treatment of immune diseases such as psoriasis. We also continued to progress our company transformation initiatives enabling us to invest in our highest priority portfolio opportunities.

In 2017, our revenues increased 7% as a result of higher demand for our prioritized brands including Opdivo and Eliquis partially offset by increased competition for established brands, primarily Daklinza. The $2.04 decrease in GAAP EPS was due to tax charges attributed to tax reform ($1.76 per share) and to a lesser extent higher license, asset acquisition and restructuring related charges and lower divestiture- related income. These items were partially offset by higher revenues, royalties and licensing income and a patent-infringement settlement. After adjusting for the impact of tax reform and other specified items, non-GAAP EPS increased $0.18 primarily as a result of higher revenues partially offset by product mix and higher R&D expenses supporting Opdivo and other IO programs.

In 2016, our revenues increased 17% as a result of higher demand for our prioritized brands including Opdivo and Eliquis partially offset by the expiration of our U.S. commercialization rights to Abilify*, the transfer of Erbitux* rights in North America and increased competition for Reyataz, Sustiva and Baraclude in certain markets. The $1.72 increase in GAAP EPS was due to higher revenues, divestiture-related income and lower license and asset acquisition charges partially offset by higher Opdivo related expenses. After adjusting for the impact of divestiture gains, R&D license and asset acquisition charges and other specified items, non-GAAP EPS increased by $0.82 primarily as a result of higher revenues partially offset by product mix.

Highlights

The following table summarizes our financial information:

	Year Ended December 31,		
Dollars in Millions, except per share data	2017	2016	2015
Total Revenues	$20,776	$19,427	$16,560
Diluted Earnings Per Share			
GAAP	0.61	2.65	0.93
Non-GAAP	3.01	2.83	2.01

Our non-GAAP financial measures, including non-GAAP earnings and related EPS information, are adjusted to exclude specified items that 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

The following is a summary of the 15 significant approvals received in 2017.

Product	Date	Approval
Opdivo	December 2017	FDA approval of injection for intravenous use for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.
	September 2017	FDA approval for the treatment of patients with HCC, a type of liver cancer, who have been previously treated with sorafenib.
		Approval in Japan for the treatment of unresectable advanced or recurrent gastric cancer which has progressed after chemotherapy, received by our alliance partner, Ono.
	August 2017	FDA approval for the treatment of adult and pediatric patients with MSI-H or dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin and irinotecan.
	June 2017	EC approval for the treatment of patients with previously treated locally advanced unresectable or metastatic urothelial carcinoma, a type of bladder cancer, in adults after failure of platinum-containing therapy.
	April 2017	EC approval for the treatment of SCCHN in adults progressing on or after platinum-based therapy.
	March 2017	Approval in Japan for the treatment of recurrent or metastatic HNC, received by our alliance partner, Ono.
	February 2017	FDA approval for the treatment of patients with previously treated locally advanced or metastatic urothelial carcinoma.
Orencia	July 2017	EC approval for the treatment of active PsA in adults for whom the response to previous disease-modifying antirheumatic drug therapy, including methotrexate, has been inadequate, and additional systemic therapy for psoriatic skin lesions is not required.
		FDA approval for the treatment of active PsA in adults.
	March 2017	FDA approval of a new subcutaneous administration option for use in patients two years of age and older with moderately to severely active polyarticular JIA.
Sprycel	November 2017	FDA expanded the indication for Sprycel tablets to include the treatment of children with Philadelphia chromosome-positive CML in chronic phase.
Yervoy	July 2017	FDA approval of an expanded indication for the treatment of unresectable or metastatic melanoma in pediatric patients.
Hepatitis C Franchise	April 2017	China FDA approval of the Daklinza and Sunvepra regimen for treatment-naive or experienced patients infected with genotype 1b chronic HCV. In addition, Daklinza was approved in China for combination use with other agents, including sofosbuvir, for adult patients with HCV genotypes 1-6 infection.

Refer to "—Product and Pipeline Developments" for all of the developments in our marketed products and late-stage pipeline in 2017 and in early 2018.

