AMGEN INC
Form 10-K
February 14, 2017

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
Form 10-K
(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016
OR
¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission file number 001-37702
Amgen Inc.
(Exact name of registrant as specified in its charter)

| | |
|---|---|
| Delaware | 95-3540776 |
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |
| One Amgen Center Drive, Thousand Oaks, California | 91320-1799 |
| (Address of principal executive offices) | (Zip Code) |

(805) 447-1000
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

| Title of Each Class | Name of Each Exchange on Which Registered |
|---|---|
| Common stock, $0.0001 par value | The NASDAQ Global Select Market |

Securities registered pursuant to Section 12(g) of the Act: None
Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý 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 ý
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or Section 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 ý 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 ý 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 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 ¨

(Do not check if a smaller reporting company)

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

The approximate aggregate market value of voting and non-voting stock held by non-affiliates of the registrant was $101,183,706,509 as of June 30, 2016.(A)

(A) Excludes 83,869,173 shares of common stock held by directors and executive officers, and any stockholders whose ownership exceeds ten percent of the shares outstanding, at June 30, 2016. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, directly or indirectly, to direct or cause the direction of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant.

736,452,791

(Number of shares of common stock outstanding as of February 9, 2017)

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's Proxy Statement with respect to the 2017 Annual Meeting of stockholders to be held May 19, 2017, are incorporated by reference into Part III of this annual report.

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PART I

Item 1. BUSINESS

Amgen Inc. (including its subsidiaries, referred to as "Amgen," "the Company," "we," "our" or "us") is committed to unlockin the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

Our strategy is to develop innovative medicines in six focused therapeutic areas that meet important unmet medical needs in addressing serious illness. We have a presence in approximately 100 countries worldwide focusing on: oncology/hematology, cardiovascular disease, inflammation, bone health, nephrology and neuroscience.

Amgen was incorporated in California in 1980 and became a Delaware corporation in 1987. Amgen operates in one business segment: human therapeutics.

Significant Developments

Following is a summary of significant developments affecting our business that have occurred and that we have reported since the filing of our Annual Report on Form 10-K for the year ended December 31, 2015, and in early 2017.

Products/Pipeline

Bone health

EVENITY™ (romosozumab)*

- In February 2016, we and UCB, our global collaboration partner in the development of EVENITY,™ announced that the phase 3 FRAME (FRActure study in postmenopausal woMen with ostEoporosis) study met its co-primary endpoints.
- In March 2016, we and UCB announced that the phase 3 BRIDGE (placeBo-contRolled study evaluatIng the efficacy anD safety of EVENITY™ in treatinG mEn with osteoporosis) study met its primary endpoint.
- In September 2016, we and UCB announced that the U.S. Food and Drug Administration (FDA) accepted for review the Biologics License Application (BLA) for EVENITY™ for the treatment of osteoporosis in postmenopausal women at increased risk for fracture. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of July 19, 2017.
- In December 2016, we and UCB announced that we submitted an application to the Pharmaceuticals and Medical Devices Agency in Japan, together with our joint venture partner Astellas Pharma, Inc., seeking marketing approval for EVENITY™ for the treatment of osteoporosis for those at high risk of fracture.

Prolia® (denosumab)

- In August 2016, we announced that the phase 3 randomized, double-blind, double-dummy, active-controlled study evaluating the safety and efficacy of Prolia® compared with risedronate in patients receiving glucocorticoid treatment met all primary and secondary endpoints at 12 months.

XGEVA® (denosumab)

- In October 2016, we announced that the phase 3 study evaluating XGEVA® versus Zometa® (zoledronic acid) in the prevention of skeletal-related events (SREs) in patients with multiple myeloma met its primary endpoint of non-inferiority in delaying the time to first on-study SRE. The secondary endpoints of superiority in delaying time to first SRE and delaying time to first-and-subsequent SREs were not met.

Cardiovascular

Repatha® (evolocumab)

- In July 2016, we announced that the FDA approved the Repatha® Pushtronex™ system (on-body infusor with prefilled cartridge), a new, monthly single-dose administration option. The Pushtronex™ system is a hands-free device designed to provide 420 mg of Repatha® in a single dose.
- In September 2016, we announced that the phase 3 GLAGOV (GLobal Assessment of Plaque ReGression with a PCSK9 AntibOdy as Measured by IntraVascular Ultrasound) study evaluating the effect of Repatha® on coronary artery disease met its primary and secondary endpoints.
- In December 2016, we announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion for an extension to the marketing authorization of a new 420 mg single-dose delivery option for Repatha®.
- In January 2017, the United States District Court in Delaware granted Amgen's request for a permanent injunction prohibiting Sanofi, Sanofi-Aventis U.S. LLC, Aventisub LLC, formerly doing business as Aventis Pharmaceuticals Inc. (collectively, Sanofi) and Regeneron Pharmaceuticals, Inc. (Regeneron) from infringing two patents that Amgen holds for Repatha® by manufacturing, using, selling or offering alirocumab for sale in the United States. Sanofi and Regeneron subsequently appealed the case to the U.S. Court of Appeals for the Federal Circuit (the Federal Circuit Court), and following a motion by Sanofi and Regeneron, in February 2017 the Federal Circuit Court entered a stay of the permanent injunction during the pendency of the appeal. See Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements.
- In February 2017, we announced that the phase 3 FOURIER (Further Cardiovascular OUtcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk) study evaluating the effects of Repatha® on cardiovascular outcomes met its primary composite endpoint (cardiovascular death, non-fatal myocardial infarction (MI), non-fatal stroke, hospitalization for unstable angina or coronary revascularization) and key secondary composite endpoint (cardiovascular death, non-fatal MI or non-fatal stroke). No new safety issues were observed.
- In February 2017, we announced that the phase 3 EBBINGHAUS (Evaluating PCSK9 Binding antiBody Influence oN coGnitive HeAlth in high cardiovascUlar risk Subjects) cognitive function study achieved its primary endpoint.

Inflammation

Enbrel® (etanercept)

- In November 2016, we announced that the FDA approved the supplemental Biologics License Application (sBLA) for the expanded use of ENBREL, making it the first and only systemic therapy to treat pediatric patients (ages 4-17) with chronic moderate-to-severe plaque psoriasis.

Nephrology

Parsabiv™ (etelcalcetide)*

- In November 2016, we announced that the European Commission (EC) granted marketing authorization for Parsabiv™ for the treatment of secondary hyperparathyroidism (sHPT) in adult patients with chronic kidney disease (CKD) who are on hemodialysis.
- In February 2017, we announced that the FDA approved Parsabiv™ for the treatment of sHPT in adult patients with CKD who are on hemodialysis.

Neuroscience

Erenumab (formerly AMG 334)

- In June 2016, we announced that the global phase 2 study evaluating the efficacy and safety of erenumab in chronic migraine prevention met its primary endpoint. Erenumab is being developed jointly with Novartis AG (Novartis).
- In September 2016, we announced that the phase 3 ARISE (A phase 3, RandomIzed, double-blind, placebo-controlled Study to Evaluate the efficacy and safety of erenumab in migraine prevention) study evaluating the efficacy of erenumab in episodic migraine prevention met its primary endpoint.
- In November 2016, we announced the positive top-line results of the global phase 3, randomized, double-blind, placebo-controlled STRIVE (STudy to evaluate the efficacy and safety of erenumab in migRaIne preVEntion) study. The study met its primary endpoint.

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Oncology/Hematology

BLINCYTO® (blinatumomab)

- In September 2016, we announced that the FDA approved the sBLA for BLINCYTO® to include new data supporting the treatment of pediatric patients with Philadelphia chromosome-negative (Ph-) relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukemia (ALL).
- In February 2017, we announced the submission of a sBLA to the FDA to include overall survival data from the Phase 3 TOWER study, supporting the conversion of BLINCYTO®'s accelerated approval to full approval. The sBLA also includes new data supporting the treatment of patients with Philadelphia chromosome-positive (Ph+) R/R B-cell precursor ALL.

KYPROLIS® (carfilzomib)

- In June 2016, the EC approved a variation to the marketing authorization for KYPROLIS® to include use in combination with dexamethasone alone for adult patients with multiple myeloma who have received at least one prior therapy. The EC approved the extended indication for KYPROLIS® based on data from the phase 3 head-to-head ENDEAVOR (RandomizEd, OpeN Label, Phase 3 Study of Carfilzomib Plus DExamethAsone Vs Bortezomib Plus DexamethasOne in Patients With Relapsed Multiple Myeloma) study.
- In September 2016, we announced the top-line results of the phase 3 CLARION (Carfilzomib, Melphalan, Prednisone vs Bortezomib, Melphalan, Prednisone in Newly Diagnosed Multiple Myeloma) study, which evaluated an investigational regimen of KYPROLIS®, melphalan and prednisone versus VELCADE® (bortezomib), melphalan and prednisone for 54 weeks in patients with newly diagnosed multiple myeloma who were ineligible for hematopoietic stem-cell transplant. The study did not meet the primary endpoint of superiority in progression-free survival (PFS).

Nplate® (romiplostim)

- In April 2016, we announced that the phase 3 study of Nplate® in children with symptomatic immune thromobocytopenia met its primary endpoint.

Biosimilars

AMJEVITA™ (adalimumab-atto) /ABP 501

- In September 2016, we announced that the FDA approved AMJEVITA™ across all eligible indications of the reference product, HUMIRA® (adalimumab), including treatment of psoriatic arthritis, ankylosing spondylitis and moderate-to-severe rheumatoid arthritis, polyarticular juvenile idiopathic arthritis in patients four years of age or older, chronic plaque psoriasis, adult Crohn's disease and ulcerative colitis. For discussion of ongoing, related litigation, see Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements.
- In January 2017, we announced that the CHMP of the EMA adopted a positive opinion for the marketing authorization of ABP 501, recommending approval for all available indications.

ABP 215

- In November 2016, we and Allergan plc (Allergan), our collaboration partner in the development and commercialization of certain biosimilar candidates, announced the submission of a BLA to the FDA for ABP 215, a biosimilar candidate to Avastin® (bevacizumab). The FDA has accepted the BLA and set the Biosimilar User Fee Act target action date of September 14, 2017.
- In December 2016, we and Allergan announced the submission of a Marketing Authorization Application (MAA) to the EMA for ABP 215.

ABP 980

- In July 2016, we and Allergan announced the results from a phase 3 study evaluating the efficacy and safety of ABP 980 compared with trastuzumab (Herceptin®) in patients with human epidermal growth factor receptor 2-positive early breast cancer. The results ruled out inferiority compared to trastuzumab but could not rule out superiority based on its primary efficacy endpoint of the difference of the percentage of patients with a pathologic complete response.

* FDA provisionally approved trade name

Marketing, Distribution and Selected Marketed Products

The largest concentration of our sales and marketing forces is based in the United States and Europe. Additionally, we continue to expand the commercialization and marketing of our products into other geographic territories, including parts of Latin America, the Middle East and Asia. This expansion is occurring by either establishing our own affiliate, acquiring existing third- party businesses or product rights or in partnering with third parties. Use of our own sales and marketing forces versus a third-party's varies across these markets. Such use typically depends on several factors including the nature of entry into the new market, the size of opportunity and the operational capabilities. Together with our partners, we market our products to healthcare providers, including physicians or their clinics, dialysis centers, hospitals and pharmacies.

In the United States, we sell primarily to pharmaceutical wholesale distributors that we utilize as the principal means of distributing our products to healthcare providers. We also market certain products directly to consumers through direct-to-consumer print and television advertising, as well as through multi-channel marketing. For further discussion, see Government Regulation—Regulation of Product Marketing and Promotion. Outside the United States, we sell principally to healthcare providers and/or pharmaceutical wholesale distributors depending on the distribution practice in each country.

Our product sales to three large wholesalers, AmerisourceBergen Corporation, McKesson Corporation and Cardinal Health, Inc., each accounted for more than 10% of total revenues for each of the years ended December 31, 2016, 2015 and 2014. On a combined basis, these wholesalers accounted for approximately 96%, 97% and 94% of our U.S. gross product sales, respectively, and approximately 81%, 81% and 77% of our worldwide gross revenues, respectively. We monitor the financial condition of our larger customers and limit our credit exposure by setting credit limits and, in certain circumstances, by requiring letters of credit.

For financial information related to our one business segment, see Part IV—Consolidated Statements of Income, Consolidated Balance Sheets, and Note 19, Segment information, to the Consolidated Financial Statements.

Our products are marketed around the world with the United States being our largest market. The following chart shows our product sales by principal product and by geography for the years ended December 31, 2016, 2015 and 2014.

Enbrel® (etanercept)

We market ENBREL primarily in the United States. It was launched in 1998 and is used primarily in indications for the treatment of adult patients with the following conditions:

- moderately to severely active rheumatoid arthritis,
- chronic moderate-to-severe plaque psoriasis patients who are candidates for systemic therapy or phototherapy, and
- active psoriatic arthritis.

Neulasta® (pegfilgrastim)

We market Neulasta®, a pegylated protein based on the filgrastim molecule, primarily in the United States and Europe. Neulasta® was launched in 2002, and is used primarily in the indication to help reduce the chance of infection due to a low white blood cell count, in people with certain types of cancer (non-myeloid) who receive anti-cancer medicines (chemotherapy) that can cause fever and a low blood cell count. In 2015, the Neulasta® Onpro® kit became available in the United States.

Aranesp® (darbepoetin alfa)

We market Aranesp® primarily in Europe and the United States. It was launched in 2001, and is indicated to treat a lower-than-normal number of red blood cells (anemia) caused by CKD (in both patients on dialysis and patients not on dialysis). Aranesp® is also indicated for the treatment of anemia due to concomitant myelosuppressive chemotherapy in patients with non-myeloid malignancies, and when chemotherapy will be used for at least two months after starting Aranesp®.

Aranesp® and EPOGEN® compete with each other in the United States, primarily in the dialysis setting.

Prolia® (denosumab)

We market Prolia® primarily in the United States and Europe. It contains the same active ingredient as XGEVA® but is approved for different indications, patient populations, doses and frequencies of administration. Prolia® was launched in the United States and Europe in 2010. In the United States, it is used primarily in the indication for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In Europe, Prolia® is used primarily for the treatment of osteoporosis in postmenopausal women at increased risk of fracture.

Sensipar®/Mimpara® (cinacalcet)

We market cinacalcet as Sensipar® primarily in the United States and as Mimpara® primarily in Europe. It was launched in 2004 and is used primarily in the indication for the treatment of sHPT in adult patients with CKD who are on dialysis.

XGEVA® (denosumab)

We market XGEVA® primarily in the United States and Europe. XGEVA® was launched in the United States in 2010, and is used primarily in the indication for the prevention of SREs (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in patients with bone metastases from solid tumors. It is not indicated for the prevention of SREs in patients with multiple myeloma. XGEVA® was launched in Europe in 2011, and is used primarily in the indication for the prevention of SREs in adults with bone metastases from solid tumors.

EPOGEN® (epoetin alfa)

We market EPOGEN® in the United States for dialysis patients. EPOGEN® was launched in 1989, and we market it for the indication to treat anemia caused by CKD in patients on dialysis to lessen the need for red blood cell transfusions. The majority of our sales are to two large dialysis providers.

NEUPOGEN® (filgrastim)

We market NEUPOGEN®, a recombinant-methionyl human granulocyte colony-stimulating factor (G-CSF), primarily in the United States, Canada and Europe. NEUPOGEN® was launched in 1991 and is used primarily in the indication to help reduce the chance of infection due to a low white blood cell count in people with certain types of cancer (non-myeloid) who receive anti-cancer medicines (chemotherapy) that can cause fever and a low blood cell count.

Other Marketed Products

We market several other products, including KYPROLIS® (carfilzomib), Vectibix® (panitumumab), Nplate® (romiplostim), Repatha® (evolocumab), BLINCYTO® (blinatumomab), IMLYGIC® (talimogene laherparepvec) and

Corlanor® (ivabradine).

Patents

The following table describes our outstanding material patents for the indicated product by territory, general subject matter and latest expiry date. Certain of the European patents are the subject of supplemental protection certificates that provide additional protection for the product in certain European countries beyond the dates listed in the table (see footnotes).

One or more patents with the same or earlier expiry date may fall under the same "general subject matter" and are not listed separately.

| Product | Territory | General Subject Matter | Expiration |
|---|---|---|---|
| Enbrel® (etanercept) | U.S. | Methods of treating psoriasis | 8/13/2019 |
| | U.S. | Aqueous formulation and methods of treatment using the formulation | 6/8/2023 |
| | U.S. | Fusion protein, and pharmaceutical compositions | 11/22/2028 |
| | U.S. | DNA encoding fusion protein, and methods of making fusion protein | 4/24/2029 |
| Neulasta® (pegfilgrastim) | Europe | Pegylated G-CSF(1) | 2/8/2015 |
| Aranesp® (darbepoetin alfa) | U.S. | Glycosylation analogs of erythropoietin proteins | 5/15/2024 |
| Prolia®/ XGEVA® (denosumab) | U.S. | RANKL antibodies; and methods of use(2) | 12/22/2017 |
| | U.S. | Methods of treatment | 6/25/2022 |
| | U.S. | Nucleic acids encoding RANKL antibodies, and methods of producing RANKL antibodies | 11/30/2023 |
| | U.S. | RANKL antibodies including sequences | 2/19/2025 |
| | Europe | RANKL antibodies(1) | 12/22/2017 |
| | Europe | Medical use of RANKL antibodies(1) | 4/15/2018 |
| | Europe | RANKL antibodies including epitope binding | 2/23/2021 |
| | Europe | RANKL antibodies including sequences(1) | 6/25/2022 |
| Sensipar®/ Mimpara® (cinacalcet) | U.S. | Calcium receptor-active molecules | 3/8/2018 |
| | U.S. | Formulation | 9/22/2026 |
| | Europe | Calcium receptor-active molecules(1) | 10/23/2015 |
| KYPROLIS® (carfilzomib) | U.S. | Compositions and compounds | 12/7/2027 |
| | U.S. | Methods of treatment | 4/14/2025 |
| | Europe | Compositions, compounds and methods of treatment(1) | 8/8/2025 |
| Vectibix® (panitumumab) | U.S. | Human monoclonal antibodies to epidermal growth factor receptor (EGFr) | 4/8/2020 |
| | Europe | Human monoclonal antibodies to EGFr(1) | 5/5/2018 |
| Nplate® (romiplostim) | U.S. | Thrombopoietic compounds | 1/19/2022 |
| | U.S. | Formulation | 2/12/2028 |
| | Europe | Thrombopoietic compounds(1) | 10/22/2019 |
| | Europe | Formulation | 4/20/2027 |
| Repatha® (evolocumab) | U.S. | Antibodies(3) | 10/25/2029 |
| | U.S. | Methods of treatment | 10/8/2030 |
| | Europe | Compositions and method of treatment | 8/22/2028 |
| BLINCYTO® (blinatumomab) | U.S. | Bifunctional polypeptides(3) | 4/21/2019 |
| | U.S. | Method of administration | 9/28/2027 |
| | Europe | Bifunctional polypeptides | 11/26/2024 |
| | Europe | Method of administration | 11/29/2026 |
| IMLYGIC® (talimogene laherparepvec) | U.S. | Compositions and method of treatment(3) | 1/22/2021 |
| | Europe | Composition and uses | 1/22/2021 |
| Parsabiv™ | U.S. | Compound and pharmaceutical composition | 7/29/2030 |

| | | | |
|---|---|---|---|
| (etelcalcetide) | Europe | Compound and pharmaceutical composition | 7/29/2030 |

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(1) A European patent with this subject matter may also be entitled to supplemental protection in one or more countries in Europe, and the length of any such extension will vary by country. For example, supplementary protection certificates have been issued related to the indicated products for patents in at least the following countries:

- pegfilgrastim — France, Germany, Italy, Spain, and the United Kingdom, expiring in August 2017
- denosumab — France, Italy, Spain and the United Kingdom, expiring in 2025
- cinacalcet — France, Germany, Italy, Spain, and the United Kingdom, expiring in 2019
- panitumumab — France, Germany, Italy, Spain, and the United Kingdom, expiring in 2022
- romiplostim — France, Italy, Spain, and the United Kingdom, expiring in 2024
- carfilzomib — France and Germany, expiring in 2028

(2) The U.S. Patent and Trademark Office has issued a Notice of Final Determination that a patent with this subject matter is eligible for patent term extension with an expiry of September 17, 2021.

(3) A patent with this subject matter may be entitled to patent term extension in the United States.

Competition

We operate in a highly competitive environment. Our products compete with other products or treatments for diseases for which our products may be indicated. Our competitors market products or are actively engaged in research and development (R&D) in areas in which we have products or in which we are developing product candidates or new indications for existing products. Our competitive positions may be based on, among other things, safety, efficacy, reliability, availability, patient convenience/delivery devices, price, reimbursement, access to and timing of market entry and patent position and expiration.

Certain of the existing patents on our principal products have expired, and we face new and increasing competition, including from biosimilars. We may also compete against biosimilar or generic versions of our competitors' products. A biosimilar is another version of a biological product for which marketing approval is sought or has been obtained based on a demonstration that it is "highly similar" to the original reference product. See Government Regulation. We expect the adverse impact from biosimilars to be more like branded biologics than generic small molecules. Although we expect biosimilars to compete on price, we believe many patients, providers and payers will continue to place high value on the reputation, reliability and safety of our products. Zarxio®, a biosimilar version of NEUPOGEN® from Sandoz, a Novartis company (Sandoz), which launched in the United States in 2015, was the first biosimilar entrant into the U.S. market. Companies have pending applications with the FDA for biosimilar versions of EPOGEN® and Neulasta®, along with additional biosimilar versions of NEUPOGEN®. We are well positioned to compete and will leverage the experience we have had in the United States versus branded competition, as well as our considerable experience in competing against epoetin alfa and filgrastim biosimilars in Europe.