Strategy

Our focus as a specialty biopharmaceutical company is on discovering, developing and delivering transformational medicines that address serious unmet medical needs. Our strategy is to combine the resources, scale and capability of a pharmaceutical company with the speed and focus on innovation of the biotech industry. Our four strategic priorities are to drive business performance, continue to build a leading franchise in IO, maintain a diversified portfolio both within and outside of IO, and continue our disciplined approach to capital allocation, including establishing partnerships, collaborations and in-licensing or acquiring investigational compounds as an essential component of successfully delivering transformational medicines to patients.

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We are developing new medicines in the following core therapeutic areas: (1) oncology with a priority in IO; (2) immunoscience with priorities in lupus, rheumatoid arthritis and inflammatory bowel disease; (3) cardiovascular with a priority in heart disease and; (4) fibrotic disease with priorities in lung and liver. We continue to advance the next wave of innovative medicines by investing significantly in our pipeline both internally and through business developments activities. In IO, we continue to invest in monotherapy studies, combination approaches, and our next wave of early assets. We have entered into several collaboration agreements and expanded others to research and develop Opdivo and other approved or investigational oncology agents in combination regimens. We remain focused and well-resourced in our cancer development programs and seek to broaden the use of Opdivo in earlier lines of therapy, expand into new tumors, accelerate next wave IO mechanisms and develop treatment options for refractory IO patients. Beyond cancer, we continue to advance our early stage portfolio in immunoscience, cardiovascular, and fibrotic diseases and strengthen our partnerships with a diverse group of companies and academic institutions in new and expanded research activities. We believe our differentiated internal and external focus contributes to the advancing of our pipeline of potentially transformational medicines.

Our commercial model has been evolving and revenues from our marketed product portfolio continue to grow which demonstrates strong execution of our strategy. We continue to drive growth of Opdivo by expanding into additional indications and tumor types both as a monotherapy and in combination with Yervoy and other anti-cancer agents. Eliquis continues to grow, leveraging its best in class clinical profile and extensive real world data, and is now the number one novel oral anticoagulant in total prescriptions in the U.S. We are building on the continued success of our other prioritized brands and remain strongly committed to Orencia and Sprycel. Through our operating model transformation, our commercial infrastructure is uniquely leveraged for potential growth.

Our operating model continues to evolve and we have been successful in focusing commercial and R&D resources on prioritized brands and markets, strengthening our R&D capabilities in tumor biology, patient selection, and new biomarkers, delivering leaner administrative functions and streamlining our manufacturing network to reflect the importance of biologics in our current and future portfolio. The evolution in our operating model will enable us to deliver the necessary strategic, financial and operational flexibility to invest in the highest priority opportunities within our portfolio.

Looking ahead, we will continue to implement our biopharma strategy by driving the growth of key brands, executing product launches, investing in our diverse and innovative pipeline, aided by strategic 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 arrangements 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, including IO, immunoscience, cardiovascular and fibrosis. Significant arrangements during the past three years are summarized below. Refer to "Item 8. Financial Statements—Note 4. Acquisitions, Divestitures and Licensing Arrangements" for further information.

2017 Arrangements

Ono: BMS acquired an exclusive license to develop and commercialize ONO-4578, Ono’s Prostaglandin E2 receptor 4 antagonist for the treatment of cancer. BMS acquired worldwide rights except in Japan, South Korea, and Taiwan where it was added to the existing collaboration and in China and ASEAN countries where Ono retained exclusive rights.

Halozyme: BMS and Halozyme entered into a global collaboration and license agreement to develop subcutaneously administered BMS IO medicines using Halozyme's ENHANZE* drug-delivery technology which may allow for more rapid delivery of large volume injectable medications.

IFM: BMS acquired all of the outstanding shares of IFM providing BMS with full rights to IFM's preclinical STING and NLRP3 agonist programs focused on enhancing the innate immune response for treating cancer.
Biogen: BMS out-licensed to Biogen exclusive rights to develop and commercialize BMS-986168, an anti-eTau compound in development for Progressive Supranuclear Palsy.
Roche: BMS out-licensed to Roche exclusive rights to develop and commercialize BMS-986089, an anti-myostatin adnectin in development for Duchenne Muscular Dystrophy.
CytomX: BMS and CytomX expanded their initial 2014 strategic collaboration to discover novel cancer treatment therapies that will include up to eight additional targets using CytomX’s proprietary Probody platform for the treatment of cancer.

2016 Arrangements

PsiOxus: BMS acquired exclusive worldwide rights to PsiOxus's NG-348, a pre-clinical stage, "armed" oncolytic virus with the goal of addressing solid tumors.

Padlock: BMS acquired all of the outstanding shares of Padlock providing BMS with full rights to Padlock’s PAD inhibitor discovery program focused on the development of treatment approaches for patients with rheumatoid arthritis.

Cormorant: BMS acquired all of the outstanding shares of Cormorant providing BMS with full rights to Cormorant's lead candidate HuMax-IL8, a monoclonal antibody that represents a potentially complementary IO mechanism of action to T-cell directed antibodies and co-stimulatory molecules.

Nitto Denko: BMS acquired an exclusive worldwide license to develop and commercialize Nitto Denko's investigational siRNA molecules targeting heat shock protein 47 (HSP47) in vitamin A containing formulations including Nitto Denko's lead asset ND-L02-s0201, currently in development for the treatment of advanced liver fibrosis, and the option to receive exclusive licenses for HSP47 siRNAs in vitamin A containing formulations for the treatment of lung and other organ fibrosis.

2015 Arrangements

Flexus: BMS acquired all of the outstanding shares of Flexus providing 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 included its IDO-selective, IDO/TDO dual and TDO-selective compounds.

Cardioxyl: BMS acquired all of the outstanding shares of Cardioxyl providing BMS with full rights to CXL-1427, a nitroxyl prodrug in development for acute decompensated heart failure.

Five Prime: BMS and Five Prime entered into an exclusive worldwide licensing and collaboration agreement to develop and commercialize Five Prime’s CSF1R antibody program, including cabiralizumab currently in development for IO indications and PVNS. BMS is responsible for the development, manufacturing and commercialization of cabiralizumab, subject to Five Prime’s option to conduct certain studies at its cost to develop cabiralizumab in PVNS and in combination with its own internal oncology pipeline assets.

Promedior: BMS acquired a warrant providing BMS exclusive rights to acquire Promedior, whose lead asset, PRM-151, is being developed for the treatment of IPF and MF. The warrant is exercisable upon being provided data following completion of either of the IPF or MF Phase II clinical studies being directed by Promedior.

Bavarian Nordic: BMS 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. In 2017, an independent Data Monitoring Committee determined that the continuation of the Phase III PROSPECT study of Prostvac* in patients with metastatic castration-resistant prostate cancer is futile.

uniQure: BMS entered into a collaboration and license agreement with uniQure granting BMS an exclusive license to uniQure’s gene therapy technology platform for up to 10 specific collaboration targets. 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.

RESULTS OF OPERATIONS

Regional Revenues

The composition of the changes in revenues was as follows:

	Year Ended December 31, Total Revenues			2017 vs. 2016 Analysis of % Change		2016 vs. 2015 Analysis of % Change	
Dollars in Millions	2017	2016	2015	Total Change	Foreign Exchange[b]	Total Change	Foreign Exchange[b]
United States	$11,358	$10,720	$8,188	6 %	—	31 %	—
Europe	4,988	4,215	3,491	18 %	1 %	21 %	(2)%
Rest of the World	3,877	3,964	4,142	(2)%	—	(4)%	(4)%
Other[a]	553	528	739	5 %	N/A	(29)%	N/A
Total	$20,776	$19,427	$16,560	7 %	—	17 %	(2)%

(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.

U.S. revenues increased in 2017 due to higher demand for Eliquis and Opdivo partially offset by lower demand for established brands due to increased competition, primarily Daklinza and HIV brands. The lower growth rate in the U.S. was due to additional competition for Opdivo and Daklinza. Average U.S. net selling prices were approximately 2% higher after charge-backs, rebates and discounts. Refer to "—Product Revenues Commentary" for additional information.

U.S. revenues increased in 2016 due to higher demand for Opdivo, Eliquis and Daklinza, partially offset by the full year impact of the expiration/transfer of commercialization rights to Abilify* and Erbitux*. Average U.S. net selling prices were approximately 5% higher after charge-backs, rebates and discounts.

Europe revenues increased in 2017 due to higher demand for Opdivo and Eliquis partially offset by lower demand for Daklinza due to increased competition. Europe revenues increased in 2016 due to higher demand for Opdivo and Eliquis partially offset by lower demand for Yervoy.