The introduction of new products, the development of new processes or technologies by competitors or the emergence of new information about existing products may result in increased competition for our marketed products, even for those protected by patents, or in reductions in the prices we receive from selling our products. In addition, the development of new treatment options or standards of care may reduce the use of our products or may limit the utility and application of ongoing clinical trials for our product candidates (as used in this document, clinical trials may include prospective clinical trials, observational studies, registries and other studies). See Item 1A. Risk Factors—Our products face substantial competition and Item 1A. Risk Factors—We currently face competition from biosimilars and expect to face increasing competition in the future.

The following table reflects our significant competitors and is not exhaustive.

| Product | Territory | Competitor Marketed Product | Competitors |
|---|---|---|---|
| | U.S. & Canada | REMICADE®* | Janssen Biotech, Inc. (Janssen)[1]/Merck & Company, Inc. (Merck) |
| ENBREL | U.S. & Canada | HUMIRA® | AbbVie Inc. |
| | U.S. & Canada | STELARA®[2] | Janssen[1] |
| Neulasta® | Europe | Filgrastim biosimilars | Various |
| | U.S. | PROCRIT®[3] | Janssen[1] |
| Aranesp® | U.S. | MIRCERA®[4] | Galenica Group (Galenica)/F. Hoffmann-La Roche Ltd. (Roche) |
| | Europe | Epoetin alfa biosimilars | Various |
| Prolia® | U.S. & Europe | Alendronate, raloxifene and zoledronate generics | Various |
| Sensipar®[5]/ Mimpara® | U.S. & Europe | Active Vitamin D analogs | Various |
| XGEVA® | U.S. & Europe | Zoledronate generics | Various |
| EPOGEN® | U.S. | MIRCERA®[4] | Galenica/Roche |
| | U.S. | Granix® | Teva Pharmacueticals Industries Ltd. (Teva) |
| NEUPOGEN® | U.S. | Zarxio® | Sandoz |
| | Europe | Filgrastim biosimilars | Various |
| | U.S. | VELCADE® | Millennium Pharmaceuticals, Inc.[6] |
| KYPROLIS®[7] | U.S. | REVLIMID® | Celgene Corporation (Celgene) |
| | U.S. | POMALYST® | Celgene |
| Repatha® | U.S. & Europe | PRALUENT® | Regeneron<br>Sanofi |

* Approved biosimilar available

(1) A subsidiary of Johnson & Johnson (J&J).

(2) Dermatology only.

(3) PROCRIT® competes with Aranesp® in the supportive cancer care and pre-dialysis settings.

(4) MIRCERA® competes with Aranesp® in the nephrology segment only.

(5) Teva and Barr Pharmaceuticals have received tentative approval from the FDA for generic versions of Sensipar® that could compete with Sensipar® in the future. There is an injunction prohibiting them from commercializing in the United States until expiration of the Sensipar® patents.

(6) A wholly owned subsidiary of Takeda Pharmaceutical Company Limited.

(7) KYPROLIS® is facing increased competition from several recently approved products.

Reimbursement

Sales of our principal products are dependent on the availability and extent of coverage and reimbursement from third-party payers. In many markets around the world, these payers, including government health systems, private health insurers and other organizations, continue to be focused on reducing the cost of healthcare. Their efforts have intensified as a result of rising healthcare costs and economic challenges. Drugs, and in particular specialty drugs such as our products, remain a focus for cost containment by these parties. As a result, payers around the world are being more restrictive regarding the use of biopharmaceutical products while requiring a higher level of clinical evidence to support the benefit such products bring to patients and the broader healthcare system.

The scrutiny of biopharmaceutical pricing in the United States remains intense and a point of focus in the discussion of rising healthcare costs. The pricing practices of certain companies have increased public media and government scrutiny of the biopharmaceutical industry, providing greater incentive for governments and private payers to limit or regulate the price of drug products and services. At the same time, value assessments of new technology, previously used predominantly outside the United States, are having an impact in the U.S. healthcare environment. Healthcare provider organizations and independent organizations are creating their own value assessments of biopharmaceutical drugs for comparison with manufacturer pricing. Although these organizations do not set drug prices, they seek to influence pricing as well as payer and provider decision making by publicly disclosing their assessments, often making assertions around what they believe to be the appropriate price to charge for a product. These developments put greater pressure on access to, pricing of and sales of our products.

In the United States, healthcare providers are reimbursed for covered services and products they deliver through Medicare, Medicaid and other government healthcare programs, as well as through private payers. Pharmacies are also reimbursed in a similar manner for drug products they dispense. We are required to provide specified rebates or discounts on the products we sell to certain government funded programs, including Medicare and Medicaid, and those rebates or discounts have increased over time. The Patient Protection and Affordable Care Act (ACA), enacted in 2010, increased many of the mandatory discounts and rebates required of us and imposed a new Branded Prescription Pharmaceutical Manufacturers and Importers fee payable each year by us and other manufacturers. The new U.S. presidential administration has identified repealing and replacing the ACA as a priority. The timing and method of repeal and replacement legislation is uncertain but changes could include the number of patient lives covered, the quality of the insurance, Medicaid eligibility and the level of patient protections provided.

Further efforts by government agencies and state legislatures in the United States could also affect us and our industry. For example, a recently enacted Vermont law requires manufacturers to submit price increase justifications to the state attorney general if certain price increase and state spending thresholds are met. Examples of other proposals that have been discussed and debated, but not yet enacted, include state ballot initiatives that would place a maximum price ceiling, or cap, on pharmaceutical products purchased by state agencies and state legislative efforts to cap pharmaceutical prices for commercial payers. Other legislative and regulatory actions that would have a significant impact on Amgen include: changes to how the Medicare program covers and reimburses current and future drugs, including for patients with End-Stage Renal Disease; changes in the Federal payment rate or new rebate requirements for covered drugs and policies for payment in Medicare or Medicaid; and changes to coverage and payment for biosimilars, including the current Medicare biosimilar coverage and payment policies intended to encourage biosimilar adoption, or other policies that provide easier substitution or reimbursement advantages.

In the U.S. private sector, healthcare providers and payers continue to institute cost reduction and containment measures that lower drug spending altogether or shift a greater portion of the costs to patients. Such measures include more limited benefit plan designs, higher tier formulary placement that increases the level of patient out of pocket costs and stricter utilization criteria before a patient may get access to a drug. In the retail pharmacy sector, in which the majority of our sales for ENBREL, Sensipar® and Repatha® occur, the use of such measures by Pharmacy Benefit Managers (PBMs) and insurers has continued to intensify which have limited Amgen product usage and revenues. PBMs are third-party organizations tasked with administrating prescription drug programs for large employers, health plans and government programs. Consolidation has resulted in a smaller number of PBMs and insurers overseeing a large portion of total covered lives in the United States; for example three PBMs oversee approximately 75% of covered lives in the United States. As a result, PBMs and insurers have greater market power and negotiating leverage

to exclude drugs from their formularies in favor of competitor drugs or alternative treatments, and/or to mandate stricter utilization criteria. Formulary exclusion effectively encourages patients and providers to seek alternative treatments or pay 100% of the cost of a drug. Recent experience with Repatha® underscores that utilization management requirements continue to be onerous for patients and physicians, limiting access to appropriate usage. In highly competitive treatment markets such as with ENBREL, PBMs are also able to exert negotiating leverage by requiring incremental rebates from manufacturers in order to maintain their formulary position. A drug's favorable position on formulary is essential to ensure patients have access.

In general, in countries outside the United States, government-sponsored healthcare systems are the primary payers for drugs and biologics. With increased budgetary constraints, payers in many countries apply a variety of measures to exert downward price pressure. These measures can include mandatory price controls, price referencing, therapeutic reference pricing, increases in mandates or incentives for generic substitution and biosimilar usage, and government-mandated price cuts. We expect that

countries will continue to take aggressive actions to reduce expenditures on drugs and biologics. Similarly, fiscal constraints may also impact the extent to which countries are willing to approve new and innovative therapies and/or allow access to new technologies. For example, many Health Technology Assessment (HTA) organizations use formal economic metrics such as cost-effectiveness to determine coverage and reimbursement of new therapies, and these organizations are proliferating in established and emerging markets.

The dynamics and developments discussed above serve to create pressure on the pricing and potential usage of our products, and the industry as a whole. We remain focused on delivering breakthrough treatments for unmet medical needs. Amgen is committed to working with the entire healthcare community to ensure continued innovation and to enable patient access to needed medicines. We do this by:

- investing billions of dollars annually in research and development;
- developing more affordable therapeutic choices in the form of high-quality and reliably-supplied biosimilars;
- pricing our medicines to reflect the value they provide;
- partnering with payers to share risk and accountability for health outcomes;
- providing patient support and education programs and helping patients in financial need access our medicines; and
- working with policymakers, patients and other stakeholders to establish a sustainable healthcare system with access to affordable care and where patients and their healthcare professionals are the primary decision makers.

See Item 1A. Risk Factors—Our sales depend on coverage and reimbursement from third-party payers, and pricing and reimbursement pressures may affect our profitability and Item 1A. Risk Factors—Guidelines and recommendations published by various organizations can reduce the use of our products.

Manufacturing, Distribution and Raw Materials

Manufacturing

We believe we are a leader in the manufacturing of biologics and that our manufacturing capabilities represent a competitive advantage. The products we manufacture consist of both biologics and small molecule drugs. The majority of our products are biologics that are produced in living cells and that are inherently complex due to naturally-occurring molecular variations. Highly specialized knowledge and extensive process and product characterization are required to transform laboratory-scale processes into reproducible commercial manufacturing processes. For additional information regarding manufacturing facilities, see Item 2. Properties.

We perform most of our bulk manufacturing, formulation, and/or fill and finish activities in our Puerto Rico, Rhode Island, California and Ireland facilities and also conduct finish activities in the Netherlands. In addition, we utilize third-party contract manufacturers to supplement our commercial manufacturing requirements.

We manufacture products to support our clinical trials primarily in our California and Rhode Island locations. We also utilize third-party contract manufacturers for certain clinical products.

See Item 1A. Risk Factors for a discussion of the factors that could adversely impact our manufacturing operations and the global supply of our products.

Distribution

We operate distribution centers in Kentucky, California and the Netherlands for worldwide distribution of the majority of our commercial and clinical products. We also use third-party distributors to supplement distribution of our products worldwide.

Other

In addition to the manufacturing and distribution activities noted above, our operations in the United States, the U.S. territory of Puerto Rico and the Netherlands include key manufacturing support functions, including quality control, process development, procurement, production scheduling and warehousing. Certain of those manufacturing and distribution activities are highly regulated by the FDA as well as other international regulatory agencies. See Government Regulation—Regulation in the United States—Regulation of Manufacturing Standards.

Manufacturing Initiatives

We have multiple ongoing initiatives that are designed to extend our manufacturing advantage by optimizing our manufacturing network and/or mitigating manufacturing risks while continuing to ensure adequate supply of our products. We have initiated the bulk process qualification campaign to facilitate licensure at our biologics manufacturing facility in Singapore. Upon licensure, this facility will expand our capability to manufacture cell culture products utilizing new technology and innovation. The facility will be fully reconfigurable, providing efficient manufacturing capabilities to help ensure supply of our products worldwide. Our first product to be manufactured in the facility will be denosumab. We are also constructing an additional new facility at the site in Singapore to enable the manufacture of the active pharmaceutical ingredient for KYPROLIS®.

In addition to these initiatives, we have projects designed to optimize manufacturing asset utilization, to continue our use of third-party contract manufacturers and to maintain a state of regulatory compliance. This includes manufacturing network consolidation initiatives as well as process improvements surrounding manufacturing. See Item 1A. Risk Factors—Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales.

Raw Materials and Medical Devices

Certain raw materials, medical devices, including companion diagnostics, and components necessary for the commercial and/or clinical manufacturing of our products are provided by and are the proprietary products of unaffiliated third-party suppliers, certain of which may be our only sources for such materials. We currently attempt to manage the risk associated with such suppliers by inventory management, relationship management and evaluation of alternative sources when feasible. We also monitor the financial condition of certain suppliers and their ability to supply our needs. See Item 1A. Risk Factors—We rely on third-party suppliers for certain of our raw materials, medical devices and components.

We perform various procedures to assist us in authenticating the source of raw materials, including intermediary materials used in the manufacture of our products, which include verification of the country of origin. The procedures are incorporated into the manufacturing processes we and our third-party contract manufacturers perform.

Government Regulation

Regulation by government authorities in the United States and other countries is a significant factor in the production and marketing of our products and our ongoing R&D activities. In order to clinically test, manufacture and market products for therapeutic use, we must satisfy mandatory procedures and safety and effectiveness standards established by various regulatory bodies. Compliance with these standards is complex and failure to comply with any of these standards can result in significant implications. See Item 1A. Risk Factors for a discussion of factors that can adversely impact our development and marketing of commercial products including global regulatory implications.

Regulation in the United States

In the United States, the Public Health Service Act, the Federal Food, Drug, and Cosmetic Act (FDCA) and the regulations promulgated thereunder, as well as other federal and state statutes and regulations govern, among other things, the production, research, development, testing, manufacture, quality control, labeling, storage, record keeping, approval, advertising and promotion, and distribution of our products, as well as the reporting of certain payments and other transfers of value to healthcare professionals and teaching hospitals.

Clinical Development and Product Approval. Drug development in our industry is complex, challenging and risky; and failure rates are high. Product development cycles are typically very long—approximately 10 to 15 years from discovery to market. A potential new medicine must undergo many years of preclinical and clinical testing to establish its safety and efficacy for use in humans at appropriate dosing levels and with an acceptable risk-benefit profile. After laboratory analysis and preclinical testing in animals, we file an Investigational New Drug Application (IND) with the FDA to begin human testing. Typically, we undertake an FDA-designated three-phase human clinical testing program.

- In phase 1, we conduct small clinical trials to investigate the safety and proper dose ranges of our product candidates in a small number of human subjects.
- In phase 2, we conduct clinical trials to investigate side effect profiles and the efficacy of our product candidates in a large number of patients who have the disease or condition under study.

- In phase 3, we conduct clinical trials to investigate the safety and efficacy of our product candidates in a large number of patients who have the disease or condition under study.

The FDA monitors the progress of each trial conducted under an IND and may, at its discretion, re-evaluate, alter, suspend or terminate the testing based on the data accumulated to that point and the FDA's risk-benefit assessment with regard to the

patients enrolled in the trial. The results of preclinical and clinical trials are submitted to the FDA in the form of a BLA for biologic products or an NDA for small molecule products. We are not permitted to market or promote a new product until the FDA has approved our marketing application.

Approval of Biosimilars. The ACA authorized the FDA to approve biosimilars via a separate, abbreviated pathway. The pathway allows sponsors of a biosimilar to seek and obtain regulatory approval based in part on the non-clinical and clinical trial data of an originator product to which the biosimilar has been demonstrated to be "highly similar" and to have no clinically meaningful differences in terms of safety, purity, and potency. The relevance of demonstrating "similarity" is that in many cases, biosimilars can be brought to market without conducting the full suite of clinical trials typically required of originators, as risk-benefit has previously been established. In order to preserve incentives for future innovation, the law establishes a period of exclusivity for originators' products, which in general prohibits biosimilars from gaining FDA approval based in part on reliance on or reference to the originator's data in their application to the FDA for 12 years after FDA approval of the originator product. The law does not change the duration of patents granted on biologic products. The FDA has released a number of guidance documents as part of the implementation of the abbreviated approval pathway for biosimilars, some of which remain in draft form. As of the end of 2016, four biosimilar applications have been approved by the FDA, including AMJEVITA.™ A number of manufacturers have announced the filing of marketing applications to the FDA under the biosimilar pathway, some of which are for biosimilars of our products.

Regulation of Product Marketing and Promotion. The FDA regulates the marketing and promotion of products. Our product promotion for approved product indications must comply with the statutory standards of the FDCA, and the FDA's implementing regulations and standards. The FDA's review of marketing and promotional activities encompasses, but is not limited to, direct-to-consumer advertising, healthcare provider-directed advertising and promotion, sales representative communications to healthcare professionals, promotional programming and promotional activities involving electronic media. The FDA may also review industry-sponsored scientific and educational activities that make representations regarding product safety or efficacy in a promotional context. The FDA may take enforcement action against a company for promoting unapproved uses of a product or for other violations of its advertising and labeling laws and regulations. Enforcement action may include product seizures, injunctions, civil or criminal penalties or regulatory letters, which may require corrective advertising or other corrective communications to healthcare professionals. Failure to comply with the FDA's regulations also can result in adverse publicity or increased scrutiny of company activities by the U.S. Congress or other legislators. Additionally, as described below, such failure may lead to additional liability under U.S. health care fraud and abuse laws.

Regulation of Manufacturing Standards. The FDA regulates and inspects equipment, facilities, laboratories and processes used in the manufacturing and testing of products prior to providing approval to market products. If after receiving approval from the FDA, we make a material change in manufacturing equipment, location or process, additional regulatory review may be required. We also must adhere to current Good Manufacturing Practice regulations and product-specific regulations enforced by the FDA through its facilities inspection program. The FDA conducts regular, periodic visits to re-inspect our equipment, facilities, laboratories and processes following an initial approval.

Regulation of Combination Products. Combination products are defined by the FDA to include products composed of two or more regulated components (e.g., a biologic and/or drug and a device). Biologics/Drugs and devices each have their own regulatory requirements, and combination products may have additional requirements. A number of our marketed products meet this definition and are regulated under this framework, and we expect that a number of our pipeline product candidates will be evaluated for regulatory approval under this framework as well.

Regulation Outside the United States

In the European Union (EU) countries as well as Switzerland, Canada, Australia and Japan, regulatory requirements and approval processes are similar in principle to those in the United States.

In the EU, there are currently two potential tracks for seeking marketing approval for a product which is not authorized in any Member State; a decentralized procedure; and a centralized procedure. In the decentralized procedure, identical applications for marketing authorization are submitted simultaneously to the national regulatory agencies. Regulatory review is led by one Member State (the Reference Member State) and its assessment—based on

safety, quality and efficacy—is reviewed and approved (assuming there are no concerns that the product poses a serious risk to public health) by the other Member States from which the applicant is seeking approval (the Concerned Member States). The decentralized procedure leads to a series of single national approvals in all relevant countries. In the centralized procedure, which is required of all products derived from biotechnology, a company submits a single MAA to the EMA, which conducts an evaluation of the dossier, drawing upon its scientific resources across Europe. If the drug product is proven to fulfill the requirements for quality, safety and efficacy, the EMA's CHMP adopts a positive opinion, which is transmitted to the EC for final decision on grant of the marketing authorization. While the EC generally follows the CHMP's opinion, it is not bound to do so. Subsequent commercialization is enabled by country-by-country reimbursement approval.

In the EU, biosimilars are approved under a specialized pathway of the centralized procedure. As with the U.S. pathway, applicants seek and obtain regulatory approval for a biosimilar once the data exclusivity period for the original reference product has expired relying in part on the data submitted for the originator product together with data evidencing that the biosimilar is "highly similar" in terms of quality, safety and efficacy to the original reference product authorized in the European Economic Area.

Other countries such as Russia, Turkey and those in Latin America and the Middle East have review processes and data requirements similar to those of the EU, and in some cases rely on prior marketing approval from U.S. or EU regulatory authorities. The regulatory process in these countries may include manufacturing/testing facility inspections, testing of drug product upon importation and other domestic requirements.

In Asia Pacific, a number of countries such as China, Japan, South Korea and Taiwan may require local clinical trial data for bridging purposes as part of the drug registration process in addition to global clinical trials, which can add to overall drug development and registration timelines. In most of the Asian markets, registration timelines depend on marketing approval in the United States or the EU. In some markets in Asia, such as China, Thailand, and Indonesia, the regulatory timelines can be less predictable. The regulatory process may also include manufacturing/testing facility inspections, testing of drug product upon importation and other domestic requirements. Countries such as Australia and Japan have more mature systems that would allow for submissions in more competitive timeframes. Regarding biosimilars, several of these countries have pathways to register biosimilars (e.g., South Korea, India, Australia, Singapore and Taiwan) and biosimilar products are already present on the markets (e.g., Australia and South Korea).

In some countries, such as Japan and those in the EU, medical devices may be subject to regulatory regimes whereby the manufacturer must establish that its medical device conforms to essential requirements set out in the law for the particular device category. For example, in the EU, with limited exceptions, medical devices placed on the market must bear the Conformité Européenne marking to indicate their conformity with legal requirements.

Post-approval Phase

After approval, we continue to monitor adverse events reported following the use of our products through post marketing routine pharmacovigilance surveillance and studies when applicable. We report such events to the appropriate regulatory agencies, as required per local regulations for individual cases and aggregate reports. We proactively monitor (according to good pharmacovigilance practices) and ensure implementation of signal detection, assessment and the communication of adverse events that may be associated with the use of our products. We may also be required by regulatory agencies to conduct further clinical trials on our marketed products as a condition of their approval or to provide additional information on safety and efficacy. Health authorities, including the FDA, have authority to mandate labeling changes to products at any point in a product's lifecycle based on new safety information or as part of an evolving label change to a particular class of products.

Health authorities, including the FDA, also have the authority, before or after approval, to require companies to implement a risk management program for a product to ensure that the benefits of the drug outweigh the risks. Each risk management program is unique and varies depending on the specific factors required. In the United States, a risk management program is known as a risk evaluation and mitigation strategy (REMS) and we currently have REMS for Prolia®, Nplate® and BLINCYTO®, as well as for our erythropoiesis-stimulating agents (ESAs), which includes EPOGEN® and Aranesp®.