Rest of the World revenues decreased in 2017 due to lower demand for established brands, including Daklinza, due to increased competition and out-licensing of a mature brand product, partially offset by higher demand for Opdivo and Eliquis. Rest of the World revenues decreased in 2016 due to increased competition for the Hepatitis C Franchise in Japan and unfavorable foreign exchange (primarily Latin America) partially offset by higher demand for Opdivo and Eliquis.

Other revenues decreased in 2016 as a result of the expiration of certain supply arrangements. 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 except for Japan which contributed 10% of total revenues in 2015.

GTN Adjustments

We recognize revenue net of GTN adjustments that are further described in "—Critical Accounting Policies". Our share of certain Abilify* and Atripla* revenues is reflected net of all GTN adjustments in alliance and other revenues.

The activities and ending reserve balances for each significant category of GTN adjustments were as follows:

Dollars in Millions	Charge-Backs and Cash Discounts	Medicaid and Medicare Rebates	Other Rebates, Returns, Discounts and Adjustments	Total
Balance at January 1, 2016	$ 97	$ 434	$ 890	$1,421
Provision related to sale made in:				
Current period	1,582	1,438	1,797	4,817
Prior period	—	(56)	(99)	(155)
Payments and returns	(1,553)	(1,296)	(1,397)	(4,246)
Foreign currency translation and other	—	—	(31)	(31)
Balance at December 31, 2016	$ 126	$ 520	$ 1,160	$1,806
Provision related to sale made in:				
Current period	2,087	2,090	2,135	6,312
Prior period	(3)	(4)	(64)	(71)
Payments and returns	(2,004)	(1,810)	(2,107)	(5,921)
Foreign currency translation and other	3	—	104	107
Balance at December 31, 2017	$ 209	$ 796	$ 1,228	$2,233

The reconciliation of gross product sales to net product sales by each significant category of GTN adjustments was as follows (excluding alliance and other revenues such as Abilify* and Atripla*):

	Year Ended December 31,			% Change	
Dollars in Millions	2017	2016	2015	2017 vs. 2016	2016 vs. 2015
Gross product sales	$25,499	$22,364	$17,166	14%	30 %
GTN Adjustments					
Charge-backs and cash discounts	(2,084)	(1,582)	(1,043)	32%	52 %
Medicaid and Medicare rebates	(2,086)	(1,382)	(859)	51%	61 %
Other rebates, returns, discounts and adjustments	(2,071)	(1,698)	(1,219)	22%	39 %
Total GTN Adjustments	(6,241)	(4,662)	(3,121)	34%	49 %
Net product sales	$19,258	$17,702	$14,045	9 %	26 %
GTN adjustments percentage	24 %	21 %	18 %	3 %	3 %
U.S.	31 %	26 %	25 %	5 %	1 %
Non-U.S.	13 %	13 %	11 %	—	2 %

GTN adjustments are primarily a function of product sales volume, regional and payer channel mix, contractual or legislative discounts and rebates. GTN adjustments are increasing at a higher rate than gross product sales due to higher U.S. Eliquis gross product sales, which has a relatively high GTN adjustment percentage as a result of competitive pressures to maintain its position on healthcare payer formularies allowing patients continued access through their medical plans.