Other Regulation

We are also subject to various laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal to solicit, offer, receive or pay any remuneration in exchange for or to induce the referral of business, including the purchase or prescription of a particular drug that is reimbursed by a state or federal program. False claims laws prohibit knowingly and willingly presenting, or causing to be presented for payment to third-party payers (including Medicare and Medicaid) any claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed or claims for medically unnecessary items or services. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and civil monetary penalties, as well as by the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid). Liability under the false claims laws may also arise when a violation of certain laws or

regulations related to the underlying products (e.g., violations regarding improper promotional activity or unlawful payments) contributes to the submission of a false claim.

In 2012, Amgen announced it had finalized a settlement agreement with the U.S. government and various other parties regarding allegations that Amgen's promotional, contracting, sales and marketing activities and arrangements caused the submission of various false claims under the Federal Civil False Claims Act and various State False Claims Acts. In connection with entering into the settlement agreement, Amgen also entered into a corporate integrity agreement with the Office of Inspector General (OIG) of the U.S. Department of Health and Human Services that requires Amgen to maintain its corporate compliance program and to undertake a set of defined corporate integrity obligations for a period of five years. Due to the breadth of the

statutory provisions and the absence of guidance in the form of regulations or court decisions addressing some of our practices, it is possible that in the future our practices might be further challenged under anti-kickback or similar laws. Additionally, the U.S. Foreign Corrupt Practices Act (FCPA) prohibits U.S. corporations and their representatives from offering, promising, authorizing or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Other countries have enacted similar anti-corruption laws and/or regulations.

Our business has been and will continue to be subject to various other U.S. and foreign laws, rules and/or regulations.

Research and Development and Selected Product Candidates

We focus our R&D on novel human therapeutics for the treatment of serious illness in the areas of oncology/hematology, cardiovascular disease, inflammation, bone health, nephrology and neuroscience. We take a modality-independent approach to R&D with a focus on biologics. We use cutting-edge science and technology to study the subtle biological mechanisms in search of therapies that will improve the lives of those who suffer from diseases. Our discovery research programs may therefore yield targets that lead to the development of human therapeutics delivered as large molecules, small molecules, or other combination or new modalities. Human genetic validation is used whenever possible to enhance the likelihood of success. For the years ended December 31, 2016, 2015 and 2014, our R&D expenses were $3.8 billion, $4.1 billion and $4.3 billion, respectively.

We have major R&D centers in several locations throughout the United States (including Thousand Oaks and San Francisco, California and Cambridge, Massachusetts), in Iceland and in the United Kingdom, as well as smaller research centers and development facilities globally. See Item 2. Properties.

We conduct clinical trial activities by using both our internal staff and third-party contract clinical trial service providers. To increase the number of patients available for enrollment in our clinical trials, we have opened clinical sites and will continue opening clinical sites and enrolling patients in a number of geographic locations. See Government Regulation—Clinical Development and Product Approval for a discussion of government regulation over clinical development. Also see Item 1A. Risk Factors—We must conduct clinical trials in humans before we can commercialize and sell any of our product candidates or existing products for new indications.

Some of our competitors are actively engaged in R&D in areas where we have products or where we are developing product candidates or new indications for existing products. For example, we compete with other clinical trials for eligible patients, which may limit the number of available patients who meet the criteria for certain clinical trials. The competitive marketplace for our product candidates is significantly dependent on the timing of entry into the market. Early entry may have important advantages in gaining product acceptance, thereby contributing to a product's eventual success and profitability. Accordingly, we expect that in some cases, the relative speed with which we can develop products, complete clinical testing, receive regulatory approval and supply commercial quantities of a product to the market will be important to our competitive position.

In addition to product candidates and marketed products generated from our internal R&D efforts, we acquire companies, acquire and license certain product and R&D technology rights and establish R&D arrangements with third parties to enhance our strategic position within our industry by strengthening and diversifying our R&D capabilities, product pipeline and marketed product base. In pursuing these R&D arrangements and licensing or acquisition activities, we face competition from other pharmaceutical and biotechnology companies that also seek to license or acquire technologies, product candidates or marketed products from those entities performing the R&D.

The following table is a selection of certain of our product candidates by phase of development in our therapeutic areas of focus as of February 13, 2017, unless otherwise indicated. Additional product candidate information can be found on our website at www.amgen.com. The website address is not intended to function as a hyperlink, and the information contained on our website is not intended to be a part of this filing. The information in this section does not include other, non-registrational clinical trials that we may conduct for purposes other than for submission to regulatory agencies for their approval of a new product indication. We may conduct non-registrational clinical trials for various reasons including to evaluate real-world outcomes or to collect additional safety information with the use of our products. In addition, the table does not include the biosimilar products we are developing, which are discussed later in this section.

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| Molecule | Disease/Condition |
|---|---|
| Phase 3 Programs | |
| Aranesp® | Myelodysplastic syndromes |
| BLINCYTO® | ALL |
| ENBREL | Psoriatic arthritis;<br>Rheumatoid arthritis remission |
| Erenumab | Episodic migraine |
| EVENITY™ | Postmenopausal osteoporosis;<br>Male osteoporosis |
| IMLYGIC® | Metastatic melanoma |
| KYPROLIS® | Multiple myeloma |
| Omecamtiv mecarbil | Chronic heart failure |
| Prolia® | Glucocorticoid-induced osteoporosis |
| Repatha® | Hyperlipidemia |
| Vectibix® | Metastatic colorectal cancer (mCRC) |
| XGEVA® | Delay or prevention of bone metastases in breast cancer;<br>Cancer-related bone damage in patients with multiple myeloma |
| Phase 2 Programs | |
| BLINCYTO® | Diffuse Large B-Cell Lymphoma (DLBCL);<br>R/R Ph+ and minimal residual disease of ALL |
| Erenumab | Chronic migraine |
| AMG 157 | Asthma;<br>Atopic dermatitis |
| AMG 520 | Alzheimer’s disease |
| AMG 899 | Dyslipidemia |
| Phase 1 Programs | |
| IMLYGIC® | Various cancer types |
| KYPROLIS® | Small-cell lung cancer |
| Oprozomib | Multiple myeloma |
| AMG 176 | Various cancer types |
| AMG 211 | Various cancer types |
| AMG 224 | Multiple myeloma |
| AMG 301 | Migraine |
| AMG 330 | Acute myeloid leukemia |
| AMG 420 | Multiple myeloma |
| AMG 557 | Systemic lupus erythematosus |
| AMG 570 | Systemic lupus erythematosus |
| AMG 592 | Inflammatory diseases |
| AMG 820 | Various cancer types |
| AMG 986 | Heart failure |

| | |
|---|---|
| Phase 3 | clinical trials investigate the safety and efficacy of product candidates in a large number of patients who have the disease or condition under study; typically performed with registrational intent. |
| Phase 2 | clinical trials investigate side effect profiles and efficacy of product candidates in a large number of patients who have the disease or condition under study. |
| Phase 1 | clinical trials investigate safety and proper dose ranges of product candidates in a small number of human subjects. |

Phase 3 Product Candidate Program Changes

As of February 15, 2016, we had 15 phase 3 programs. As of February 13, 2017, we also had 15 phase 3 programs, as omecamtiv mecarbil for the treatment of chronic heart failure advanced from phase 2 trials to phase 3 trials and Parsabiv™ was approved by the EC and FDA for the treatment of sHPT in patients with CKD on hemodialysis.

Phase 3 Product Candidate Patent Information

The following table describes our outstanding composition of matter patents that have issued thus far for our product candidates in phase 3 development that have yet to be approved for any indication. Patents for products already approved for one or more indications but currently undergoing phase 3 clinical trials for additional indications are previously described. See Marketing, Distribution and Selected Marketed Products—Patents.

| Molecule | Territory | General Subject Matter | Estimated Expiration* |
|---|---|---|---|
| Erenumab | U.S. | Polypeptides | 2031 |
| EVENITY™ | U.S. | Polypeptides | 2026 |
| | Europe | Polypeptides | 2026 |
| Omecamtiv mecarbil | U.S. | Compound | 2027 |

* Patent expiration estimates are based on issued patents, which may be challenged, invalidated, or circumvented by competitors. The patent expiration estimates do not include any term adjustments, extensions or supplemental protection certificates that may be obtained in the future and extend these dates. Corresponding patent applications are pending in other jurisdictions. Additional patents may be filed or issued and may provide additional exclusivity for the product candidate or its use.

Phase 3 and 2 Program Descriptions

The following text provides additional information about selected product candidates that have advanced into human clinical trials.

Aranesp®

Aranesp® is a recombinant human protein agonist of the erythropoietin receptor.

In February 2016, we announced that the randomized, double-bind, placebo controlled phase 3 ARCADE trial met its primary endpoint of reducing the incidence of red blood cell transfusions in anemic patients with low and intermediate-1 risk myelodysplastic syndromes.

BLINCYTO®

BLINCYTO® is an anti-CD19 x anti-CD3 (BiTE®) bispecific antibody construct.

A phase 3 study in pediatric patients with high-risk first relapse B-precursor ALL is ongoing. Phase 2 studies in adult patients with R/R Ph+ and minimal residual disease of ALL are ongoing. A phase 2/3 study in patients with R/R DLBCL is ongoing.

In February 2017, we announced the submission of a sBLA to the FDA to include overall survival data from the Phase 3 TOWER study, supporting the conversion of BLINCYTO®'s accelerated approval to full approval. The sBLA also includes new data supporting the treatment of patients with Ph+ R/R B-cell precursor ALL.

Denosumab

Denosumab is a human monoclonal antibody that inhibits RANKL.

Prolia®

In August 2016, we announced that the phase 3 randomized, double-blind, double-dummy, active controlled study evaluating the safety and efficacy of Prolia® compared with risedronate in patients receiving glucocorticoid treatment met all primary and secondary endpoints at 12 months.

XGEVA®

In October 2016, we announced that a phase 3 study evaluating XGEVA® versus Zometa® in the prevention of SRE in patients with multiple myeloma met its primary endpoint of non-inferiority in delaying the time to first on-study SRE. The secondary endpoints of superiority in delaying time to first SRE and delaying time to first-and-subsequent SRE were not met.

A phase 3 study for the delay or prevention of bone metastases in patients with adjuvant breast cancer is ongoing.

ENBREL

ENBREL is a fusion protein that inhibits tumor necrosis factor.

A phase 3 study to evaluate ENBREL as a monotherapy for psoriatic arthritis treatment is ongoing. A phase 3 study to evaluate ENBREL as a monotherapy in maintaining remission in rheumatoid arthritis is ongoing.

Erenumab (formerly AMG 334)

Erenumab is a human monoclonal antibody that inhibits the receptor for calcitonin gene-related peptide. It is being evaluated for the prophylaxis of migraine. Erenumab is being developed jointly with Novartis.

In June 2016, we announced that the global phase 2 study evaluating the efficacy and safety of erenumab in chronic migraine prevention met its primary endpoint.

In September 2016, we announced that the phase 3 ARISE study evaluating the efficacy of erenumab in episodic migraine prevention, met its primary endpoint. Patients enrolled in ARISE study were randomized to receive either placebo, or erenumab 70 mg subcutaneously, once monthly for three months.

In November 2016, we announced that the global phase 3 STRIVE study evaluating the efficacy of erenumab in episodic migraine prevention, met its primary endpoint. Patients enrolled in STRIVE were randomized to receive either placebo, or one of two erenumab doses—70 mg or 140 mg—subcutaneously, once monthly for six months.

EVENITY™

EVENITY™ is a humanized monoclonal antibody that inhibits the action of sclerostin. It is being evaluated as a treatment for osteoporosis. EVENITY™ is being developed in collaboration with UCB.

In February 2016, we and UCB announced that the phase 3 FRAME study met its co-primary endpoints.

In March 2016, we and UCB announced that the phase 3 BRIDGE study met its primary endpoint.

In September 2016, we and UCB announced that the FDA accepted for review the BLA for EVENITY™ for the treatment of osteoporosis in postmenopausal women at increased risk for fracture. The FDA has set a PDUFA target action date of July 19, 2017. Phase 3 studies for the treatment of postmenopausal women with osteoporosis are ongoing.

IMLYGIC®

IMLYGIC® is an oncolytic immunotherapy derived from HSV-1.

A phase 1b/3 study to evaluate IMLYGIC® in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in patients with mid- to late-stage metastatic melanoma is ongoing.

KYPROLIS®

KYPROLIS® is a proteasome inhibitor.

A phase 3 study, ARROW (RAndomized, Open-label, Phase 3 Study in Subjects with Relapsed and Refractory Multiple Myeloma Receiving Carfilzomib in Combination with Dexamethasone, Comparing Once-Weekly versus Twice-weekly Carfilzomib Dosing), with weekly dosing in relapsed and refractory multiple myeloma is ongoing.

Omecamtiv mecarbil

Omecamtiv mecarbil is a small molecule activator of cardiac myosin. It is being evaluated for the treatment of chronic heart failure. Omecamtiv mecarbil is being developed by Amgen in collaboration with Cytokinetics, Inc. and in an alliance with Servier for certain territories.

A phase 3 cardiovascular outcomes study for the treatment of chronic heart failure is ongoing.

Repatha®

Repatha® is a human monoclonal antibody that inhibits PCSK9.

In September 2016, we announced that the phase 3 GLAGOV study evaluating the effect of Repatha® on coronary artery disease met its primary and secondary endpoints.

In February 2017, we announced that the phase 3 FOURIER study evaluating the effects of Repatha® on cardiovascular outcomes met its primary composite endpoint and key secondary composite endpoint. No new safety issues were observed.

In February 2017, we announced that the phase 3 EBBINGHAUS cognitive function study achieved its primary endpoint.

Additional phase 3 studies to evaluate Repatha® in diabetes, statin intolerant subjects, with coronary imaging, and to reduce the need for future apheresis are ongoing.

Vectibix®

Vectibix® is a human monoclonal antibody antagonist of the EGFr.

In June 2015, we announced that results of a phase 3 study evaluating Vectibix® and best supportive care (BSC) met its primary endpoint, demonstrating a statistically significant improvement in overall survival in patients with chemorefractory wild-type KRAS (exon2) mCRC compared to those patients treated with BSC alone.

AMG 157

AMG 157 is a human monoclonal antibody that inhibits the action of TSLP. It is being evaluated as a treatment for asthma and atopic dermatitis, with phase 2 studies ongoing. AMG 157 is being jointly developed in collaboration with AstraZeneca plc (AstraZeneca).

AMG 520

AMG 520 is a small molecule inhibitor of BACE. It is being evaluated for the prevention of Alzheimer's disease, with phase 2 studies ongoing. AMG 520 is being jointly developed in collaboration with Novartis.

AMG 899

AMG 899 is a small molecule CETP inhibitor. It is being evaluated for the treatment of dyslipidemia and has completed certain phase 2 studies. Development of AMG 899 is delayed pending competitor clinical trials in the class.

Amgen Development of Biosimilars

We continue to develop and commercialize biosimilar medicines. Our biosimilar product candidates are in varying stages of commercialization and clinical development as described in the following table:

| Program | Reference product | Status |
|---|---|---|
| AMJEVITA™/ABP 501 | adalimumab (HUMIRA®) | Approved by FDA across all eligible indications of reference product and MAA submitted to EMA |
| ABP 215* | bevacizumab (Avastin®) | BLA and MAA submitted to FDA and EMA, respectively |
| ABP 710 | infliximab (REMICADE®) | Phase 3 rheumatoid arthritis study ongoing |
| ABP 798* | rituximab (Rituxan® / Mabthera®) | Phase 3 rheumatoid arthritis study ongoing<br>Phase 3 non-Hodgkin's lymphoma study ongoing |
| ABP 959 | eculizumab (Soliris®) | Phase 1 ongoing |
| ABP 980* | trastuzumab (Herceptin®) | Phase 3 breast cancer study completed |

* Developed in collaboration with Allergan

Business Relationships

From time to time, we enter into business relationships, including joint ventures and collaborative arrangements, for the R&D, manufacture and/or commercialization of products and/or product candidates. In addition, we also acquire product and R&D technology rights and establish R&D collaborations with third parties to enhance our strategic position within our industry by strengthening and diversifying our R&D capabilities, product pipeline and marketed product base. These arrangements generally provide for non-refundable, upfront license fees; development and commercial performance milestone payments; cost sharing; royalty payments and/or profit sharing. The activities under these collaboration agreements are performed with no guarantee of either technological or commercial success, and each is unique in nature.

Trade secret protection for our unpatented confidential and proprietary information is important to us. To protect our trade secrets, we generally require counterparties to execute confidentiality agreements upon the commencement of the business relationship with us. However, others could either develop independently the same or similar information or unlawfully obtain access to our information.

Kirin-Amgen, Inc.

Kirin-Amgen, Inc. (K-A) is a 50-50 joint venture with Kirin Holdings Company, Limited (Kirin). K-A develops and then out-licenses to third parties certain product rights which have been transferred to this joint venture from Amgen and Kirin.

K-A has given us exclusive licenses to manufacture and market: (i) G-CSF and pegfilgrastim in the United States, Europe, Canada, Australia, New Zealand, all Central American, South American, Middle Eastern and African countries and certain countries in Asia; (ii) darbepoetin alfa and romiplostim in the United States, Europe, Canada, Australia, New Zealand, Mexico, all Central and South American countries and certain countries in Central Asia, Africa and the Middle East; and (iii) recombinant human erythropoietin in the United States. We currently market pegfilgrastim, G-CSF, darbepoetin alfa, recombinant human erythropoietin and romiplostim under the brand names Neulasta®, NEUPOGEN®/GRANULOKINE®, Aranesp®, EPOGEN® and Nplate®, respectively. Under these agreements, we pay K-A royalties based on product sales. In addition, we also receive payments from K-A for milestones earned and for conducting certain R&D activities on its behalf. See Part IV—Note 8, Related party transactions, to the Consolidated Financial Statements.

K-A has also given Kirin exclusive licenses to manufacture and market: (i) G-CSF and pegfilgrastim in Japan, Taiwan and South Korea; (ii) darbepoetin alfa, romiplostim and brodalumab in Japan, China, Taiwan, South Korea and in certain other countries and/or regions in Asia; and (iii) recombinant human erythropoietin in Japan. K-A also gave Kirin and Amgen co-exclusive licenses to manufacture and market G-CSF, pegfilgrastim and recombinant human erythropoietin in China, which Amgen subsequently assigned to Kirin, and as a result, Kirin now exclusively manufactures and markets G-CSF and recombinant human erythropoietin in China. Kirin markets G-CSF, pegfilgrastim, darbepoetin alfa, romiplostim, recombinant human erythropoietin, and brodalumab under the brand names GRAN®/Grasin®, Peglasta®/Neulasta®/G-Lasta®, NESP®/Aranesp®, ROMIPLATE®, ESPO®, and LUMICEF®, respectively. Under these agreements, Kirin pays K-A royalties based on product sales. In addition, Kirin also receives payments from K-A for conducting certain R&D activities on its behalf.

K-A has also given J&J exclusive licenses to manufacture and market recombinant human erythropoietin for all geographic areas of the world outside the United States, China and Japan. Under this agreement, J&J pays royalties to K-A based on product sales.

Pfizer Inc.

The co-promotion term of our ENBREL collaboration agreement with Pfizer Inc. (Pfizer) in the United States and Canada expired on October 31, 2013. Under this agreement, we paid Pfizer a profit share until October 31, 2013, and residual royalties from November 1, 2013 to October 31, 2016, which were significantly less than the profit share payments. In 2016, the residual royalty payments were 10% of the annual net ENBREL sales in the United States and Canada. Effective November 1, 2016, there are no further royalty payments.

UCB

We are in a collaboration with UCB for the development and commercialization of EVENITY™. In 2016, we amended the commercialization rights and responsibilities of the parties. Under the amended agreement, we have the rights to commercialize EVENITY™ for all indications in the United States and Japan. UCB has the rights for Europe, China, and Brazil. The rest of the countries have been allocated to Amgen. Generally, development costs and future worldwide commercialization profits and losses related to the collaboration after accounting for expenses are shared equally.

Bayer HealthCare Pharmaceuticals Inc.

We are in a collaboration with Bayer HealthCare Pharmaceuticals Inc. (Bayer) to jointly develop and commercialize Nexavar® (sorafenib). In 2015, we amended the terms of our collaboration agreement with Bayer, which terminated the co-promotion agreement in the United States, and transferred all U.S. operational responsibilities to Bayer, including commercial and medical affairs activities. Prior to the termination of the co-promotion agreement, we

co-promoted Nexavar® with Bayer and shared equally in the profits in the United States. In lieu of this profit share, Bayer now pays us a royalty on U.S. sales of Nexavar® at a percentage rate in the high 30s. Outside of the United States, excluding Japan, Bayer manages all commercialization activities and incurs all of the sales and marketing expenditures and mutually agreed R&D expenses, and we reimburse Bayer for half of those expenditures. In all countries outside of the United States, except Japan, we receive 50% of net profits on sales of Nexavar® after deducting certain Bayer-related costs. The rights to develop and market Nexavar® in Japan are reserved to Bayer.

DaVita Inc.

In January 2017, we entered into a new six-year supply agreement with DaVita Inc. (DaVita), which supercedes the existing seven-year supply agreement that commenced in 2012. Pursuant to the new agreements, we will supply EPOGEN® and Aranesp® in amounts necessary to meet specified annual percentages of DaVita's and its affiliates' requirements for ESAs used in providing dialysis services in the United States and Puerto Rico. Such percentage varies during the term of the agreement, but each year is at least 90%. The new agreement expires in 2022. The agreement may be terminated by either party before expiration of its term in the event of certain breaches of the agreement by the other party.

Human Resources

As of December 31, 2016, Amgen had approximately 19,200 staff members. We consider our staff relations to be good.