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Product Revenues

Dollars in Millions	Year Ended December 31, 2017	2016	2015	% Change 2017 vs. 2016	2016 vs. 2015
Prioritized Brands					
Opdivo	$4,948	$3,774	$ 942	31 %	**
U.S.	3,102	2,664	823	16 %	**
Non-U.S.	1,846	1,110	119	66 %	**
Eliquis	4,872	3,343	1,860	46 %	80 %
U.S.	2,887	1,963	1,023	47 %	92 %
Non-U.S.	1,985	1,380	837	44 %	65 %
Orencia	2,479	2,265	1,885	9 %	20 %
U.S.	1,704	1,532	1,271	11 %	21 %
Non-U.S.	775	733	614	6 %	19 %
Sprycel	2,005	1,824	1,620	10 %	13 %
U.S.	1,105	969	829	14 %	17 %
Non-U.S.	900	855	791	5 %	8 %
Yervoy	1,244	1,053	1,126	18 %	(6)%
U.S.	908	802	602	13 %	33 %
Non-U.S.	336	251	524	34 %	(52)%
Empliciti	231	150	3	54 %	**
U.S.	151	133	3	14 %	**
Non-U.S.	80	17	—	**	N/A
Established Brands					
Baraclude	1,052	1,192	1,312	(12)%	(9)%
U.S.	53	66	135	(20)%	(51)%
Non-U.S.	999	1,126	1,177	(11)%	(4)%
Sustiva Franchise	729	1,065	1,252	(32)%	(15)%
U.S.	622	901	1,041	(31)%	(13)%
Non-U.S.	107	164	211	(35)%	(22)%
Reyataz Franchise	698	912	1,139	(23)%	(20)%
U.S.	327	484	591	(32)%	(18)%
Non-U.S.	371	428	548	(13)%	(22)%
Hepatitis C Franchise	406	1,578	1,603	(74)%	(2)%
U.S.	109	827	323	(87)%	**
Non-U.S.	297	751	1,280	(60)%	(41)%
Other Brands	2,112	2,271	3,818	(7)%	(41)%

U.S.	390	379	1,547	3 %	(76)%
Non-U.S.	1,722	1,892	2,271	(9)%	(17)%
Total Revenues	20,776	19,427	16,560	7 %	17 %
U.S.	11,358	10,720	8,188	6 %	31 %
Non-U.S.	9,418	8,707	8,372	8 %	4 %

** Change in excess of 100%

Opdivo (nivolumab) — a fully human monoclonal antibody that binds to the PD-1 on T and NKT cells that has been approved for several anti-cancer indications including bladder, blood, colon, head and neck, kidney, liver, lung, melanoma and stomach and continues to be investigated across other tumor types and disease areas.

- U.S. revenues increased in both periods due to higher demand. We expect increased competition for Opdivo to continue in the future due to new product entrants and expanded indications.
- International revenues increased in both periods due to higher demand as a result of launches of additional indications and approvals in new countries.

Eliquis (apixaban) — an oral Factor Xa inhibitor, targeted at stroke prevention in adult patients with non-valvular atrial fibrillation and the prevention and treatment of VTE disorders.

- U.S. and international revenues increased in both periods due to higher demand resulting from increased commercial acceptance of novel oral anticoagulants and market share gains.

Orencia (abatacept) — a fusion protein indicated for adult patients with moderate to severe active RA and PsA 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 due to higher demand.

Sprycel (dasatinib) — an oral inhibitor of multiple tyrosine kinase 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 CML with resistance or intolerance to prior therapy, including Gleevec* (imatinib meslylate).

- U.S. revenues increased in both periods due to higher demand and average net selling prices.
- International revenues increased in both periods due to higher demand. We may experience a decline in European revenues in the event that generic datasinib product enters the market.

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

- U.S. revenues increased in both periods primarily due to higher demand.
- International revenues increased in 2017 due to higher demand in Europe following the approval of the Opdivo+Yervoy combination therapy for melanoma. International revenues decreased in 2016 due to lower demand resulting from the introduction of other IO products being used to treat patients with melanoma, including Opdivo.

Empliciti (elotuzumab) — a humanized monoclonal antibody for the treatment of multiple myeloma.

- Empliciti was launched in the U.S. in December 2015, in the EU in May 2016 and in Japan in September 2016.

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

- International revenues continued to decrease in both periods due to lower demand resulting from increased competition.

Sustiva (efavirenz) 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 continued to decrease in both periods due to lower demand resulting from increased competition from new product entrants. The decrease in 2016 was partially offset by higher average net selling prices. The LOE occurred in December 2017. Gilead terminated BMS's participation in the U.S. and Canada joint venture following the launch of a generic version of Sustiva in the U.S. As a result, BMS's share of Atripla* revenues will further decline during the next three years. Refer to "Item 8. Financial Statements—Note 3. Alliances" for further discussion.

Reyataz (atazanavir sulfate) Franchise — Includes Reyataz - a protease inhibitor for the treatment of HIV and Evotaz (atazanavir 300 mg and cobicistat 150 mg) - a combination therapy containing Reyataz and Tybost* (cobicistat).