Executive Officers of the Registrant

The executive officers of the Company as of February 7, 2017, are set forth below.

Mr. Robert A. Bradway, age 54, has served as a director of the Company since October 2011 and Chairman of the Board of Directors since January 1, 2013. Mr. Bradway has been the Company's President since May 2010 and Chief Executive Officer since May 2012. From May 2010 to May 2012, Mr. Bradway served as the Company's President and Chief Operating Officer. Mr. Bradway joined the Company in 2006 as Vice President, Operations Strategy and served as Executive Vice President and Chief Financial Officer from April 2007 to May 2010. Prior to joining the Company, he was a Managing Director at Morgan Stanley in London where, beginning in 2001, he had responsibility for the firm's banking department and corporate finance activities in Europe.

Mr. Bradway has been a director of Norfolk Southern Corporation, a transportation company, since July 2011, and The Boeing Company, an aerospace company and manufacturer of commercial airplanes, defense, space and securities systems, since October 2016. He has served on the board of trustees of the University of Southern California since April 2014, and on the advisory board of the Leonard D. Schaeffer Center for Health Policy and Economics at that university since 2012.

Mr. Jonathan P. Graham, age 56, became Senior Vice President, General Counsel and Secretary in July 2015. From July 2006 to May 2015, Mr. Graham was Senior Vice President and General Counsel at Danaher Corporation. From October 2004 to June 2006, Mr. Graham was Vice President, Litigation and Legal Policy at General Electric Company (GE). Prior to GE, Mr. Graham was a partner at Williams & Connolly LLP.

Dr. Sean E. Harper, age 54, became Executive Vice President, Research and Development in February 2012. Dr. Harper joined the Company in 2002, and has held leadership roles in early development, medical sciences and global regulatory and safety. Dr. Harper served as Senior Vice President, Global Development and Corporate Chief Medical Officer from March 2007 to February 2012. Prior to joining the Company, Dr. Harper worked for five years at Merck Research Laboratories.

Mr. Anthony C. Hooper, age 62, became Executive Vice President, Global Commercial Operations in October 2011. From March 2010 to October 2011, Mr. Hooper was Senior Vice President, Commercial Operations and President, U.S., Japan and Intercontinental of BMS. From January 2009 to March 2010, Mr. Hooper was President, Americas of BMS. From January 2004 to January 2009, Mr. Hooper was President, U.S. Pharmaceuticals, Worldwide Pharmaceuticals Group, a division of BMS. Prior to this, Mr. Hooper held various senior leadership positions at BMS. Prior to joining BMS, Mr. Hooper was Assistant Vice President of Global Marketing for Wyeth Laboratories.

Ms. Lori A. Johnston, age 52, became Senior Vice President in December 2016. From October 2012 to December 2016, Ms. Johnston was Executive Vice President and Chief Administrative Officer of Celanese Corporation. From February 2006 to September 2012, Ms. Johnston served in a series of progressive leadership roles at Amgen, with her last position being Vice President, Human Resources. Prior to joining the Company, Ms. Johnston held human resources and other positions at Dell Inc.

Mr. Brian McNamee, age 60, became Executive Vice President, Full Potential Initiatives in October 2013. Mr. McNamee joined the Company in June 2001 as Senior Vice President, Human Resources. From November 1999 to June 2001, Mr. McNamee served as Vice President of Human Resources at Dell Computer Corp. From 1998 to 1999, Mr. McNamee served as Senior Vice President, Human Resources for the National Broadcasting Corporation, a

division of the GE. From July 1988 to November 1999, Mr. McNamee held human resources positions at GE.

Mr. David W. Meline, age 59, became Executive Vice President and Chief Financial Officer in July 2014. From April 2011 to July 2014, Mr. Meline served as Senior Vice President and Chief Financial Officer at 3M Company (3M). From September 2008 to March 2011, Mr. Meline served as Vice President, Corporate Controller and Chief Accounting Officer of 3M. Prior to 2008, Mr. Meline served in a variety of senior leadership roles for General Motors Company for over 20 years, with his last position being Vice President and Chief Financial Officer, North America. Mr. Meline has been a director of ABB Ltd., a global industrial technology company based in Switzerland, since February 2016, serving as a member of the Finance, Audit and Compliance Committee. Mr. Meline was a director of TRW Automotive Holdings, Corp., a supplier of automotive systems, modules and components, from February 2014 until its acquisition by ZF Friedrichshafen AG in May 2015.

Ms. Cynthia M. Patton, age 55, became Senior Vice President and Chief Compliance Officer in October 2012. Ms. Patton joined the Company in 2005. From July 2005 to September 2010, Ms. Patton was Associate General Counsel. From September 2010 to October 2012, Ms. Patton was Vice President, Law. Previously, Ms. Patton served as Senior Vice President, General Counsel and Secretary of SCAN Health Plan from 1999 to 2005.

Mr. David A. Piacquad, age 60, became Senior Vice President, Business Development in March 2014. Mr. Piacquad joined the Company in June 2010 and, until January 2014, served as Vice President, Strategy and Corporate Development. From January 2014 to March 2014, Mr. Piacquad served as Vice President, Business Development. Prior to joining the Company, from December 2009 to June 2010, Mr. Piacquad was Principal of David A. Piacquad Consulting LLC. From March 2006 to December 2009, Mr. Piacquad served as Senior Vice President, Business Development and Licensing for Schering-Plough Corporation. Prior to Schering-Plough, Mr. Piacquad served in a series of leadership roles in finance and business development at J&J, with his last position being Vice President, Ventures and Business Development.

Mr. Esteban Santos, age 49, became Executive Vice President, Operations in July 2016. Mr. Santos joined the Company in 2007 as Executive Director, Manufacturing Technologies. From October 2008 to May 2013, Mr. Santos held a number of Vice President roles at the Company in engineering, manufacturing, site operations and drug product. From May 2013 to July 2016, Mr. Santos was Senior Vice President, Manufacturing. Prior to joining the Company, Mr. Santos served as Site General Manager for J&J's Cordis operation in Puerto Rico. Prior to J&J, Mr. Santos held several management positions in GE's industrial and transportation businesses.

Geographic Area Financial Information

For financial information concerning the geographic areas in which we operate, see Part IV—Note 19, Segment information—Geographic information, to the Consolidated Financial Statements.

Investor Information

Financial and other information about us is available on our website at www.amgen.com. We make available on our website, free of charge, copies of our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the U.S. Securities and Exchange Commission (SEC). In addition, we have previously filed registration statements and other documents with the SEC. Any document we file may be inspected, without charge, at the SEC's public reference room at 100 F Street NE, Washington, DC 20549, or at the SEC's website at www.sec.gov. These website addresses are not intended to function as hyperlinks, and the information contained in our website and in the SEC's website is not intended to be a part of this filing. Information related to the operation of the SEC's public reference room may be obtained by calling the SEC at 800-SEC-0330.

Item 1A. RISK FACTORS

This report and other documents we file with the SEC contain forward-looking statements that are based on current expectations, estimates, forecasts and projections about us, our future performance, our business, our beliefs and our management's assumptions. The statements are not guarantees of future performance and involve certain risks, uncertainties and assumptions that are difficult to predict. You should carefully consider the risks and uncertainties our business faces. The risks described below are not the only ones we face. Our business is also subject to the risks that affect many other companies, such as employment relations, general economic conditions, geopolitical events and international operations. Further, additional risks not currently known to us or that we currently believe are immaterial

may in the future materially and adversely affect our business, operations, liquidity and stock price.

Our sales depend on coverage and reimbursement from third-party payers, and pricing and reimbursement pressures may affect our profitability.

Sales of our products depend on the availability and extent of coverage and reimbursement from third-party payers, including government healthcare programs and private insurance plans. Governments and private payers continue to pursue aggressive initiatives to contain costs and manage drug utilization and are increasingly focused on the effectiveness, benefits and costs of similar treatments, which could result in lower reimbursement rates for our products or narrower populations for whom our products will be reimbursed by payers. Public scrutiny of the price of drugs and other healthcare costs is increasing and greater focus on pricing and price increases may limit our ability to set or increase the price of our products based on their value, which could have a material adverse effect on our product sales, business and results of operations.

A substantial portion of our U.S. business relies on reimbursement from U.S. federal government healthcare programs and private insurance plans regulated by the U.S. federal government. See Item 1. Business—Reimbursement. Changes to U.S. federal reimbursement policy may come through legislative actions. U.S. President Donald Trump and other U.S. lawmakers have made statements about potentially repealing and/or replacing the ACA, although specific legislation for such a repeal or replacement has not yet been introduced. While we are unable to predict what changes may ultimately be enacted, to the extent that future changes affect how our products are paid for and reimbursed by government and private payers our business could be adversely impacted. For example, discussions continue about proposals that would allow the U.S. federal government to directly negotiate drug prices with pharmaceutical manufacturers or require manufacturers to pay higher rebates in the Medicare Part D setting. Changes in U.S. federal reimbursement policy may also arise as a result of regulations or demonstration projects implemented by the Centers for Medicare & Medicaid Services (CMS), the federal agency responsible for administering Medicare, Medicaid and the Health Insurance Marketplaces. CMS has substantial power to quickly implement policy changes that can significantly affect how our products are covered and reimbursed. State government actions or ballot initiatives can also affect how our products are covered and reimbursed or create additional pressure on how our products are priced. Many states have discussed and debated and are considering new pricing legislation, including state proposals designed to require biopharmaceutical manufacturers to publicly report proprietary pricing information or to place a maximum price ceiling, or cap, on pharmaceutical products purchased by state agencies. For example, Ohio voters are expected to consider in their November 2017 election a ballot proposition that would prohibit the state from paying a greater price for drugs than the lowest price paid by the U.S. Department of Veterans Affairs. Passage of this proposition could lead to the introduction of additional ballot initiatives in other states. Legislative or regulatory changes or other government initiatives that decrease the coverage or reimbursement available for our products, require that we pay increased rebates, limit our ability to offer co-pay payment assistance to commercial patients or limit the pricing of pharmaceutical products could have a material adverse effect on our business and results of operations.

Payers, including healthcare insurers, PBMs and group purchasing organizations, increasingly seek price discounts or rebates in connection with the placement of our products on their formularies or those they manage. Consolidation in the health insurance industry has resulted in a few large insurers and PBMs exerting greater pressure in pricing and usage negotiations with drug manufacturers, significantly increasing such discounts and rebates and limiting patient access and usage. Three PBMs currently oversee approximately 75% of total covered lives in the United States. Payers continue to adopt benefit plan changes that shift a greater portion of prescription costs to patients, and some payers may attempt to limit the use of programs assisting commercial patients with their co-payments. Payers also control costs by imposing restrictions on access to our products, such as by requiring prior authorizations or step therapy, and may choose to exclude certain indications for which our products are approved or even choose to exclude coverage entirely. For example, since the launch of Repatha® in August 2015, the application of utilization management criteria by some payers, including PBMs, has resulted in denials of coverage for a significant number of patients for whom Repatha® has been prescribed, slowing Repatha® sales. In early February 2017, we announced that our phase 3 outcomes study evaluating the ability of Repatha® to prevent cardiovascular events met its primary composite endpoint and key secondary composite endpoint. See Item 1. Business—Significant Developments. However, in the current competitive environment, the application of restrictive utilization management criteria by some payers

may continue until the clinical data is reflected in approved product labeling, or even thereafter. Ultimately, further discounts, rebates, coverage or plan changes, restrictions or exclusions as described above could have a material adverse effect on sales of our affected products.

We also face risks relating to the reporting of pricing data that affects the reimbursement of and discounts provided for our products to U.S. government healthcare programs. Pricing data that we submit impacts the payment rates for providers, rebates we pay, and discounts we are required to provide under Medicare, Medicaid and other government drug programs. Government price reporting regulations are complex and may require a manufacturer to update certain previously submitted data. Our price reporting data calculations are reviewed monthly and quarterly, and based on such reviews we have on occasion restated previously reported pricing data to reflect changes in calculation methodology, reasonable assumptions and/or underlying data. If our submitted pricing data are incorrect, we may become subject to substantial fines and penalties or other government enforcement actions, which could have a material adverse effect on our business and results of operations. In addition, as a result of restating previously reported price data, we also may be required to pay additional rebates and provide additional discounts.

Outside the United States, we expect countries will continue to take aggressive actions to reduce their healthcare expenditures. See Item 1. Business—Reimbursement. For example, international reference pricing (IRP) is widely used by a large number of countries to control costs based on an external benchmark of a product's price in other countries. IRP policies can quickly and frequently change and may not reflect differences in the burden of disease, indications, market structures, or affordability differences across countries or regions. Any deterioration in the coverage and reimbursement available for our products or in the timeliness or certainty of payment by payers to physicians and other providers could negatively impact the ability or willingness of healthcare providers to prescribe our products for their patients or could otherwise negatively affect the use of our products or the prices we receive for them. Such changes could have a material adverse effect on our product sales, business and results of operations.

Our products face substantial competition.

We operate in a highly competitive environment. See Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition. We expect that our products will compete with new drugs currently in development, drugs currently approved for other indications that may later be approved for the same indications as those of our products and drugs approved for other indications that are used off-label. Large pharmaceutical companies and generics manufacturers of pharmaceutical products are expanding into the biotechnology field, and some pharmaceutical companies and generics manufacturers have formed partnerships to pursue biosimilars. In addition, some of our competitors may have technical, competitive or other advantages over us for the development of technologies and processes or greater experience in particular therapeutic areas, and consolidation among pharmaceutical and biotechnology companies can enhance such advantages. These advantages may make it difficult for us to compete with them to successfully discover, develop and market new products and for our current products to compete with new products or new product indications they may bring to market. As a result, our products may compete against products that have lower prices, equivalent or superior performance, better safety profiles, easier administration, earlier market availability or other competitive features. If we are unable to compete effectively, this could reduce sales, which could have a material adverse effect on our business and results of operations.

We currently face competition from biosimilars and expect to face increasing competition in the future.

We currently face competition from biosimilars in both Europe and the United States, and we expect to face increasing biosimilar competition in the next year and beyond. Expiration or successful challenge of applicable patent rights could accelerate such competition, and we could face more litigation regarding the validity and/or scope of our patents. Our products may also experience greater competition from lower-cost biosimilars or generics that come to market when branded products that compete with our products lose their own patent protection. To the extent that governments adopt more permissive approval frameworks and competitors are able to obtain broader or expedited marketing approval for biosimilars, the rate of increased competition for our products could accelerate.

In the EU, biosimilars are evaluated and authorized pursuant to a set of general and product class-specific guidelines. In addition, in an effort to spur biosimilar utilization and/or increase potential healthcare savings, some EU countries have adopted or are attempting to adopt biosimilar uptake measures such as requiring physician prescribing quotas or promoting switching or pharmacy substitution of biosimilars for the corresponding reference products, and other countries may adopt similar measures. Some EU countries may impose automatic price reductions upon market entry of the second or third biosimilar competitor.

In the United States, the ACA authorized the FDA to approve biosimilars via a separate, abbreviated pathway. See Item 1. Business—Government Regulation—Regulation in the United States—Approval of Biosimilars. The first biosimilar entrant into the U.S. market, Sandoz's Zarxio®, is a biosimilar version of NEUPOGEN®, and was launched in the United States in 2015. Since then, the FDA has approved additional biosimilars, including a biosimilar version of ENBREL. In addition, a growing number of companies have announced that they are in varying stages of development of biosimilar versions of existing biotechnology products, including biosimilars that would compete with our products. Companies pursuing development of biosimilar versions of our products have challenged and may continue to, challenge our patents well in advance of the expiration of our material patents. For information related to our biosimilars patent litigation, including our litigation regarding ENBREL, see Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements. See also Our intellectual property positions may be challenged, invalidated or circumvented, or we may fail to prevail in present and future intellectual property litigation.

The U.S. pathway includes the option for biosimilar products that meet certain criteria to be approved as interchangeable with their reference products. Some companies currently developing biosimilars may seek to register their products as interchangeable biologics, which could make it easier for pharmacists to substitute those biosimilars for our products or could encourage prescribers who are inclined to select the interchangeable biosimilar over our innovative products. In addition, critics of the 12-year exclusivity period in the biosimilar pathway law will likely continue to seek to shorten the data exclusivity period and/or to encourage the FDA to interpret narrowly the law's provisions regarding which new products receive data exclusivity, which could expose us to biosimilar competition at an earlier time. While we are unable to predict the precise impact of biosimilars on our products, we are currently facing and expect to face greater competition in the United States and Europe in the next year and beyond as a result of biosimilars and downward pressure on our product prices and sales. This biosimilar competition has had and could increasingly have a material adverse effect on our business and results of operations.

Our current products and products in development cannot be sold without regulatory approval.

Our business is subject to extensive regulation by numerous state and federal government authorities in the United States, including the FDA, and by foreign regulatory authorities, including the EMA. We are required in the United States and in foreign countries to obtain approval from regulatory authorities before we manufacture, market and sell our products. Once our products are approved, the FDA and other U.S. and foreign regulatory agencies have substantial authority to require additional testing and reporting, perform inspections, change product labeling or mandate withdrawals of our products. Failure to comply with applicable regulatory requirements may subject us to administrative and/or judicially imposed sanctions or monetary penalties as well as reputational and other harms. The sanctions could include the FDA's or foreign regulatory authorities' refusals to approve pending applications, delays in obtaining or withdrawals of approvals, delays or suspensions of clinical trials, warning letters, product recalls or seizures, total or partial suspensions of our operations, injunctions, fines, civil penalties and/or criminal prosecutions.

Obtaining and maintaining regulatory approval have been, and will continue to be, increasingly difficult, time-consuming and costly. Legislative bodies or regulatory agencies could enact new laws or regulations, change existing laws or regulations, or change their interpretations of laws or regulations at any time, which could affect our ability to obtain or maintain approval of our products or product candidates. The rate and degree of change in existing laws and regulations and regulatory expectations have accelerated in established markets, and regulatory expectations continue to evolve in emerging markets. We are unable to predict whether and when any further changes to laws or regulatory policies affecting our business could occur, such as changes to regulations governing manufacturer communications concerning drug products and drug product candidates, and whether such changes could have a material adverse effect on our business and results of operations.

Regulatory authorities may also question the sufficiency for approval of the endpoints we select for our clinical trials. A number of our products and product candidates have been evaluated in clinical trials using surrogate endpoints that measure an effect that is known to correlate with an ultimate clinical endpoint. For example, a therapeutic oncology product candidate may be evaluated for its ability to extend the length of time during and after the treatment that a patient lives without the disease worsening PFS. Demonstrating that the product candidate produces a statistically significant improvement in PFS does not necessarily mean that the product candidate will show a statistically significant improvement in overall survival or the time that the patients remain alive. In the cardiovascular setting, a heart disease therapeutic candidate may be evaluated for its ability to reduce LDL-C levels, as elevated LDL-C level has been a surrogate endpoint for cardiovascular events such as death, heart attack and stroke. The use of surrogate endpoints such as PFS and LDL-C reduction, in the absence of other measures of clinical benefit, may not be sufficient for broad usage or approval even when such results are statistically significant. Regulatory authorities could also add new requirements, such as the completion of enrollment in a confirmatory study or the completion of an outcomes study or a meaningful portion of an outcomes study, as conditions for obtaining approval or obtaining an indication. For example, our initial FDA application for Repatha® sought approval for a broader patient population based on data demonstrating that Repatha® reduced LDL-C levels. However, the FDA ultimately approved Repatha® only for a subset of those patients, citing among other things the absence of positive outcomes data showing that Repatha® prevents cardiovascular events. We subsequently announced that our phase 3 outcomes study evaluating the ability of Repatha® to prevent cardiovascular events met its primary composite endpoint and key secondary composite endpoint. See Item 1. Business—Significant Developments. However, we cannot predict the degree to which the results of this study will be incorporated into the Repatha® label by regulators. There may also be situations in which demonstrating the efficacy and safety of a product candidate may not be sufficient to gain regulatory approval unless superiority to comparative products can be shown. The imposition of additional requirements or our inability to meet them in a timely fashion or at all may delay our clinical development and regulatory filing efforts, delay or prevent us from obtaining regulatory approval for new product candidates or new indications for existing products, or prevent us from maintaining our current labels.

Some of our products have been approved by U.S. and foreign regulatory authorities on a conditional basis with full approval conditioned upon fulfilling the requirements of regulators. For example, in December 2014, we received accelerated approval for BLINCYTO® for the treatment of patients with Ph- relapsed or refractory B-cell precursor ALL in the United States, with continued approval contingent upon clinical benefit in subsequent trials. BLINCYTO®

also received conditional marketing authorization for the treatment of patients with Ph- relapsed or refractory B-cell precursor ALL from the EC in November 2015. Regulatory authorities are placing greater focus on monitoring products originally approved on an accelerated or conditional basis and on whether the sponsors of such products have met the conditions of the accelerated or conditional approvals. If we are unable to fulfill the regulators' requirements that were conditions of a product's accelerated or conditional approval and/or if regulators re-evaluate the data or risk-benefit profile of our product, the conditional approval may not result in full approval or may be revoked or not renewed. Alternatively, we may be required to change the product's labeled indications or even withdraw the product from the market.

Safety problems or signals can arise as our products and product candidates are evaluated in clinical trials, including investigator sponsored studies, or as our marketed products are used in clinical practice. We are required to continuously collect and assess adverse events reported to us and to communicate to regulatory agencies these adverse events and safety signals regarding

our products. Regulatory agencies periodically perform inspections of our pharmacovigilance processes, including our adverse event reporting. In 2012, pharmacovigilance legislation became effective in the EU that enhanced the authority of European regulators to require companies to conduct additional post-approval clinical efficacy and safety studies and increased the requirements on sponsor companies to analyze and evaluate the risk-benefit profiles of their products. Similarly, for our products with approved REMS (see Item 1. Business—Government Regulation—Post-Approval Phase) we are required to submit periodic assessment reports to the FDA to demonstrate that the goals of the REMS are being met. REMS and other risk management programs are designed to ensure that a drug's benefits outweigh the risks, and vary in the elements they contain. For example, our ESA REMS requires applicable healthcare providers and institutions to enroll in the program, receive education about the product and the REMS and document and report certain information to us over time. We are responsible for tracking and documenting certain elements of healthcare provider and institution compliance with the ESA REMS, and we use third-party service providers to assist in the administration of certain portions of our REMS. If the FDA is not satisfied with the results of the periodic assessment reports we submit for any of our REMS, the FDA may also modify our REMS or take other regulatory actions, such as implementing revised or restrictive labeling. If regulatory agencies determine that we or other parties (including our clinical trial investigators, those operating our patient support programs or licensees of our products) have not complied with the applicable reporting or other pharmacovigilance requirements, we may become subject to additional inspections, warning letters or other enforcement actions, including fines, marketing authorization withdrawal and other penalties. Our product candidates and marketed products can also be affected by safety problems or signals occurring with respect to products that are similar to ours and that implicate an entire class of products. Further, as a result of clinical trials, including sub-analyses or meta-analyses of earlier clinical trials (a meta-analysis involves the use of various statistical methods to combine results from previous separate but related studies) performed by us or others, concerns may arise about the sufficiency of the data or studies underlying a product's approved label. Such actual or perceived safety problems or concerns can lead to:

- revised or restrictive labeling for our products, or the potential for restrictive labeling that may result in our decision not to commercialize a product candidate;
- requirement of risk management activities or other regulatory agency compliance actions related to the promotion and sale of our products;
- mandated post-marketing commitments or pharmacovigilance programs for our approved products;
- product recalls of our approved products;
- revocation of approval for our products from the market completely, or within particular therapeutic areas or patient types;
- increased timelines or delays in being approved by the FDA or other regulatory bodies; and/or
- fewer treatments or product candidates being approved by regulatory bodies.

For example, since 2006, when adverse safety results involving ESAs were observed, ESAs continue to be the subject of ongoing review and scrutiny. Reviews by regulatory authorities of the risk-benefit profile of ESAs have resulted in, and may continue to result in, changes to ESA labeling, our ESA REMS and usage in both the oncology and nephrology clinical settings.

In addition to our innovative products, we are working to develop and commercialize biosimilar versions of a number of products currently manufactured, marketed and sold by other pharmaceutical companies. In some markets, there is not yet a legislative or regulatory pathway for the approval of biosimilars. In the United States, the ACA provided for such a pathway; while the FDA continues to implement it, questions remain as to the evidence needed to demonstrate biosimilarity or interchangeability for specific products and what information can be included in biosimilar labeling. See We currently face competition from biosimilars and expect to face increasing competition in the future. Delays or uncertainties in the development of such pathways could result in delays or difficulties in getting our biosimilar products approved by regulatory authorities, subject us to unanticipated development costs or otherwise reduce the value of the investments we have made in the biosimilars area. Further, we cannot predict whether any repeal or reform of the ACA would affect the biosimilar pathway or have a material adverse effect on our development of biosimilars. In addition, if we are unable to bring our biosimilar products to market on a timely basis, and secure "first-to-market" positions, our future biosimilar sales and results of operations could be materially and adversely

affected.

We may not be able to develop commercial products despite significant investments in R&D.

Amgen invests heavily in R&D. Successful product development in the biotechnology industry is highly uncertain, and very few R&D projects produce commercial products. Product candidates, including biosimilar product candidates, or new indications

for existing products (collectively, product candidates) that appear promising in the early phases of development may fail to reach the market for a number of reasons, such as:

- the product candidate did not demonstrate acceptable clinical trial results even though it demonstrated positive preclinical trial results, for reasons that could include changes in the standard of care of medicine;
- the product candidate was not effective or not more effective than currently available therapies in treating a specified condition or illness;
- the product candidate was not cost effective in light of existing therapeutics;
- the product candidate had harmful side effects in humans or animals;
- the necessary regulatory bodies, such as the FDA or EMA, did not approve the product candidate for an intended use;
- the product candidate was not economical for us to manufacture and commercialize;
- the biosimilar product candidate failed to demonstrate the requisite biosimilarity to the applicable reference product, or was otherwise determined by a regulatory authority to not meet applicable standards for approval;
- other parties had or may have had proprietary rights relating to our product candidate, such as patent rights, and did not let us sell it on reasonable terms, or at all;
- we and certain of our licensees, partners or independent investigators may have failed to effectively conduct clinical development or clinical manufacturing activities; and
- the pathway to regulatory approval or reimbursement for product candidates was uncertain or not well-defined.

A number of our product candidates have failed or been discontinued at various stages in the product development process. For example, in May 2015, we terminated our participation in the co-development and commercialization of brodalumab with AstraZeneca. The decision was based on events of suicidal ideation and behavior in the brodalumab program, which we believed likely would necessitate restrictive labeling that would limit the appropriate patient population. Inability to bring a product to market or a significant delay in the expected approval and related launch date of a new product for any of the reasons discussed could potentially have a negative impact on our product sales and earnings and could result in a significant impairment of in-process research and development (IPR&D) or other intangible assets.

We must conduct clinical trials in humans before we commercialize and sell any of our product candidates or existing products for new indications.

Before we sell any products, we must conduct clinical trials to demonstrate that our product candidates are safe and effective for use in humans. The results of those clinical trials are used as the basis to obtain approval from regulatory authorities such as the FDA and EMA. See Our current products and products in development cannot be sold without regulatory approval. We are required to conduct clinical trials using an appropriate number of trial sites and patients to support the product label claims. The length of time, number of trial sites and number of patients required for clinical trials vary substantially and therefore, we may spend several years and incur substantial expense in completing certain clinical trials. In addition, we may have difficulty finding a sufficient number of clinical trial sites and patients to participate in our clinical trials, particularly if competitors are conducting clinical trials in similar patient populations. Patients may withdraw from clinical trials at any time, and privacy laws and/or other restrictions in certain countries may restrict the ability of clinical trial investigators to conduct further follow-up on such patients, which may adversely affect the interpretation of study results. Delays and complications in planned clinical trials can result in increased development costs, associated delays in regulatory approvals and in product candidates reaching the market and revisions to existing product labels.

Further, to increase the number of patients available for enrollment in our clinical trials, we have and will continue to open clinical sites and enroll patients in a number of locations where our experience conducting clinical trials is limited, including Russia, India, China, South Korea, the Philippines, Singapore and some Central and South American countries, either through utilization of third-party contract clinical trial providers entirely or in combination with local staff. Conducting clinical trials in locations where we have limited experience requires substantial time and resources to understand the unique regulatory environments of individual countries. Further, we must ensure the timely production, distribution and delivery of the clinical supply of our product candidates to numerous and varied clinical trial sites. If we fail to adequately manage the design, execution and diverse regulatory aspects of our large and complex clinical trials or to manage the production or distribution of our clinical supply, corresponding regulatory

approvals may be delayed or we may fail to gain approval for our product candidates or could lose our ability to market existing products in certain therapeutic areas or altogether. If we are unable to market and sell our products or product candidates or to obtain approvals in the timeframe needed to execute our product strategies, our business and results of operations could be materially and adversely affected.

We rely on independent third-party clinical investigators to recruit patients and conduct clinical trials on our behalf in accordance with applicable study protocols, laws and regulations. Further, we rely on unaffiliated third-party vendors to perform certain aspects of our clinical trial operations. We also may acquire companies that have ongoing clinical trials. These trials may not have been conducted to the same standards as ours; however, once an acquisition has been completed we assume responsibility for the conduct of these trials, including any potential risks and liabilities associated with the past and prospective conduct of those trials. If regulatory authorities determine that we or others, including our licensees or the independent investigators selected by us or by a company we have acquired, have not complied with regulations applicable to the clinical trials, those authorities may refuse or reject some or all of the clinical trial data or take other actions that could negatively impact our ability to obtain or maintain marketing approval of the product or indication. If we were unable to market and sell our products or product candidates, our business and results of operations could be materially and adversely affected.

In addition, some of our clinical trials involve drugs manufactured and marketed by other pharmaceutical companies. These drugs may be administered in clinical trials in combination with one of our products or product candidates or in a head-to-head study comparing the products' or product candidates' relative efficacy and safety. In the event that any of these vendors or pharmaceutical companies have unforeseen issues that negatively impact the quality of their work or create a shortage of supply or if we are otherwise unable to obtain an adequate supply of these other drugs, our ability to complete our applicable clinical trials and/or evaluate clinical results may also be negatively impacted. As a result, this could adversely affect our ability to timely file for, gain or maintain regulatory approvals worldwide.

Clinical trials must be designed based on the current standard of medical care. However, in certain diseases, such as cancer, the standard of care is evolving rapidly. In such diseases, the duration of time needed to complete certain clinical trials may result in the design of such clinical trials being based on standards of medical care that are no longer the current standards by the time such trials are completed, limiting the utility and application of such trials.

We may not obtain favorable clinical trial results and therefore may not be able to obtain regulatory approval for new product candidates or new indications for existing products and/or maintain our current product labels. Participants in clinical trials of our products and product candidates may also suffer adverse medical events or side effects that could, among other factors, delay or terminate clinical trial programs and/or require additional or longer trials to gain approval.

Even after a product is on the market, safety concerns may require additional or more extensive clinical trials as part of a risk management plan for our product or for approval of a new indication. For example, in connection with the June 2011 ESA label changes, we agreed to conduct additional clinical trials examining the use of ESAs in CKD. Additional clinical trials we initiate, including those required by the FDA, could result in substantial additional expense and the outcomes could result in further label restrictions or the loss of regulatory approval for an approved indication, each of which could have a material adverse effect on our business and results of operations. Additionally, any negative results from such trials could materially affect the extent of approvals, the use, reimbursement and sales of our products, our business and results of operations.

Some of our products are used with drug delivery or companion diagnostic devices that have their own regulatory, manufacturing and other risks.

Many of our products and product candidates may be used in combination with a drug delivery device, such as an injector or other delivery system. In addition, Vectibix® is used in combination with a test kit (which is a companion diagnostic device), and some of our product candidates may also be used in combination with a companion diagnostic device. Our product candidates or expanded indications of our products used with such devices may not be approved or may be substantially delayed in receiving regulatory approval if such devices do not also gain or maintain regulatory approval or clearance. When approval of the product and device is sought under a single marketing drug application, the increased complexity of the review process may delay receipt of regulatory approval. In addition, some of these devices may be provided by single-source unaffiliated third-party companies. We are dependent on the sustained cooperation and effort of those third-party companies both to supply the devices and, in some cases, to conduct the studies required for approval or clearance by the applicable regulatory agencies. We are also dependent on those third-party companies continuing to meet applicable regulatory or other requirements. Failure to successfully develop or supply the devices, delays in or failures of the Amgen or third-party studies, or failure of us or the

third-party companies to obtain or maintain regulatory approval or clearance of the devices could result in increased development costs; delays in, or failure to obtain, regulatory approval; and/or associated delays in a product candidate reaching the market or in the addition of new indications for existing products. Actual or perceived safety problems or concerns with a device used with our product can lead to regulatory actions and impacts to our products. See Our current products and products in development cannot be sold without regulatory approval. Loss of regulatory approval or clearance of a device that is used with our product may also result in the removal of our product from the market. Further, failure to successfully develop, supply, or gain or maintain approval for these devices could adversely affect sales of the related, approved products.

Our intellectual property positions may be challenged, invalidated or circumvented, or we may fail to prevail in present and future intellectual property litigation.

Our success depends in part on our ability to obtain and defend patent rights and other intellectual property rights that are important to the commercialization of our products and product candidates. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and often involve complex legal, scientific and factual questions. Third parties may challenge, invalidate or circumvent our patents and patent applications relating to our products, product candidates and technologies. Challenges to patents may come from potential competitors or from parties other than those who seek to market a potentially-infringing product. In addition, our patent positions might not protect us against competitors with similar products or technologies because competing products or technologies may not infringe our patents. For certain of our product candidates, there are third parties who have patents or pending patent applications that they may claim necessitate payment of a royalty or prevent us from commercializing these product candidates in certain territories. Patent disputes are frequent, costly and can preclude, delay or increase the cost of commercialization of products. We have been in the past, and are currently and may be in the future, involved in patent litigation. These matters have included and may in the future include litigation with manufacturers of products that purport to be biosimilars of certain of our products for patent infringement and for failure to comply with certain provisions of the Biologics Price Competition and Innovation Act, including the requirement to provide 180 days' notice in advance of commercial marketing. A determination made by a court, agency or tribunal concerning infringement, validity, enforceability, injunctive or economic remedy, or the right to patent protection, for example, are typically subject to appellate or administrative review. Upon review, such initial determinations may be afforded little or no deference by the reviewing tribunal and may be affirmed, reversed, or made the subject of reconsideration through further proceedings. A patent dispute or litigation may not discourage a potential violator from bringing the allegedly-infringing product to market prior to a final resolution of the dispute or litigation. The period from inception until resolution of a patent dispute or litigation is subject to the availability and schedule of the court, agency or tribunal before which the dispute or litigation is pending. We may be subject to competition during this period and may not be able to fully recover from the losses, damages, and harms we incur from infringement by the competitor product even if we prevail. Moreover, if we lose or settle current or future litigations at certain stages or entirely, we could be subject to competition and/or significant liabilities, be required to enter into third-party licenses for the infringed product or technology or be required to cease using the technology or product in dispute. In addition, we cannot guarantee that such licenses will be available on terms acceptable to us, or at all.

Further, under the Hatch-Waxman Act, our products approved by the FDA under the FDCA may be the subject of patent litigation with generics competitors before expiry of the five-year period of data exclusivity provided for under the Hatch-Waxman Act and prior to the expiration of the patents listed for the product. Likewise, our innovative biologic products may be the subject of patent litigation prior to the expiration of our patents and, with respect to competitors seeking approval as a biosimilar or interchangeable version of our products, prior to the 12-year exclusivity period provided under the ACA. In addition, we may face additional patent litigation involving claims that the biosimilar product candidates we are working to develop infringe the patents of other companies that manufacture, market or sell the applicable reference products. While we may attempt to challenge such patents, our efforts may be unsuccessful. For information related to our biosimilars patent litigation, see Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements.

Certain of the existing patents on our products have recently expired. See Item 1. Business—Marketing, Distribution and Selected Marketed Products—Patents. As our patents expire, competitors are able to legally produce and market similar products or technologies, including biosimilars, which may have a material adverse effect on our product sales, business and results of operations. In addition, competitors may be able to invalidate, design around or otherwise circumvent our patents and sell competing products.

Guidelines and recommendations published by various organizations can reduce the use of our products.

Government agencies promulgate regulations and guidelines directly applicable to us and to our products. However, professional societies, practice management groups, insurance carriers, physicians groups, private health and science foundations and organizations involved in various diseases also publish guidelines and recommendations to healthcare providers, administrators and payers, as well as patient communities. Recommendations by government agencies or

other groups and organizations may relate to such matters as usage, dosage, route of administration and use of related therapies, and a growing number of organizations are providing assessments of the value and pricing of pharmaceutical products. These assessments may come from private organizations, such as the Institute for Clinical and Economic Review, which publish their findings and offer recommendations relating to the products' reimbursement by government and private payers. In addition, government HTA organizations, such as the National Institute for Health and Clinical Excellence in the United Kingdom and the Canadian Agency for Drugs and Technologies in Health, make reimbursement recommendations to payers in their jurisdictions based on the clinical effectiveness, cost-effectiveness and service impact of new, emerging and existing medicines and treatments. Such HTA organizations may recommend reimbursement for our product for a narrower indication than was approved by applicable regulatory agencies, or may recommend against reimbursement entirely. Such recommendations or guidelines may affect our reputation, and any

recommendations or guidelines that result in decreased use, dosage or reimbursement of our products could have a material adverse effect on our product sales, business and results of operations. In addition, the perception by the investment community or stockholders that such recommendations or guidelines will result in decreased use and dosage of our products could adversely affect the market price of our common stock.

The adoption of new tax legislation or exposure to additional tax liabilities could affect our profitability.

We are subject to income and other taxes in the United States and other jurisdictions in which we do business. As a result, our provision for income taxes is derived from a combination of applicable tax rates in the various places we operate. Significant judgment is required for determining our provision for income tax. Our tax returns are routinely examined by tax authorities in the United States and other jurisdictions in which we do business, and a number of audits are currently underway. Tax authorities are becoming more aggressive in their audits and are particularly focused on the allocations of income and expense among tax jurisdictions. We believe our accrual for income tax liabilities is appropriate based on past experience, interpretations of tax law, and judgments about potential actions by tax authorities; however, due to the complexity of the provision for income taxes, the ultimate resolution of any tax matters may result in payments greater or less than amounts accrued. See Part IV—Note 5, Income Taxes, to the Consolidated Financial Statements. Our provision for income taxes and results of operations in the future could be adversely affected by changes to our operating structure, changes in the mix of income and expenses in countries with differing tax rates, changes in the valuation of deferred tax assets and liabilities, and changes in applicable tax laws, regulations or administrative interpretations thereof. President Trump has indicated that U.S. corporate tax reform is a high priority for his Administration, and the U.S. Congress is expected to propose sweeping changes to the U.S. tax system including changes to corporate tax rates, the taxation of income earned outside the U.S. (including the taxation of previously unrepatriated foreign earnings), as well as a potential destination-based tax system. A change to the U.S. tax system, a change to the tax system in a jurisdiction where we have significant operations, such as the U.S. territory of Puerto Rico, or a change in tax law in other jurisdictions where we do business, could have a material and adverse effect on our business and on the results of our operations.

We rely on third-party suppliers for certain of our raw materials, medical devices and components.

We rely on unaffiliated third-party suppliers for certain raw materials, medical devices and components necessary for the manufacturing of our commercial and clinical products. Certain of those raw materials, medical devices and components are proprietary products of those unaffiliated third-party suppliers and are specifically cited in our drug applications with regulatory agencies so that they must be obtained from that specific sole source or sources and could not be obtained from another supplier unless and until the regulatory agency approved such supplier. For example, Insulet Corporation is our single source of the on-body injector for our Neulasta® Onpro® kit. Also, certain of the raw materials required in the commercial and clinical manufacturing of our products are sourced from other countries and/or derived from biological sources, including mammalian tissues, bovine serum and human serum albumin. Among the reasons we may be unable to obtain these raw materials, medical devices and components include:

- regulatory requirements or action by regulatory agencies or others;
- adverse financial or other strategic developments at or affecting the supplier, including bankruptcy;
- unexpected demand for or shortage of raw materials, medical devices or components;
- failure to comply with our quality standards which results in quality and product failures, product contamination and/or recall;
- a material shortage, contamination, recall and/or restrictions on the use of certain biologically derived substances or other raw materials;
- discovery of previously unknown or undetected imperfections in raw materials, medical devices or components; and
- labor disputes or shortages, including from the effects of health emergencies and natural disasters.

These events could negatively impact our ability to satisfy demand for our products or conduct clinical trials, which could have a material adverse effect on our product use and sales and our business and results of operations. For example, in prior years we have experienced shortages in certain components necessary for the formulation, fill and finish of certain of our products in our Puerto Rico facility. Further quality issues that result in unexpected additional demand for certain components may lead to shortages of required raw materials or components (such as we have experienced with EPOGEN® glass vials). We may experience or continue to experience these or other shortages in the

future resulting in delayed shipments, supply constraints, clinical trial delays, contract disputes and/or stock-outs of our products.

Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales. Manufacturing biologic human therapeutic products is difficult, complex and highly regulated. We currently are involved in the manufacture of many of our products and plan to manufacture many of our product candidates. In addition, we currently use third-party contract manufacturers to produce, or assist in the production of, a number of our products, and we currently use contract manufacturers to produce, or assist in the production of, a number of our late-stage product candidates and drug delivery devices. See Item 1. Business—Manufacturing, Distribution and Raw Materials—Manufacturing. Our ability to adequately and timely manufacture and supply our products and product candidates is dependent on the uninterrupted and efficient operation of our facilities and those of our third-party contract manufacturers, which may be impacted by:

•capacity of manufacturing facilities;
•contamination by microorganisms or viruses, or foreign particles from the manufacturing process;
•natural or other disasters, including hurricanes, earthquakes, volcanoes or fires;
•labor disputes or shortages, including the effects of health emergencies or natural disasters;
•compliance with regulatory requirements;
•changes in forecasts of future demand;
•timing and actual number of production runs and production success rates and yields;
•updates of manufacturing specifications;
•contractual disputes with our suppliers and contract manufacturers;
•timing and outcome of product quality testing;
•power failures and/or other utility failures; and/or
•breakdown, failure, substandard performance or improper installation or operation of equipment.

If the efficient manufacture and supply of our products or product candidates is interrupted, we may experience delayed shipments, delays in our clinical trials, supply constraints, stock-outs, adverse event trends, contract disputes and/or recalls of our products. From time to time we have initiated voluntary recalls of certain lots of our products. For example, in July 2014, we initiated a voluntary recall of an Aranesp® lot distributed in the EU after particles were detected in a quality control sample following distribution of that lot. If we are at any time unable to provide an uninterrupted supply of our products to patients, we may lose patients and physicians may elect to prescribe competing therapeutics instead of our products, which could have a material adverse effect on our product sales, business and results of operations.