- U.S. revenues continued to decrease due to lower demand resulting from new product entrants. The decrease in 2016 was partially offset by higher average net selling prices. The LOE occurred in December 2017 and will result in a higher decline in revenues in future periods due to generic competition.
- International revenues continued to decrease in both periods due to lower demand resulting from increased competition. The decrease in 2016 was also impacted by unfavorable foreign exchange.

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Hepatitis C Franchise — Daklinza (daclatasvir) - an NS5A replication complex inhibitor; Sunvepra (asunaprevir) - an NS3 protease inhibitor; and beclabuvir - an NS5B inhibitor.

- U.S. revenues decreased in 2017 due to lower demand resulting from new product entrants. U.S. revenues increased in 2016 due to the launch of Daklinza in July 2015.
- International revenues decreased in both periods due to lower demand resulting from increased competition due to new product entrants.

Other Brands — includes all other brands, including those which have lost exclusivity in major markets, OTC brands and royalty revenue.

- U.S. revenues decreased in 2016 due to the expiration of BMS's commercialization rights to Abilify* in April 2015 and the transfer of BMS's North American Erbitux* rights to Lilly in October 2015. Refer to "Item 8. Financial Statements—Note 3. Alliances" for further discussion.
- International revenues decreased in 2017 due to out-licensing and divestiture of certain other brands and continued generic erosion. International revenues decreased in 2016 due to the expiration of certain supply arrangements, divestiture of certain other brands, increased competition for OTC brands and unfavorable foreign exchange.

Estimated End-User Demand

Pursuant to the SEC Consent Order described 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. At December 31, 2017, Daklinza had 1.7 months of inventory on hand in the U.S. as a result of minimum required stock levels to support patient demand. We expect inventory on hand levels of Daklinza to exceed one month over the near term. Below are international products that had estimated levels of inventory in the distribution channel in excess of one month on hand at September 30, 2017.

Dafalgan, an analgesic product sold principally in Europe, had 1.2 months of inventory on hand internationally at direct customers compared to also 1.2 months of inventory on hand at June 30, 2017. The level of inventory on hand was primarily attributable to France to support product seasonality.

Efferalgan, an analgesic product sold principally in Europe, had 1.2 months of inventory on hand internationally at direct customers compared to 0.8 months of inventory on hand at June 30, 2017. The level of inventory on hand was primarily attributable to France to support product seasonality.

Fervex, a cold and flu product, had 3.0 months of inventory on hand at direct customers compared to 4.0 months of inventory on hand at June 30, 2017. The level of inventory on hand was attributable to France to support product seasonality.

Perfalgan, an analgesic product, had 2.6 months of inventory on hand internationally at direct customers compared to 1.5 months of inventory on hand at June 30, 2017. The level of inventory on hand was primarily in the Gulf Countries due to extended delivery lead time.

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.

Our non-U.S. businesses have significantly more direct customers. Information on available direct customer product level inventory and corresponding out-movement information and the reliability of third-party demand information varies widely. We limit our direct customer sales channel inventory reporting to where we can influence demand. When this information does not exist or is otherwise not available, we have developed a variety of methodologies to estimate such data, including using historical sales made to direct customers and third-party market research data

related to prescription trends and end-user demand. Given the difficulties inherent in estimating third-party demand information, we evaluate our methodologies to estimate direct customer product level inventory and to calculate months on hand on an ongoing basis and make changes as necessary. Factors that may affect our estimates include generic competition, seasonality of products, 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, 2017 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

Dollar in Millions	2017	2016	2015	% Change 2017 vs. 2016	% Change 2016 vs. 2015
Cost of products sold	$6,066	$4,946	$3,909	23 %	27 %
Marketing, selling and administrative	4,687	4,911	4,841	(5)%	1 %
Research and development	6,411	4,940	5,920	30 %	(17)%
Other income (net)	(1,519)	(1,285)	(187)	18 %	**
Total Expenses	$15,645	$13,512	$14,483	16 %	(7)%

** Change in excess of 100%

Cost of products sold

Cost of products sold include material, internal labor and overhead costs from our owned manufacturing sites, third-party product supply costs and other supply chain costs managed by our global manufacturing and supply organization. Cost of products sold also includes royalties and profit sharing, certain excise taxes, foreign currency hedge settlement gains and losses and the amortization of acquired developed technology costs. Cost of products sold typically vary between periods as a result of product mix and volume (particularly royalties and profit sharing), and to a lesser extent changes in foreign currency, price, inflation and costs attributed to manufacturing site exits.