Our manufacturing processes and those of our third-party contract manufacturers must undergo regulatory approval processes and are subject to continued review by the FDA and other regulatory authorities. It can take longer than five years to build, validate and license another manufacturing plant and it can take longer than three years to qualify and license a new contract manufacturer. We have initiated the drug substance process qualification campaign to facilitate licensure at our biologics manufacturing facility in Singapore. This Singapore facility will utilize a novel manufacturing technology that has not been previously approved by the FDA or other regulatory authorities. In addition, we are in the process of commercially validating and licensing a new facility at the site in Singapore to enable the manufacture of the active pharmaceutical ingredient for KYPROLIS®. If we are unable to obtain needed licenses for either of these facilities on a timely basis, it could adversely affect our ability to achieve our planned risk mitigation and cost reductions which, as a result, could have a material adverse effect on our product sales, business and results of operations.

If regulatory authorities determine that we or our third-party contract manufacturers or certain of our third-party service providers have violated regulations or if authorities restrict, suspend or revoke our prior approvals, they could prohibit us from manufacturing our products or conducting clinical trials or selling our marketed products until we or the affected third-party contract manufacturers or third-party service providers comply, or indefinitely. Such issues may also delay the approval of product candidates we have submitted for regulatory review, even if such product candidates are not directly related to the products, devices or processes at issue with regulators. Because our third-party contract manufacturers and certain of our third-party service providers are subject to the FDA and foreign regulatory authorities, alternative qualified third-party contract manufacturers and third-party service providers may not be available on a timely basis or at all. If we or our third-party contract manufacturers or third-party service

providers cease or interrupt production or if our third-party contract manufacturers and third-party service providers fail to supply materials, products or services to us, we may experience delayed shipments, supply constraints, stock-outs and/or recalls of our products. Additionally, we distribute a substantial volume of our commercial products through our primary distribution centers in Louisville, Kentucky for the United States and in Breda, Netherlands for Europe and much of the rest of the world. We also conduct all the labeling and packaging of our products distributed in Europe and much of the rest of the world in Breda. Our

ability to timely supply products is dependent on the uninterrupted and efficient operations of our distribution and logistics centers, our third-party logistics providers and our labeling and packaging facility in Breda. Further, we rely on commercial transportation, including air freight, for the distribution of our products to our customers, which may be negatively impacted by natural disasters or security threats.

We perform a substantial majority of our commercial manufacturing activities at our facility in the U.S. territory of Puerto Rico and substantially all of our clinical manufacturing activities at our facility in Thousand Oaks, California; if significant disruptions or production failures occur at the Puerto Rico facility, we may not be able to supply these products or, at the Thousand Oaks facility, we may not be able to continue our clinical trials.

We currently perform a substantial majority of our commercial manufacturing activities at our facility in the U.S. territory of Puerto Rico and substantially all of our clinical manufacturing activities at our facility in Thousand Oaks, California. The global supply of our products and product candidates for commercial sales and for use in our clinical trials is significantly dependent on the uninterrupted and efficient operation of these facilities. See Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales.

The operation of our manufacturing facility in Puerto Rico is also subject to local economic challenges. Since June 2015, when the Governor of Puerto Rico announced that the government (including certain government entities) was unable to pay its roughly $72 billion in debt, the government's liquidity position has continued to deteriorate and public reports indicate that the Puerto Rico government is not making certain payments with respect to its obligations. On June 30, 2016, President Obama signed into law the Puerto Rico Oversight, Management, and Economic Stability Act (PROMESA) to provide a mechanism for Puerto Rico to restructure its debt, achieve fiscal responsibility, and gain access to capital markets. PROMESA established a federal Financial Oversight and Management Board (Oversight Board) to provide fiscal oversight through the development and approval of fiscal plans and budgets for Puerto Rico and to assist in the debt restructuring. The establishment of the Oversight Board initially provided for an automatic stay of creditor actions against the Puerto Rico government until February 15, 2017, and recently extended the automatic stay until May 1, 2017. The Puerto Rico government is expected to submit a fiscal plan to the Oversight Board by February 28, 2017. Additionally, on January 29, 2017, the Puerto Rico government signed into law the Puerto Rico Fiscal Emergency and Fiscal Responsibility Act (the Act), which is intended to facilitate and encourage a voluntary negotiation process under PROMESA between the Puerto Rico government and its creditors. The Act declares a state of financial emergency in Puerto Rico until May 1, 2017, and authorizes the Governor to designate certain services as essential services, and other services as non-essential in order to prioritize the use of available resources to satisfy Puerto Rico's obligations. While PROMESA and the actions above continue to be important factors in moving Puerto Rico toward economic stability, there is still a risk that Puerto Rico's economic situation could impact the territorial government's provision of utilities or other services in Puerto Rico that we use in the operation of our business, create the potential for increased taxes or fees to operate in Puerto Rico, result in a migration of workers from Puerto Rico to the mainland United States, and/or make it more expensive or difficult for us to operate in Puerto Rico.

Concentration of sales at certain of our wholesaler distributors and free-standing dialysis clinic businesses and consolidation of private payers may negatively impact our business.

Certain of our distributors, customers and payers have substantial purchasing leverage, due to the volume of our products they purchase or the number of patient lives for which they provide coverage. The substantial majority of our U.S. product sales is made to three pharmaceutical product wholesaler distributors: AmerisourceBergen Corporation, McKesson Corporation and Cardinal Health, Inc. These distributors, in turn, sell our products to their customers, which include physicians or their clinics, dialysis centers, hospitals and pharmacies. One of our products, EPOGEN®, is sold primarily to free-standing dialysis clinics. Two organizations, DaVita and Fresenius Medical Care North America, own or manage a large number of the outpatient dialysis facilities located in the United States and account for approximately 75% of all EPOGEN® sales. Similarly, as discussed above, there has been significant consolidation in the health insurance industry, including that three PBMs now oversee approximately 75% of total covered lives in the United States. See Item 1A. Risk Factors—Our sales depend on coverage and reimbursement from third-party payers, and pricing and reimbursement pressures may affect our profitability. The concentration of purchasing and negotiating power by these entities may put pressure on our pricing due to their ability to extract price discounts on

our products, fees for other services or rebates, negatively impacting our bargaining position, sales and/or profit margins. In addition, decisions by these entities to purchase or cover less or none of our products in favor of competitive products could have a material adverse effect on our business and results of operations due to their purchasing volume.

We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

The capital and credit markets may experience extreme volatility and disruption which may lead to uncertainty and liquidity issues for both borrowers and investors. We expect to access the capital markets to supplement our existing funds and cash generated from operations in satisfying our needs for working capital; capital expenditure and debt service requirements; our plans to pay dividends and repurchase stock; and other business initiatives we plan to strategically pursue, including acquisitions and licensing

activities. In the event of adverse capital and credit market conditions, we may be unable to obtain capital market financing on similar favorable terms, or at all, which could have a material adverse effect on our business and results of operations. Changes in credit ratings issued by nationally recognized credit-rating agencies could adversely affect our ability to obtain capital market financing and the cost of such financing and have an adverse effect on the market price of our securities.

Our efforts to acquire other companies or products and to integrate their operations may not be successful, and may result in unanticipated costs, delays or failures to realize the benefits of the transactions.

We have an ongoing process of evaluating potential merger, acquisition, partnering and in-license opportunities that we expect will contribute to our future growth and expand our geographic footprint, product offerings and/or our R&D pipeline. Acquisitions may result in unanticipated costs, delays or other operational or financial problems related to integrating the acquired company and business with our company, which may result in the diversion of our management's attention from other business issues and opportunities. Failures or difficulties in integrating or retaining new personnel or in integrating the operations of the businesses we acquire (including their technology, compliance programs, distribution and general business operations and procedures), while preserving important R&D, distribution, marketing, promotion and other relationships, may affect our ability to grow and may result in our incurring asset impairment or restructuring charges. For example, on October 1, 2013, we acquired Onyx Pharmaceuticals, Inc. (Onyx), a biopharmaceutical company with several currently marketed products as well as pipeline candidates progressing through the development process, and failures or difficulties in the integration of Onyx could result in a material adverse impact on our business and results of operations.

Our sales and operations are subject to the risks of doing business in emerging markets.

As we continue our expansion efforts in emerging markets around the world, through acquisitions and licensing transactions as well as through the development and introduction of our products in new markets, we face numerous risks to our business. There is no guarantee that our efforts and strategies to expand sales in emerging markets will succeed. Emerging market countries may be especially vulnerable to periods of global political, legal, regulatory and financial instability, including sovereign debt issues and/or the imposition of international sanctions in response to certain state actions. As we expand internationally, we are subject to fluctuations in foreign currency exchange rates relative to the U.S. dollar. While we have a program in place that is designed to reduce our exposure to foreign currency exchange rate fluctuations through foreign currency hedging arrangements, our hedging efforts do not completely offset the effect of these fluctuations on our revenues and earnings. We may also be required to increase our reliance on third-party agents and unfamiliar operations and arrangements previously utilized by companies we partner with or acquire in emerging markets. See We must conduct clinical trials in humans before we commercialize and sell any of our product candidates or existing products for new indications. Our international operations and business may also be subject to less protective intellectual property or other applicable laws, diverse data privacy and protection requirements, changing tax laws and tariffs, far-reaching anti-bribery and anti-corruption laws and regulations and/or evolving legal and regulatory environments. These legal and operational challenges along with government controls, the challenges of attracting and retaining qualified personnel and obtaining and/or maintaining necessary regulatory or pricing approvals of our products may result in a material adverse impact on our international product sales, business and results of operations.

Our business may be affected by litigation and government investigations.

We and certain of our subsidiaries are involved in legal proceedings. See Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements. Civil and criminal litigation is inherently unpredictable, and the outcome can result in costly verdicts, fines and penalties, exclusion from federal healthcare programs and/or injunctive relief that affect how we operate our business. Defense of litigation claims can be expensive, time-consuming and distracting, and it is possible that we could incur judgments or enter into settlements of claims for monetary damages or change the way we operate our business, which could have a material adverse effect on our business and results of operations. In addition, product liability is a major risk in testing and marketing biotechnology and pharmaceutical products. We may face substantial product liability exposure in human clinical trials and for products we sell after regulatory approval. Product liability claims, regardless of their merits, could be costly and divert management's attention and could adversely affect our reputation and the demand for our products. We and

certain of our subsidiaries have previously been named as defendants in product liability actions for certain of our products.

We are also involved in government investigations that arise in the ordinary course of our business. In recent years, there has been a trend of increasing government investigations and litigations against companies operating in our industry, both in the United States and around the world. Our business activities outside of the United States are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the UK Bribery Act. As we announced on December 19, 2012, we finalized a settlement agreement with the U.S. government and various other parties to settle certain allegations regarding our sales and marketing practices. In connection with that settlement, we are now operating under a Corporate Integrity Agreement (CIA) with the OIG of the U.S. Department of Health and Human Services that requires us to maintain our corporate compliance program and to undertake a set of defined corporate integrity obligations until December 2017. The CIA also provides for an independent third-party review organization to assess and report on our compliance

program. While we expect to fully comply with all of our obligations under the CIA, failure to do so could result in substantial penalties and our being excluded from government healthcare programs. We may also be subject to actions by government entities, including those not participating in the settlement, and may in the future become subject to claims by other parties, in each case with respect to the alleged conduct that is the subject of the settlement. We may see new government investigations of or actions against us citing novel theories of recovery. Any of these results could have a material adverse effect on our business and results of operations.

We are increasingly dependent on information technology systems, infrastructure, network connected control systems and data security.

We are increasingly dependent on information technology systems, infrastructure, network connected control systems and data security. The breadth, complexity and business process integration of our computer systems and the potential value of our data make these systems targets of service interruption, destruction, malicious intrusion and attack. Likewise, data privacy or security breaches by employees, contractors or others may pose risks that sensitive data including intellectual property, trade secrets or personal information belonging us, our patients, customers and/or other business partners may be exposed to unauthorized persons or the public. As a global biotechnology company, our systems are subject to frequent cyber-attacks. Moreover, these attacks are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect. As the cyber-threat landscape evolves, such attacks are also increasingly difficult to detect when carried out by motivated, well-resourced, skilled and persistent actors including nation states and organized crime groups. Such attacks could include the deployment of harmful malware, key loggers, a denial-of-service, a delivery of malware through malicious websites, the use of social engineering and/or other means to affect the confidentiality, integrity and availability of our information technology systems, processes, infrastructure and data. Key business partners, third-party service and product providers and any companies we may acquire face similar risks and any security breaches of their systems could adversely affect our security and resiliency posture. Although in the past we have experienced cyber-attacks and intrusions into our computer systems, we do not believe such attacks have had a material adverse effect on our operations. While we continue to invest in the protection and monitoring of our critical or sensitive data and information technology, there can be no assurance that our efforts will prevent service interruptions or detect all breaches to our systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us.

Global economic conditions may negatively affect us and may magnify certain risks that affect our business.

Our operations and performance have been, and may continue to be, affected by global economic conditions. Financial pressures may cause government or other third-party payers to more aggressively seek cost containment measures. See Our sales depend on coverage and reimbursement from third-party payers, and pricing and reimbursement pressures may affect our profitability. As a result of global economic conditions, some third-party payers may delay or be unable to satisfy their reimbursement obligations. Job losses or other economic hardships may also affect patients' ability to afford health care as a result of increased co-pay or deductible obligations, greater cost sensitivity to existing co-pay or deductible obligations, lost healthcare insurance coverage or for other reasons. We believe such conditions have led and could continue to lead to reduced demand for our products, which could have a material adverse effect on our product sales, business and results of operations. Economic conditions may also adversely affect the ability of our distributors, customers and suppliers to obtain the liquidity required to buy inventory or raw materials and to perform their obligations under agreements with us, which could disrupt our operations. Although we monitor our distributors', customers' and suppliers' financial condition and their liquidity to mitigate our business risks, some of our distributors, customers and suppliers may become insolvent, which could have a material adverse effect on our product sales, business and results of operations.

We maintain a significant portfolio of investments disclosed as cash equivalents and marketable securities on our Consolidated Balance Sheets. The value of our investments may be adversely affected by interest rate fluctuations, downgrades in credit ratings, illiquidity in the capital markets and other factors that may result in other-than-temporary declines in the value of our investments. Any of those events could cause us to record impairment charges with respect to our investment portfolio or to realize losses on sales of investments.

Our stock price is volatile.

Our stock price, like that of our peers in the biotechnology and pharmaceutical industries, is volatile. Our revenues and operating results may fluctuate from period to period for a number of reasons. Events such as a delay in product development, changes to our expectations or strategy or even a relatively small revenue shortfall may cause financial results for a period to be below our expectations or projections. As a result, our revenues and operating results and, in turn, our stock price may be subject to significant fluctuations. Announcements or discussions of possible restrictive actions by government or private payers that would impact our business or industry if ultimately enacted or adopted may also cause our stock price to fluctuate, whether or not such restrictive actions ever actually occur. Similarly, actual or perceived safety issues with our products or similar products or unexpected clinical trial results can have an immediate and rapid impact on our stock price, whether or not our operating results are materially impacted.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

As of December 31, 2016, we owned or leased approximately 190 properties. The locations and primary functions of significant properties are summarized in the following tables:

Excluded from the tables above are undeveloped land and leased properties that have been abandoned and certain buildings that we still own but are no longer used in our business. There are no material encumbrances on our owned properties.

We believe that our facilities are suitable for their intended use and, in conjunction with our third-party contracting manufacturing agreements, provide adequate capacity and are sufficient to meet our expected needs. See Item 1A. Risk Factors for a discussion on the factors that could adversely impact our manufacturing operations and the global supply of our products.

See Item 1. Business—Manufacturing, Distribution and Raw Materials.

Item 3. LEGAL PROCEEDINGS

Certain of the legal proceedings in which we are involved are discussed in Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements and are hereby incorporated by reference.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Common stock

Our common stock trades on the NASDAQ Global Select Market under the symbol AMGN. As of February 9, 2017, there were approximately 6,444 holders of record of our common stock.

The following table sets forth, for the periods indicated, the range of high and low quarterly closing sales prices of the common stock as quoted on the NASDAQ Global Select Market:

| Year ended December 31, 2016 | High | Low |
|---|---|---|
| Fourth quarter | $168.31 | $135.22 |
| Third quarter | $175.62 | $154.27 |
| Second quarter | $164.35 | $144.58 |
| First quarter | $158.34 | $140.90 |
| Year ended December 31, 2015 | | |
| Fourth quarter | $164.58 | $140.23 |
| Third quarter | $176.59 | $132.24 |
| Second quarter | $169.17 | $151.60 |
| First quarter | $170.10 | $150.01 |

Performance graph

The following graph shows the value of an investment of $100 on December 31, 2011, in each of Amgen common stock, the Amex Biotech Index, the Amex Pharmaceutical Index and Standard & Poor's 500 Index (S&P 500). All values assume reinvestment of the pretax value of dividends and are calculated as of December 31 of each year. The historical stock price performance of the Company's common stock shown in the performance graph is not necessarily indicative of future stock price performance.

Amgen vs. Amex Biotech, Amex Pharmaceutical and S&P 500 Indices

Comparison of Five-Year Cumulative Total Return

Value of Investment of $100 on December 31, 2011

| | 12/31/2011 | 12/31/2012 | 12/31/2013 | 12/31/2014 | 12/31/2015 | 12/31/2016 |
|---|---|---|---|---|---|---|
| Amgen (AMGN) | $100.00 | $136.26 | $183.30 | $260.87 | $271.23 | $250.75 |
| Amex Biotech (BTK) | $100.00 | $141.60 | $213.50 | $315.79 | $351.76 | $284.40 |
| Amex Pharmaceutical (DRG) | $100.00 | $114.09 | $150.77 | $175.77 | $183.11 | $167.84 |
| S&P 500 (SPX) | $100.00 | $115.80 | $152.90 | $173.82 | $176.21 | $197.27 |

The material in this performance graph is not soliciting material, is not deemed filed with the SEC, and is not incorporated by reference in any filing of the Company under the Securities Act or the Exchange Act, whether made on, before or after the date of this filing and irrespective of any general incorporation language in such filing.

Stock repurchase program

During the three months and year ended December 31, 2016, we had one outstanding stock repurchase program, under which the repurchasing activity was as follows:

| | Total number of shares purchased | Average price paid per share[1] | Total number of shares purchased as part of publicly announced program | Maximum dollar value that may yet be purchased under the program[2] |
|---|---|---|---|---|
| October 1 - October 31 | 1,302,682 | $ 159.91 | 1,302,682 | $4,865,695,995 |
| November 1 - November 30 | 2,296,195 | $ 144.14 | 2,296,195 | $4,534,720,376 |
| December 1 - December 31 | 3,150,296 | $ 145.71 | 3,150,296 | $4,075,684,217 |
| | 6,749,173 | $ 147.92 | 6,749,173 | |
| January 1 - December 31 | 19,693,193 | $ 153.68 | 19,693,193 | |

(1) Average price paid per share includes related expenses.

(2) In October 2016, our Board of Directors authorized an increase that resulted in a total of $5.0 billion available under the stock repurchase program.

Dividends

For the years ended December 31, 2016 and 2015, we paid quarterly dividends. We expect to continue to pay quarterly dividends, although the amount and timing of any future dividends are subject to approval by our Board of Directors. Additional information required by this item is incorporated herein by reference to Part IV—Note 15, Stockholders' equity, to the Consolidated Financial Statements.

Securities Authorized for Issuance Under Existing Equity Compensation Plans

Information about securities authorized for issuance under existing equity compensation plans is incorporated by reference from Item 12—Securities Authorized for Issuance Under Existing Equity Compensation Plans.

Item 6. SELECTED FINANCIAL DATA

| | Years ended December 31, | | | | |
|---|---|---|---|---|---|
| Consolidated Statement of Income Data: | 2016 | 2015 | 2014 | 2013 | 2012 |
| | (In millions, except per share data) | | | | |
| Revenues: | | | | | |
| Product sales | $21,892 | $20,944 | $19,327 | $18,192 | $16,639 |
| Other revenues | 1,099 | 718 | 736 | 484 | 626 |
| Total revenues | $22,991 | $21,662 | $20,063 | $18,676 | $17,265 |
| Operating expenses: | | | | | |
| Cost of sales | $4,162 | $4,227 | $4,422 | $3,346 | $3,199 |
| Research and development | $3,840 | $4,070 | $4,297 | $4,083 | $3,380 |
| Selling, general and administrative | $5,062 | $4,846 | $4,699 | $5,184 | $4,814 |
| Net income | $7,722 | $6,939 | $5,158 | $5,081 | $4,345 |
| Diluted earnings per share | $10.24 | $9.06 | $6.70 | $6.64 | $5.52 |
| Dividends paid per share | $4.00 | $3.16 | $2.44 | $1.88 | $1.44 |
| | As of December 31, | | | | |
| Consolidated Balance Sheet Data: | 2016 | 2015 | 2014 | 2013 | 2012 |
| | (In millions) | | | | |
| Total assets | $77,626 | $71,449 | $68,882 | $65,974 | $54,180 |
| Total debt[(1)] | $34,596 | $31,429 | $30,588 | $31,977 | $26,411 |
| Total stockholders' equity[(2)] | $29,875 | $28,083 | $25,778 | $22,096 | $19,060 |

In addition to the following notes, see Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations and the Consolidated Financial Statements and accompanying notes and previously filed Annual Reports on Form 10-K for further information regarding our consolidated results of operations and financial position for periods reported therein and for known factors that will impact comparability of future results. Also, see Part IV—Note 15, Stockholders' equity, to the Consolidated Financial Statements, for information regarding cash dividends declared per share of common stock for each of the four quarters of 2016, 2015, and 2014, respectively. In addition, our Board of Directors declared dividends per share of $0.47 and $0.36 that were paid in each of the four quarters of 2013 and 2012, respectively.

(1) See Part IV—Note 14, Financing arrangements, to the Consolidated Financial Statements for discussion of our financing arrangements. In 2013, we issued long-term debt of $8.1 billion and repaid an aggregate amount of $3.4 billion. In 2012, we issued $5.0 billion aggregate principal amount of notes.

(2) Throughout the five years ended December 31, 2016, we had a stock repurchase program authorized by the Board of Directors through which we repurchased $3.0 billion, $1.9 billion, $0.2 billion, $0.8 billion and $4.7 billion, respectively, of Amgen common stock.

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

The following management's discussion and analysis (MD&A) is intended to assist the reader in understanding Amgen's business. MD&A is provided as a supplement to, and should be read in conjunction with, our consolidated financial statements and accompanying notes. Our results of operations discussed in MD&A are presented in conformity with U.S. generally accepted accounting principles (GAAP). Amgen operates in one business segment: human therapeutics. Therefore, our results of operations are discussed on a consolidated basis.

### Forward-looking statements

This report and other documents we file with the SEC contain forward-looking statements that are based on current expectations, estimates, forecasts and projections about us, our future performance, our business, our beliefs and our management's assumptions. In addition, we, or others on our behalf, may make forward-looking statements in press releases or written statements, or in our communications and discussions with investors and analysts in the normal course of business through meetings, webcasts, phone calls and conference calls. Such words as "expect," "anticipate," "outlook," "could," "target," "project," "intend," "plan," "believe," "seek," "estimate," "should," "may," "assume," and "contin variations of such words and similar expressions are intended to identify such forward-looking statements. These statements are not guarantees of future performance and they involve certain risks, uncertainties and assumptions that are difficult to predict. We describe our respective risks, uncertainties and assumptions that could affect the outcome or results of operations in Item 1A. Risk Factors. We have based our forward-looking statements on our management's beliefs and assumptions based on information available to our management at the time the statements are made. We caution you that actual outcomes and results may differ materially from what is expressed, implied or forecast by our forward-looking statements. Reference is made in particular to forward-looking statements regarding product sales, regulatory activities, clinical trial results, reimbursement, expenses, earnings per share (EPS), liquidity and capital resources, trends, planned dividends, stock repurchases and restructuring plans. Except as required under the federal securities laws and the rules and regulations of the SEC, we do not have any intention or obligation to update publicly any forward-looking statements after the distribution of this report, whether as a result of new information, future events, changes in assumptions or otherwise.

Overview

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology. Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

Our strategy is to develop innovative medicines in six focused therapeutic areas that meet important unmet medical needs in addressing serious illness. We have a presence in approximately 100 countries worldwide focusing on: oncology/hematology, cardiovascular disease, inflammation, bone health, nephrology and neuroscience. Our principal products include ENBREL, Neulasta®, Aranesp®, Prolia®, Sensipar®/Mimpara®, XGEVA®, EPOGEN®, and NEUPOGEN®. For additional information about our products, see Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products.

In 2016, we made substantial progress on our strategic priorities with strong execution across the business.

- Over the past year, our financial performance was strong, as total revenues increased 6%. Net income increased 11% and diluted EPS increased by 13% driven by higher total revenues and continued improvement in operating leverage enabled by the transformation initiatives.
- Our pipeline continued to advance with the U.S. regulatory filing for EVENITY™, approval of Parsabiv™ in the EU, and in early 2017, approval in the United States. We announced positive phase 2 and phase 3 results for erenumab for chronic and episodic migraine, respectively, and positive phase 3 results for XGEVA® for the prevention of SREs in patients with multiple myeloma. We also announced positive phase 3 results for Repatha® for the treatment of coronary artery disease and in early 2017, positive top-line results in our phase 3 cardiovascular outcomes and cognitive function trials. We received new indications for KYPROLIS®, Nplate®, BLINCYTO® and ENBREL. Additionally, we continued to advance our biosimilar program, including the U.S. approval and EU regulatory submission for AMJEVITA™, ABP 501, global regulatory submission of ABP 215, and phase 3 data for ABP 980. Throughout the course of the year, we invested in external early-stage innovation to augment our internal research efforts.
- We built the foundation for long-term growth through our product launches in new parts of the world, as seen by our ability to secure 94 country product launches.
- We made investments in next-generation biomanufacturing that build on our expertise in manufacturing, including our new Singapore facility for which licensure is under way. We believe that our next-generation biomanufacturing will reduce the scale and cost of making biologics while retaining a reliable, high-quality, compliant supply of medicines.

- We continue to innovate with patient- and provider-friendly delivery systems to differentiate our products, as seen by our U.S. launch of the Repatha® Pushtronex™ system, a new monthly single-dose administration option, and the continued growth of the Neulasta® OnPro® kit in the United States.
- Cash flows from operating activities grew 6% to $10.4 billion, enabling us to invest for the future and return capital to shareholders, consistent with our expectations for long-term growth. We increased our dividend 27% to $1.00 per share of common stock in each of the four quarters of 2016. In December 2016, the Board of Directors declared a cash dividend of $1.15 per share of common stock for the first quarter of 2017, an increase of 15% for this period, to be paid in March 2017. We also repurchased 19.7 million shares of our common stock throughout 2016 at an aggregate cost of $3.0 billion.
- We have focused our business and operating model through significant transformation and process improvement efforts. Our transformation has established a foundation for longer-term growth and we are approaching the development of promising new medicines with greater understanding, speed and confidence.

While 2016 execution was strong, we expect 2017 to be an increasingly challenging environment. Our long-term success depends to a great extent on our ability to continue to discover, develop and commercialize innovative products and acquire or collaborate on therapies currently in development by other companies. We must develop new products over time in order to provide for revenue growth and to offset revenue losses when products lose their exclusivity or competing products are launched. Certain of our products will face increasing pressure from competitive product launches, including from biosimilars. For additional information, including information on the expiration of patents for various products, see Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products—Patents and see Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition.

We devote considerable resources to R&D activities. However, successful product development in the biotechnology industry is highly uncertain. We are also confronted by increasing regulatory scrutiny of safety and efficacy both before and after products launch.

Rising healthcare costs and economic conditions also continue to pose challenges to our business, including continued pressure by third-party payers, such as governments and private payers, to reduce healthcare expenditures. As a result of public and private health care provider focus, the industry continues to experience significant pricing pressures and other cost containment measures.

Finally, wholesale and end-user buying patterns can affect our product sales. These effects can cause fluctuations in quarterly product sales and have generally not been significant when comparing full-year product performance to the prior year. See Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products and Part I, Item 1A. Risk Factors for further discussion of certain of the factors that could impact our future product sales.

We believe we are well positioned for the challenges and opportunities in the coming year. Challenges and opportunities led us to begin our transformation at Amgen, which will continue to be an important part of our strategy and execution. We have enthusiasm for the future and long-term growth based on innovative medicines that make a difference for patients suffering from serious illness. We are focused on executing our strategy and delivering results.

Selected financial information

The following is an overview of our results of operations (in millions, except percentages and per share data):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 |
|---|---|---|---|
| Product sales: | | | |
| U.S. | $ 17,325 | 5 % | $ 16,523 |
| Rest of world (ROW) | 4,567 | 3 % | 4,421 |
| Total product sales | 21,892 | 5 % | 20,944 |
| Other revenues | 1,099 | 53 % | 718 |
| Total revenues | $ 22,991 | 6 % | $ 21,662 |
| Operating expenses | $ 13,197 | — % | $ 13,192 |
| Operating income | $ 9,794 | 16 % | $ 8,470 |
| Net income | $ 7,722 | 11 % | $ 6,939 |
| Diluted EPS | $ 10.24 | 13 % | $ 9.06 |
| Diluted shares | 754 | (2 )% | 766 |

In the following discussion of changes in product sales, any reference to unit demand growth or decline refers to changes in the purchases of our products by healthcare providers, such as physicians or their clinics, dialysis centers, hospitals and pharmacies.

U.S. product sales for 2016 increased across the portfolio except for EPOGEN® and NEUPOGEN®, which declined by 31% and 33%, respectively. The U.S. increase was driven primarily by increases in net selling prices. The increase in ROW product sales for 2016 was driven primarily by higher unit demand from new product launches, offset by unfavorable changes in foreign exchange rates and declines in net selling prices.

Operating expenses for 2016 were flat as the savings from transformation and process improvement efforts were offset by increased support for launch products.

Although changes in foreign currency exchange rates result in increases or decreases in our reported international product sales, the benefit or detriment that such movements have on our international product sales is offset partially by corresponding increases or decreases in our international operating expenses and our related foreign currency hedging activities. Our hedging activities seek to offset the impacts, both positive and negative, that foreign currency exchange rate changes may have on our net income by hedging our net foreign currency exposure, primarily with respect to product sales denominated in euros. The net impact from changes in foreign currency exchange rates was not material in 2016, 2015 or 2014.

Results of Operations

Product sales

Worldwide product sales were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| ENBREL | $ 5,965 | 11 % | $ 5,364 | 14 % | $ 4,688 |
| Neulasta® | 4,648 | (1 )% | 4,715 | 3 % | 4,596 |
| Aranesp® | 2,093 | 7 % | 1,951 | 1 % | 1,930 |
| Prolia® | 1,635 | 25 % | 1,312 | 27 % | 1,030 |
| Sensipar®/Mimpara® | 1,582 | 12 % | 1,415 | 22 % | 1,158 |
| XGEVA® | 1,529 | 9 % | 1,405 | 15 % | 1,221 |
| EPOGEN® | 1,282 | (31 )% | 1,856 | (9 )% | 2,031 |
| NEUPOGEN® | 765 | (27 )% | 1,049 | (9 )% | 1,159 |
| Other products | 2,393 | 27 % | 1,877 | 24 % | 1,514 |
| Total product sales | $ 21,892 | 5 % | $ 20,944 | 8 % | $ 19,327 |
| Total U.S. | $ 17,325 | 5 % | $ 16,523 | 12 % | $ 14,732 |
| Total ROW | 4,567 | 3 % | 4,421 | (4 )% | 4,595 |
| Total product sales | $ 21,892 | 5 % | $ 20,944 | 8 % | $ 19,327 |

Future sales of our products will depend, in part, on the factors discussed in the Overview, Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition, in Part I, Item 1A. Risk Factors and any additional factors discussed in the individual product sections below. In addition, for a list of our products' significant competitors, see Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition.

ENBREL

Total ENBREL sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| ENBREL — U.S. | $ 5,719 | 12 % | $ 5,099 | 16 % | $ 4,404 |
| ENBREL — Canada | 246 | (7 )% | 265 | (7 )% | 284 |
| Total ENBREL | $ 5,965 | 11 % | $ 5,364 | 14 % | $ 4,688 |

The increases in ENBREL sales for 2016 and 2015 were driven primarily by an increase in net selling price, offset partially by the impact of competition.

In 2017, we expect intensifying competition and relatively little benefit from net selling price changes.

Neulasta®

Total Neulasta® sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| Neulasta® — U.S. | $ 3,925 | 1 % | $ 3,891 | 7 % | $ 3,649 |
| Neulasta® — ROW | 723 | (12 )% | 824 | (13 )% | 947 |
| Total Neulasta® | $ 4,648 | (1 )% | $ 4,715 | 3 % | $ 4,596 |

The decrease in global Neulasta® sales for 2016 was driven primarily by lower unit demand, offset by an increase in net selling price in the United States. As of the end of December 2016, utilization of the Neulasta® Onpro® kit continues to grow in the United States.

The increase in global Neulasta® sales for 2015 was driven primarily by an increase in net selling price in the United States, offset partially by unfavorable changes in foreign currency exchange rates.

Our final material U.S. patent for pegfilgrastim (Neulasta®) expired in October 2015. Therefore, we expect to face competition in the United States, which over time may have a material adverse impact on future sales of Neulasta®. Apotex, Inc. (Apotex), Sandoz and Coherus BioSciences, Inc., announced that the FDA has accepted their applications for proposed biosimilar versions of Neulasta®. Novartis indicated that it received a Complete Response Letter from the FDA. For discussion of ongoing litigation between us and Apotex and Sandoz, see Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements.

In addition, supplementary protection certificates issued by certain countries, including France, Germany, Italy, Spain, and the United Kingdom, relating to our European patent for pegfilgrastim (Neulasta®) will expire in August 2017. For further information regarding our patents, see Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products—Patents.

Future Neulasta® sales will also depend, in part, on the development of new protocols, tests and/or treatments for cancer and/or new chemotherapy treatments or alternatives to chemotherapy that may have reduced and may continue to reduce the use of chemotherapy in some patients.

Aranesp®

Total Aranesp® sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| Aranesp® — U.S. | $ 1,082 | 20 % | $ 900 | 13 % | $ 794 |
| Aranesp® — ROW | 1,011 | (4)% | 1,051 | (7)% | 1,136 |
| Total Aranesp® | $ 2,093 | 7 % | $ 1,951 | 1 % | $ 1,930 |

The increases in global Aranesp® sales for 2016 and 2015 were driven by unit demand growth, including a shift from EPOGEN® in the United States, offset partially by a decrease in net selling price in ROW.

Prolia®

Total Prolia® sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| Prolia® — U.S. | $ 1,049 | 25 % | $ 837 | 34 % | $ 625 |
| Prolia® — ROW | 586 | 23 % | 475 | 17 % | 405 |
| Total Prolia® | $ 1,635 | 25 % | $ 1,312 | 27 % | $ 1,030 |

The increases in global Prolia® sales for 2016 and 2015 were driven primarily by unit demand growth.

Sensipar®/Mimpara®

Total Sensipar®/Mimpara® sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| Sensipar® — U.S. | $ 1,240 | 16 % | $ 1,069 | 34 % | $ 796 |
| Sensipar®/Mimpara® — ROW | 342 | (1)% | 346 | (4)% | 362 |
| Total Sensipar®/Mimpara® | $ 1,582 | 12 % | $ 1,415 | 22 % | $ 1,158 |

The increase in global Sensipar®/Mimpara® sales for 2016 was driven primarily by an increase in net selling price in the United States and unit demand growth.

The increase in global Sensipar®/Mimpara® sales for 2015 was driven primarily by unit demand growth and an increase in net selling price in the United States. ROW Sensipar®/Mimpara® sales were negatively impacted by changes in foreign currency exchange rates.

XGEVA®

Total XGEVA® sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| XGEVA® — U.S. | $ 1,115 | 11 % | $ 1,006 | 17 % | $ 857 |
| XGEVA® — ROW | 414 | 4 % | 399 | 10 % | 364 |
| Total XGEVA® | $ 1,529 | 9 % | $ 1,405 | 15 % | $ 1,221 |

The increases in global XGEVA® sales for 2016 and 2015 were driven primarily by unit demand growth.

EPOGEN®

Total EPOGEN® sales were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| EPOGEN® — U.S. | $ 1,282 | (31 )% | $ 1,856 | (9 )% | $ 2,031 |

The decrease in EPOGEN® sales for 2016 was driven by a decline in unit demand resulting from competition and a shift in dialysis sales to Aranesp®.

The decrease in EPOGEN® sales for 2015 was driven by a decline in unit demand resulting from competition and a shift in dialysis sales to Aranesp®, offset partially by an increase in net selling price.

Our final material U.S. patent for EPOGEN® expired in May 2015. There is competition in the United States, which has had, and will continue to have, a material adverse impact on EPOGEN® sales. Further in December 2014, Hospira, Inc. (Hospira), a subsidiary of Pfizer, submitted a BLA to the FDA for Retacrit™, a proposed biosimilar to EPOGEN®. For discussion of ongoing litigation between us and Hospira, see Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements.

NEUPOGEN®

Total NEUPOGEN® sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| NEUPOGEN® — U.S. | $ 534 | (33 )% | $ 793 | (5 )% | $ 839 |
| NEUPOGEN® — ROW | 231 | (10 )% | 256 | (20 )% | 320 |
| Total NEUPOGEN® | $ 765 | (27 )% | $ 1,049 | (9 )% | $ 1,159 |

The decreases in global NEUPOGEN® sales for 2016 and 2015 were driven by a decline in unit demand due primarily to the impact of short-acting competition in the United States.

There is competition, which has intensified and will continue to have a material adverse impact on sales of NEUPOGEN®. We expect competitive trends to continue into 2017 from existing branded and new and existing biosimilar competition. See Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition and Part IV—Note 18, Contingencies and commitments, to the Consolidated Financial Statements for discussion of ongoing litigation.

Future NEUPOGEN® sales will also depend, in part, on the development of new protocols, tests and/or treatments for cancer and/or new chemotherapy treatments or alternatives to chemotherapy that may have reduced and may continue to reduce the use of chemotherapy in some patients.

Other products

Other product sales by geographic region were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| KYPROLIS® — U.S. | $ 554 | 19 % | $ 467 | 53 % | $ 306 |
| KYPROLIS® — ROW | 138 | * | 45 | 80 % | 25 |
| Vectibix® — U.S. | 229 | 12 % | 204 | 21 % | 168 |
| Vectibix® — ROW | 382 | 11 % | 345 | 2 % | 337 |
| Nplate® — U.S. | 350 | 10 % | 317 | 22 % | 260 |
| Nplate® — ROW | 234 | 13 % | 208 | — % | 209 |
| Repatha® — U.S. | 101 | * | 7 | * | — |
| Repatha® — ROW | 40 | * | 3 | * | — |
| BLINCYTO® — U.S. | 85 | 27 % | 67 | * | 3 |
| BLINCYTO® — ROW | 30 | * | 10 | * | — |
| Other — U.S. | 60 | * | 10 | * | — |
| Other — ROW | 190 | (2 )% | 194 | (6 )% | 206 |
| Total other product sales | $ 2,393 | 27 % | $ 1,877 | 24 % | $ 1,514 |
| Total U.S. — other products | $ 1,379 | | $ 1,072 | | $ 737 |
| Total ROW — other products | 1,014 | | 805 | | 777 |
| Total other product sales | $ 2,393 | | $ 1,877 | | $ 1,514 |

* Change in excess of 100%

Operating expenses

Operating expenses were as follows (dollar amounts in millions):

| | Year ended December 31, 2016 | Change | Year ended December 31, 2015 | Change | Year ended December 31, 2014 |
|---|---|---|---|---|---|
| Operating expenses: | | | | | |
| Cost of sales | $ 4,162 | (2 )% | $ 4,227 | (4 )% | $ 4,422 |
| % of product sales | 19.0 % | | 20.2 % | | 22.9 % |
| % of total revenues | 18.1 % | | 19.5 % | | 22.0 % |
| Research and development | $ 3,840 | (6 )% | $ 4,070 | (5 )% | $ 4,297 |
| % of product sales | 17.5 % | | 19.4 % | | 22.2 % |
| % of total revenues | 16.7 % | | 18.8 % | | 21.4 % |
| Selling, general and administrative | $ 5,062 | 4 % | $ 4,846 | 3 % | $ 4,699 |
| % of product sales | 23.1 % | | 23.1 % | | 24.3 % |
| % of total revenues | 22.0 % | | 22.4 % | | 23.4 % |
| Other | $ 133 | * | $ 49 | (89 )% | $ 454 |

* Change in excess of 100%

Transformation and process improvement

During 2014, we announced transformation and process improvement initiatives that we continue to execute on. As part of these efforts, we committed to a more agile and efficient operating model. Our transformation and process improvement efforts across the Company are enabling us to reallocate resources to fund many of our innovative pipeline and growth opportunities that deliver value to patients and stockholders.

The transformation includes a restructuring plan that will result in pre-tax accounting charges in the range of $800 million to $900 million. As of December 31, 2016, restructuring costs incurred to date were $709 million. During the years ended December 31, 2016, 2015 and 2014, we incurred restructuring costs of $37 million, $114 million and $558 million, respectively. We expect that we will incur most of the remaining estimated costs in 2017 in order to support our ongoing transformation and process improvement efforts. Since 2014, we have realized approximately $1.2 billion of transformation and process improvement savings. Net savings were not significant in 2016, 2015 and 2014 as savings were reinvested in product launches, clinical programs and external business development. Additional information required for our restructuring plan is incorporated herein by reference to Part IV—Note 2, Restructuring, to the Consolidated Financial Statements.

Cost of sales

Cost of sales decreased to 18.1% of total revenues for 2016, driven primarily by manufacturing efficiencies.

Cost of sales decreased to 19.5% of total revenues for 2015, driven primarily by lower royalties, higher net selling prices, manufacturing efficiencies and lower costs related to our restructuring plan. The year ended December 31, 2014, also had a $99 million charge related to the termination of the supply contract with Roche as a result of acquiring the licenses to filgrastim and pegfilgrastim effective January 1, 2014.

The excise tax imposed by Puerto Rico on the gross intercompany purchase price of goods and services from our manufacturer in Puerto Rico (Puerto Rico excise tax) is recorded as a cost of sales expense. Excluding the impact of the Puerto Rico excise tax, cost of sales would have been 16.5%, 17.8% and 20.1% of total revenues for 2016, 2015 and 2014, respectively. See Part IV—Note 5, Income taxes, to the Consolidated Financial Statements.