- Cost of products sold increased in 2017 due to higher Eliquis profit sharing of $719 million and a $146 million impairment charge to reduce the carrying value of the small molecule active pharmaceutical ingredient manufacturing operations in Swords, Ireland. The remaining increase was primarily due to higher sales volume, inventory charges, manufacturing startup costs and foreign currency. Refer to "Item 8. Financial Statements—Note 4. Acquisitions, Divestitures and Licensing Arrangements" for further information.
- Cost of products sold increased in 2016 due to higher Eliquis profit sharing of $700 million, lower foreign currency hedge settlement gains and higher Puerto Rico excise tax.

Marketing, selling and administrative

Marketing, selling and administrative expenses primarily include salary and benefit costs, third-party professional and marketing fees, outsourcing fees, shipping and handling costs, advertising and product promotion. Expenses are managed through regional commercialization organizations or global enabling functions such as finance, legal, information technology and human resources. Certain expenses are shared with alliance partners based upon contractual agreements. Expenses typically vary between periods due to new product launch promotional activities.

- Marketing, selling and administrative expenses decreased in 2017 due to lower advertising, promotion and sales-force expenses supporting Daklinza and other established brands and lower BMS foundation grants.
- Marketing, selling and administrative expenses increased in 2016 due to higher advertising, promotion and sales-force expenses supporting Opdivo partially offset by lower spend for established brands and favorable foreign exchange.

Research and development

Research and development activities include discovery research, preclinical and clinical development, drug formulation and medical support of marketed products. Expenses include salary and benefit costs, third-party grants and fees paid to clinical research organizations, supplies, upfront and contingent milestone payments for licensing and asset acquisitions of investigational compounds, IPRD impairment charges and proportionate allocations of enterprise-wide costs. The allocations include facilities, information technology, employee stock compensation costs and other appropriate costs. Certain expenses are shared with alliance partners based upon contractual agreements. Expenses typically vary between periods for a number of reasons, including the timing of license and asset acquisition

charges and IPRD impairment charges.

- Research and development expenses increased in 2017 due to higher license and asset acquisition charges, site exit charges, IPRD impairment charges and expansion of Opdivo and other IO development programs.
- Research and development expenses decreased in 2016 due to lower license and asset acquisition and IPRD impairment charges, partially offset by the acceleration and expansion of Opdivo development programs.

Significant charges included in R&D expense were as follows:

	Year Ended December 31,		
Dollars in Millions	2017	2016	2015
IFM	$311 [a]	$—	$—
CytomX	200 [a]	25 [a]	—
Halozyme	105 [a]	—	—
Flexus	324 [b]	100 [b]	800 [a]
Cardioxyl	100 [b]	—	167 [a]
PsiOxus	50 [a]	—	—
Ono	40 [a]	—	—
Padlock	—	139 [a]	—
Cormorant	—	35 [a]	—
Nitto Denko	—	100 [a]	—
Five Prime	—	—	350 [a]
Promedior	—	—	84 [c]
Bavarian Nordic	—	—	60 [c]
uniQure	—	—	50 [a]
Other	—	40	168
License and asset acquisition charges	1,130	439	1,679
F-Star Alpha	75	—	—
LPA1 Antagonist	—	—	160
Other	—	13	—
IPRD impairments	75	13	160
Site exit costs	383	83	30
Other	—	—	14
Site exit costs and other	383	83	44
Research and development significant charges	$1,588	$535	$1,883

(a) Upfront payment
(b) Milestone payment
(c) Option fee

- License and asset acquisition charges resulted from strategic transactions to acquire or license certain investigational oncology, cardiovascular, immunoscience and fibrotic disease compounds (or options to acquire or license) as disclosed in "—Acquisition and Licensing Arrangements".
- IPRD impairment charges were related to the discontinued development of an investigational compound which was part of our alliance with F-Star Alpha in 2017 and LPA1 Antagonist Phase II study in 2015.
- Site exit costs resulted from the expected exit of R&D sites in the U.S. through 2020 primarily due to the reduction in the estimated useful lives of the related assets and an impairment charge to reduce the carrying value of a R&D facility in Wallingford, Connecticut.