Research and development

The Company groups all of its R&D activities and related expenditures into three categories: (1) Discovery Research and Translational Sciences (DRTS), (2) later-stage clinical programs and (3) marketed products. These categories include the Company's R&D activities as set forth in the following table:

| Category | Description |
|---|---|
| DRTS | R&D expenses incurred in activities substantially in support of early research through the completion of phase 1 clinical trials. These activities encompass our DRTS functions, including drug discovery, toxicology, pharmacokinetics and drug metabolism, and process development. |
| Later-stage clinical programs | R&D expenses incurred in or related to phase 2 and phase 3 clinical programs intended to result in registration of a new product or a new indication for an existing product in the United States or the EU. |
| Marketed products | R&D expenses incurred in support of the Company's marketed products that are authorized to be sold in the United States or the EU. Includes clinical trials designed to gather information on product safety (certain of which may be required by regulatory authorities) and their product characteristics after regulatory approval has been obtained, as well as the costs of obtaining regulatory approval of a product in a new market after approval in either the United States or the EU has been obtained. |

R&D expense by category was as follows (in millions):

| | Years ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| DRTS | $1,039 | $997 | $1,212 |
| Later-stage clinical programs | 1,054 | 1,876 | 2,287 |
| Marketed products | 1,747 | 1,197 | 798 |
| Total R&D expense | $3,840 | $4,070 | $4,297 |

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The decreases in R&D expenses for 2016 and 2015 were driven primarily by decreased costs associated with later-stage clinical programs support of $822 million and $411 million, respectively, offset partially by increased costs associated with marketed products support of $550 million and $399 million, respectively. All categories of R&D spend benefited from savings from transformation and process improvement efforts. The decreases were offset partially by reinvestment for the long-term benefit of the company, including increases in DRTS for up-front milestone payments related to several collaboration transactions. Prior to approval, costs related to our launch products were categorized largely as later-stage clinical programs.

Selling, general and administrative

The increase in Selling, general and administrative (SG&A) expense for 2016 was driven primarily by further investments in product launches, offset partially by the expiration of the ENBREL residual royalty payments on October 31, 2016.

The increase in SG&A expense for 2015 was driven primarily by new product launches, offset partially by savings from transformation and process improvement efforts under our restructuring plan.

The ENBREL co-promotion term expired in October 2013, and we were required to pay Pfizer residual royalties on a declining percentage of net ENBREL sales in the United States and Canada. Effective November 2016, there were no further residual royalty payments. The residual royalty percentage ranged from 10% to 12% in 2014, 2015, and 2016.

Other

Other operating expenses for 2016 included $105 million of charges related to legal proceedings.

Other operating expenses for 2015 included $91 million of charges related to legal proceedings, certain charges related to our restructuring initiatives, including separation costs of $49 million, $31 million of write-offs of non-key assets acquired in a prior year business combination, and $111 million of gains from the sale of assets related to our site closures.

Other operating expenses for 2014 included certain charges related to our restructuring plan, primarily separation costs of $377 million. It also included a $46 million write-off of a non-key IPR&D program acquired in a prior year business combination.

Non-operating expenses/income and provision for income taxes

Non-operating expenses/income and provision for income taxes were as follows (dollar amounts in millions):

| | Years ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Interest expense, net | $1,260 | $1,095 | $1,071 |
| Interest and other income, net | $629 | $603 | $465 |
| Provision for income taxes | $1,441 | $1,039 | $427 |
| Effective tax rate | 15.7 % | 13.0 % | 7.6 % |

Interest expense, net

The increases in interest expense, net in 2016 and 2015 were due primarily to a higher average amount of debt outstanding compared with the respective prior year.

Interest and other income, net

The increase in interest and other income, net for 2016 compared with 2015 was due primarily to higher interest income as a result of higher average cash and investment balances in 2016, offset partially by higher gains on strategic equity investments in 2015. The increase in interest and other income, net for 2015 compared with 2014 was due primarily to higher interest income as a result of higher average cash and investment balances with a modestly higher portfolio yield, offset partially by higher net losses on sales of interest bearing securities in 2015.

Income taxes

The increase in our effective tax rate for 2016 compared with 2015 was due primarily to the unfavorable tax impact of changes in jurisdictional mix of income and expenses, offset partially by the adoption of a new accounting standard that amends certain aspects of the accounting for employee share-based compensation payments. One aspect of the standard requires that excess tax benefits and deficiencies that arise upon vesting or exercise of share-based payments be recognized as an income tax benefit and expense in the income statement.

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The increase in our effective tax rate for 2015 compared with 2014 was due primarily to the unfavorable tax impact of changes in the jurisdictional mix of income and expenses and lower domestic restructuring costs in 2015.

The effective tax rates for 2016, 2015 and 2014 would have been approximately 18.6%, 16.4% and 12.8%, respectively, without the impact of the tax credits associated with the Puerto Rico excise tax.

As permitted under GAAP, we do not provide for U.S. income taxes on undistributed earnings of our foreign operations that are intended to be invested indefinitely outside the United States.

See Summary of Critical Accounting Policies—Income taxes and Part IV—Note 5, Income taxes, to the Consolidated Financial Statements.

Financial Condition, Liquidity and Capital Resources

Selected financial data was as follows (in millions):

| | December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Cash, cash equivalents and marketable securities | $38,085 | $31,382 |
| Total assets | $77,626 | $71,449 |
| Current portion of long-term debt | $4,403 | $2,247 |
| Long-term debt | $30,193 | $29,182 |
| Stockholders' equity | $29,875 | $28,083 |

We intend to continue to return capital to stockholders through the payment of cash dividends and stock repurchases reflecting our confidence in the future cash flows of our business. The timing and amount of future dividends and stock repurchases will vary based on a number of factors, including future capital requirements for strategic transactions, the availability of financing on acceptable terms, debt service requirements, our credit rating, changes to applicable tax laws or corporate laws, changes to our business model and periodic determination by our Board of Directors that cash dividends and/or stock repurchases are in the best interests of stockholders and are in compliance with applicable laws and agreements of the Company. In addition, the timing and amount of stock repurchases may also be affected by the stock price and blackout periods, during which we are restricted from repurchasing stock. The manner of stock repurchases may include private block purchases, tender offers and market transactions.

The Board of Directors declared quarterly cash dividends of $0.61 per share of common stock in 2014, increased our quarterly cash dividend by 30% to $0.79 per share of common stock in 2015, and increased our quarterly cash dividend by 27% to $1.00 per share of common stock in 2016. In December 2016, the Board of Directors declared a cash dividend of $1.15 per share of common stock for the first quarter of 2017, an increase of 15% for this period, to be paid in March 2017.

We have also returned capital to stockholders through our stock repurchase program. During 2016 and 2015, we repurchased $3.0 billion and $1.9 billion of our common stock, respectively. During the fourth quarter of 2014, we repurchased $153 million of our common stock, of which $138 million was paid in cash by December 31, 2014. As of December 31, 2016, $4.1 billion remained available under the stock repurchase program.

We believe that existing funds, cash generated from operations and existing sources of and access to financing are adequate to satisfy our needs for working capital; capital expenditure and debt service requirements; our plans to pay dividends and repurchase stock; and other business initiatives we plan to strategically pursue, including acquisitions and licensing activities. We anticipate that our liquidity needs can be met through a variety of sources, including cash provided by operating activities, sales of marketable securities, borrowings through commercial paper and/or our syndicated credit facilities and access to other domestic and foreign debt markets and equity markets. With respect to our U.S. operations, we believe that existing funds intended for use in the United States; cash generated from our U.S. operations, including intercompany payments and receipts; and existing sources of and access to financing (collectively, U.S. funds) are adequate to continue meeting our U.S. obligations, including our plans to pay dividends and repurchase stock with U.S. funds, for the foreseeable future. See Part I, Item 1A. Risk Factors—Global economic conditions may negatively affect us and may magnify certain risks that affect our business.

Cash, cash equivalents, and marketable securities

Of our cash, cash equivalents and marketable securities totaling $38.1 billion as of December 31, 2016, approximately $35.9 billion was generated from operations in foreign tax jurisdictions and is intended to be invested indefinitely

outside the United States. Under current tax laws, if these funds were repatriated for use in our U.S. operations, we would be required to pay additional income taxes at the tax rates then in effect.

The primary objective of our investment portfolio is to enhance overall returns in an efficient manner while maintaining safety of principal, prudent levels of liquidity and acceptable levels of risk. Our investment policy limits interest-bearing security investments to certain types of debt and money market instruments issued by institutions with primarily investment-grade credit ratings and places restrictions on maturities and concentration by asset class and issuer.

Financing arrangements

The current and noncurrent portions of our long-term borrowings at December 31, 2016, were $4.4 billion and $30.2 billion, respectively. The current and noncurrent portions of our long-term borrowings at December 31, 2015, were $2.2 billion and $29.2 billion, respectively. As of December 31, 2016, Standard & Poor's Financial Services LLC (S&P), Moody's Investor Service, Inc. (Moody's) and Fitch Ratings Inc. assigned credit ratings to our outstanding senior notes of A with a stable outlook, Baa1 with a stable outlook and BBB with a stable outlook, respectively, which are considered investment grade. Unfavorable changes to these ratings may have an adverse impact on future financings.

During the years ended December 31, 2016, 2015 and 2014, we issued debt with aggregate principal amounts of $7.3 billion, $3.5 billion and $4.5 billion, respectively. During the years ended December 31, 2016, 2015 and 2014, we repaid debt of $3.7 billion, $2.4 billion and $5.6 billion, respectively. For information regarding specific issuances and repayments of debt, see Part IV—Note 14, Financing arrangements, to the Consolidated Financial Statements.

To achieve a desired mix of fixed and floating interest rate debt, we entered into interest rate swap contracts that effectively converted a fixed-rate interest coupon for certain of our debt issuances to a floating London Interbank Offered Rates (LIBOR)-based coupon over the life of the respective note. These interest rate swap contracts qualified and are designated as fair value hedges. As of December 31, 2016 and 2015, we had interest rate swap contracts with aggregate notional amounts of $6.65 billion. See Part IV—Note 14, Financing arrangements, and Note 17, Derivative instruments, to the Consolidated Financial Statements.

To hedge our exposure to foreign currency exchange rate risk associated with certain of our long-term notes denominated in foreign currencies, we entered into cross-currency swap contracts, which effectively convert the interest payments and principal repayment of the respective notes from euros, pounds sterling and Swiss francs to U.S. dollars. These cross-currency swap contracts qualified and are designated as cash flow hedges. As of December 31, 2016 and 2015, we had cross-currency swap contracts with aggregate notional amounts of $5.6 billion and $2.7 billion, respectively. See Part IV—Note 17, Derivative instruments, to the Consolidated Financial Statements.

As of December 31, 2016, we had a commercial paper program that allows us to issue up to $2.5 billion of unsecured commercial paper to fund our working capital needs. At December 31, 2016 and 2015, we had no amounts outstanding under our commercial paper program, although we anticipate utilizing the commercial paper program in 2017.

In 2014, we entered into a $2.5 billion syndicated, unsecured, revolving credit agreement which is available for general corporate purposes or as a liquidity backstop to our commercial paper program. The commitments under the revolving credit agreement may be increased by up to $500 million with the agreement of the banks. Each bank which is a party to the agreement has an initial commitment term of five years. We extended this term by one year during 2016 and may extend the term for an additional year with the agreement of the banks. Annual commitment fees for this agreement are 0.09% of the unused portion of the facility based on our current credit rating. Generally, we would be charged interest at LIBOR plus 1% for any amounts borrowed under this facility. As of December 31, 2016 and 2015, no amounts were outstanding under this facility.

In 2014, we filed a shelf registration statement with the SEC that allows us to issue unspecified amounts of debt securities; common stock; preferred stock; warrants to purchase debt securities, common stock, preferred stock or depositary shares; rights to purchase common stock or preferred stock; securities purchase contracts; securities purchase units; and depositary shares. Under this shelf registration statement, all of the securities available for issuance may be offered from time to time with terms to be determined at the time of issuance. This shelf registration statement expires on February 23, 2017, and is expected to be renewed before its expiration date.

In 1997, we established a $400 million medium-term note program under which medium-term debt securities may be offered from time to time with terms to be determined at the time of issuance. As of December 31, 2016 and 2015, no

securities were outstanding under this medium-term note program.

Certain of our financing arrangements contain non-financial covenants. In addition, our revolving credit agreement includes a financial covenant with respect to the level of our borrowings in relation to our equity, as defined. We were in compliance with all applicable covenants under this arrangement as of December 31, 2016. See Part IV—Note 14, Financing arrangements, to the Consolidated Financial Statements.

Cash flows

A summary of our cash flow activity was as follows (in millions):

| | Years ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Net cash provided by operating activities | $10,354 | $9,731 | $8,952 |
| Net cash used in investing activities | $(8,658) | $(5,547) | $(5,752) |
| Net cash used in financing activities | $(2,599) | $(3,771) | $(3,274) |

Operating

Cash provided by operating activities has been and is expected to continue to be our primary recurring source of funds. Cash provided by operating activities increased during 2016 due primarily to an improved operating margin and the timing of customer payments, offset partially by inventory build, the monetization of foreign currency forward contracts in 2015 and the timing of tax payments. Cash provided by operating activities increased during 2015 due primarily to improvement in our operating margin and the monetization of foreign currency contracts that resulted in the receipt of $340 million in cash, offset by the timing of payments to vendors and cash received from customers.

Investing

Capital expenditures, which were associated primarily with manufacturing capacity expansions in Singapore, Puerto Rico and Ireland, as well as other site developments, totaled $738 million, $594 million and $718 million in 2016, 2015 and 2014, respectively. We currently estimate 2017 spending on capital projects and equipment to be consistent with 2016 spend.

Cash used in investing activities during the years ended December 31, 2015 and 2014, also included the cost of acquiring certain businesses, net of cash acquired, which totaled $359 million and $165 million, respectively.

Net cash invested in marketable securities was $7.7 billion, $4.4 billion and $5.0 billion in 2016, 2015 and 2014, respectively. In addition, restricted investments provided $533 million in 2014.

Financing

Cash used in financing activities during 2016 was due primarily to the repayment of debt of $3.7 billion, the payment of dividends of $3.0 billion, repurchases of our common stock of $3.0 billion and withholding taxes arising from shares withheld for share-based payments of $260 million, offset partially by net proceeds from the issuance of debt of $7.3 billion. Cash used in financing activities during 2015 was due primarily to the repayment of long-term debt of $2.4 billion, the payment of dividends of $2.4 billion, repurchases of our common stock of $1.9 billion, withholding taxes arising from shares withheld for share-based payments of $401 million and the settlement of contingent consideration obligations incurred in connection with the acquisition of a business of $253 million. These payments were offset partially by net proceeds from the issuance of long-term debt of $3.5 billion. Cash used in financing activities during 2014 was due primarily to the repayment of long-term debt of $5.6 billion, the payment of dividends of $1.9 billion, withholding taxes arising from shares withheld for share-based payments of $225 million and repurchases of our common stock of $138 million. These payments were offset partially by net proceeds from the issuance of long-term debt of $4.5 billion and net proceeds from the issuance of common stock in connection with the Company’s equity award programs of $186 million.

See Part IV—Note 14, Financing arrangements, and Note 15, Stockholders’ equity, to the Consolidated Financial Statements.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that are material or reasonably likely to become material to our consolidated financial position or consolidated results of operations.

Contractual Obligations

Contractual obligations represent future cash commitments and liabilities under agreements with third parties, and exclude contingent liabilities for which we cannot reasonably predict future payment. Additionally, the expected timing of payment of the obligations presented below is estimated based on current information. Timing of payments and actual amounts paid may be different depending on the timing of receipt of goods or services or changes to agreed-upon terms or amounts for some obligations.

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The following table represents our contractual obligations aggregated by type (in millions):

| | Payments due by period as of December 31, 2016 | | | | |
|---|---|---|---|---|---|
| Contractual obligations | Total | Year 1 | Years 2 and 3 | Years 4 and 5 | Years 6 and beyond |
| Long-term debt obligations [1] [2] [3] [4] | $57,297 | $5,741 | $7,009 | $7,612 | $ 36,935 |
| Operating lease obligations [5] | 787 | 156 | 284 | 231 | 116 |
| Purchase obligations [6] | 2,914 | 1,592 | 540 | 285 | 497 |
| Unrecognized tax benefits (UTBs) [7] | — | — | — | — | — |
| Total contractual obligations | $60,998 | $7,489 | $7,833 | $8,128 | $ 37,548 |

(1) Long-term debt obligations include future interest payments on our fixed rate obligations at the contractual coupon rates. To achieve a desired mix of fixed and floating interest rate debt, we entered into interest rate swap contracts that effectively converted a fixed rate interest coupon for certain of our debt issuances to a floating LIBOR-based coupon over the life of the respective note. We used an interest rate forward curve at December 31, 2016, in computing net amounts to be paid or received under our interest rate swap contracts which resulted in an aggregate net decrease in future interest payments of $39 million. See Part IV—Note 14, Financing arrangements, to the Consolidated Financial Statements.

(2) Long-term debt obligations include future interest payments on our LIBOR-based variable rate obligations. We used an interest rate forward curve at December 31, 2016, in computing the LIBOR-based portion of interest payments on these debt obligations. See Part IV—Note 14, Financing arrangements, to the Consolidated Financial Statements.

(3) Long-term debt obligations include contractual interest payments and principal repayment of our foreign-denominated debt obligations. In order to hedge our exposure to foreign currency exchange rate risk associated with certain of our pound sterling and euro denominated long-term debt, we entered into cross-currency swap contracts that effectively convert interest payments and principal repayment on this debt from euros/pounds sterling to U.S. dollars. For purposes of this table, we used the contracted exchange rates in the cross-currency swap contracts to compute the net amounts of future interest payments and principal repayments on this debt. See Part IV—Note 17, Derivative instruments, to the Consolidated Financial Statements.

(4) Interest payments and the repayment of principal on our 4.375% 2018 euro Notes were translated into U.S. dollars at the foreign currency exchange rate in effect at December 31, 2016. See Part IV—Note 14, Financing arrangements, to the Consolidated Financial Statements.

(5) Operating lease obligations exclude $228 million of future receipts under noncancelable subleases of abandoned facilities.

(6) Purchase obligations relate primarily to: (i) R&D commitments (including those related to clinical trials) for new and existing products; (ii) capital expenditures; and (iii) open purchase orders for the acquisition of goods and services in the ordinary course of business. Our obligation to pay certain of these amounts may be reduced based on certain future events.

(7) Liabilities for UTBs (net of foreign tax credits and federal tax benefit of state taxes) and related accrued interest and penalties totaling approximately $2.5 billion at December 31, 2016, are not included in the table above because, due to their nature, there is a high degree of uncertainty regarding the timing of future cash outflows and other events that extinguish these liabilities.

In addition to amounts in the table above, we are contractually obligated to pay additional amounts, which in the aggregate are significant, upon the achievement of various development, regulatory and commercial milestones for agreements we have entered into with third parties, including contingent consideration incurred in the acquisitions of Dezima Pharma B.V. (Dezima) and Biovex Group Inc. (BioVex). These payments are contingent upon the occurrence of various future events, substantially all of which have a high degree of uncertainty of occurring. These contingent payments have not been included in the table above, and, except with respect to the fair value of the contingent consideration obligations, are not recorded on our Consolidated Balance Sheets. As of December 31, 2016, the

maximum amount that may be payable in the future for agreements we have entered into with third parties is approximately $7.5 billion, including $1.6 billion of contingent consideration payments in connection with the acquisitions of Dezima and BioVex. See Part IV—Note 16, Fair value measurement to the Consolidated Financial Statements.

Summary of Critical Accounting Policies

The preparation of our consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the notes to the financial statements. Some of those judgments can be subjective and complex, and therefore, actual results could differ materially from those estimates under different assumptions or conditions.

Product sales and sales deductions

Revenues from sales of our products are recognized when the products are shipped and title and risk of loss have passed. Product sales are recorded net of accruals for estimated rebates, wholesaler chargebacks, cash discounts and other deductions (collectively, sales deductions) and returns, which are established at the time of sale.

We analyze the adequacy of our accruals for sales deductions quarterly. Amounts accrued for sales deductions are adjusted when trends or significant events indicate that adjustment is appropriate. Accruals are also adjusted to reflect actual results. Amounts recorded in Accrued liabilities in the Consolidated Balance Sheets for sales deductions were as follows (in millions):

| | Rebates | Chargebacks | Other deductions | Total |
|---|---|---|---|---|
| Balance as of January 1, 2014 | $895 | $ 251 | $ 102 | $1,248 |
| Amounts charged against product sales | 2,499 | 3,399 | 688 | 6,586 |
| Payments | (2,274) | (3,454) | (727) | (6,455) |
| Balance as of December 31, 2014 | 1,120 | 196 | 63 | 1,379 |
| Amounts charged against product sales | 2,734 | 4,275 | 732 | 7,741 |
| Payments | (2,735) | (4,198) | (701) | (7,634) |
| Balance as of December 31, 2015 | 1,119 | 273 | 94 | 1,486 |
| Amounts charged against product sales | 3,479 | 5,270 | 905 | 9,654 |
| Payments | (3,181) | (5,201) | (884) | (9,266) |
| Balance as of December 31, 2016 | $1,417 | $ 342 | $ 115 | $1,874 |

For the years ended December 31, 2016, 2015 and 2014, total sales deductions were 31%, 27% and 25% of gross product sales, respectively. Included in the amounts are immaterial net adjustments related to prior-year sales due to changes in estimates. Such amounts represent less than 1% of the aggregate sales deductions charged against product sales in each of the three years ended December 31, 2016.

In the United States, we utilize wholesalers as the principal means of distributing our products to healthcare providers, such as physicians or their clinics, dialysis centers, hospitals and pharmacies. Products we sell in Europe are distributed principally to hospitals and/or wholesalers depending on the distribution practice in each country where the product is sold. We monitor the inventory levels of our products at our wholesalers by using data from our wholesalers and other third parties, and we believe wholesaler inventories have been maintained at appropriate levels (generally two to three weeks) given end-user demand. Accordingly, historical fluctuations in wholesaler inventory levels have not significantly impacted our method of estimating sales deductions and returns.

Accruals for sales deductions are based primarily on estimates of the amounts earned or to be claimed on the related sales. These estimates take into consideration current contractual and statutory requirements, specific known market events and trends, internal and external historical data and forecasted customer buying patterns. Sales deductions are substantially product-specific and, therefore, for any given