AMGEN INC
Form 10-K
February 13, 2019

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, 2018
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 every Interactive Data File required to be submitted 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 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

| Large accelerated filer | Accelerated filer | Non-accelerated filer | Smaller reporting company | Emerging growth company |
|---|---|---|---|---|
| ý | ¨ | ¨ | ¨ | ¨ |

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

Indicate by check mark 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 $119,629,312,769 as of June 30, 2018.(A)

(A) Excludes 884,143 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, 2018. 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.

622,278,034
(Number of shares of common stock outstanding as of February 7, 2019)

DOCUMENTS INCORPORATED BY REFERENCE
Specified portions of the registrant's Proxy Statement with respect to the 2019 Annual Meeting of Stockholders to be held May 21, 2019, are incorporated by reference into Part III of this annual report.

INDEX

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.

Amgen was incorporated in California in 1980 and became a Delaware corporation in 1987. We have a presence in approximately 100 countries worldwide. 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, 2017, and in early 2018.

Products/Pipeline

Oncology/Hematology

BLINCYTO® (blinatumomab)

- In March 2018, we announced that the U.S. Food and Drug Administration (FDA) approved under accelerated approval the supplemental Biologics License Application (sBLA) for BLINCYTO® for the treatment of adults and children with B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease greater than or equal to 0.1 percent.
- In June 2018, we announced that the European Commission (EC) granted a full marketing authorization for BLINCYTO® based on the overall survival data from the phase 3 TOWER study in adult patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL.
- In August 2018, we announced that the EC approved an expanded indication for BLINCYTO® as monotherapy for the treatment of pediatric patients aged one year or older with Philadelphia chromosome-negative CD19 positive B-cell precursor ALL, which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation.
- In January 2019, we announced that the EC approved an expanded indication for BLINCYTO® as monotherapy to include adult patients with Philadelphia chromosome-negative CD19 positive B-cell precursor ALL in first or second complete remission with minimal residual disease greater than or equal to 0.1 percent.

KYPROLIS® (carfilzomib)

- In January 2018, we announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion resulting in a label variation for KYPROLIS® to include updated overall survival 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 patients with relapsed or refractory multiple myeloma.
- In April 2018, we announced that the CHMP of the EMA adopted a positive opinion resulting in a label variation for KYPROLIS® to include the final overall survival data from the phase 3 ASPIRE (CArfilzomib, Lenalidomide, and DexamethaSone versus Lenalidomide and Dexamethasone for the treatment of PatIents with Relapsed Multiple MyEloma) study. In June 2018, we announced that the FDA approved the supplemental New Drug Application (sNDA) to add the positive overall survival data from the ASPIRE study to the U.S. Prescribing Information for patients with relapsed or refractory myeloma.

- In October 2018, we announced that the FDA approved the sNDA to expand the Prescribing Information for KYPROLIS® to include a once-weekly dosing option in combination with dexamethasone for patients with relapsed or refractory multiple myeloma.

Neulasta® (pegfilgrastim)

- In February 2018, we announced that the CHMP of the EMA issued a positive opinion recommending a label variation for Neulasta® to include the Neulasta® Onpro® kit.

Cardiovascular

Repatha® (evolocumab)

- In May 2018, we announced that the EC approved a new indication in the Repatha® label for adults with established atherosclerotic cardiovascular disease (myocardial infarction, stroke or peripheral arterial disease) to reduce cardiovascular risk by lowering low-density lipoprotein (LDL) cholesterol levels.
- In October 2018, we announced a set of new National Drug Codes (NDCs) to make Repatha® available at a 60% lower list price of $5,850 per year to address affordability for patients, particularly those on Medicare.
- In January 2019, we announced that the National Medical Products Administration approved a new indication for Repatha® as the first PCSK9 inhibitor in China for adults with established atherosclerotic cardiovascular disease to reduce the risk of myocardial infarction, stroke and coronary revascularization.

Neuroscience

Aimovig® (erenumab-aooe)

- In May 2018, we announced that the FDA approved Aimovig® for the preventive treatment of migraine in adults. Aimovig® is part of a joint development and commercialization collaboration with Novartis AG (Novartis).

Inflammation

Tezepelumab

- In September 2018, we announced that the FDA granted Breakthrough Therapy Designation for tezepelumab in patients with severe asthma without an eosinophilic phenotype. Tezepelumab is being developed jointly in collaboration with AstraZeneca plc (AstraZeneca).

Bone health

EVENITY™* (romosozumab)

- In January 2019, we and UCB, our global collaboration partner in the development of EVENITY™, announced that the FDA Bone, Reproductive and Urologic Drugs Advisory Committee (BRUDAC) voted to recommend approval of EVENITY™ for the treatment of osteoporosis in postmenopausal women at high risk for fracture. Also in January 2019, the Japanese Ministry of Health, Labor and Welfare granted a marketing authorization for the treatment of osteoporosis in men and postmenopausal women at high risk of fracture.

Prolia® (denosumab)

- In May 2018 and June 2018, the FDA and the EC, respectively, approved a new indication for Prolia® for the treatment of glucocorticoid-induced osteoporosis in adult patients at high risk of fracture.

XGEVA® (denosumab)

- In April 2018, we announced that the EC approved an expanded indication for XGEVA® for the prevention of skeletal-related events (SREs) in patients with multiple myeloma.

Biosimilars

AMGEVITA™ (biosimilar adalimumab)

- In October 2018, we began launching AMGEVITA™ in markets across Europe.

KANJINTI™* (biosimilar trastuzumab / formerly ABP 980)

- In May 2018, the EC granted marketing authorization for KANJINTI™, a biosimilar candidate to Herceptin®, for the treatment of HER2-positive metastatic breast cancer, HER2-positive early breast cancer and HER2-positive metastatic adenocarcinoma of the stomach or gastroesophageal junction. KANJINTI™ is being developed in collaboration with Allergan plc (Allergan).
- In May 2018, we announced that we received a Complete Response Letter from the FDA for the Biologics License Application (BLA) for KANJINTI™. In December 2018, we refiled our BLA with the FDA for KANJINTI™.

ABP 710 (biosimilar infliximab)

- In June 2018, we announced results from a phase 3 study evaluating the efficacy and safety of biosimilar candidate ABP 710 compared with REMICADE® (infliximab) in patients with moderate-to-severe rheumatoid arthritis. The results confirmed noninferiority compared to infliximab but could not rule out superiority based on its primary efficacy endpoint.
- In December 2018 and January 2019, we submitted a BLA to the FDA and a Marketing Authorization Application (MAA) to the EMA, respectively, for ABP 710.

ABP 798 (biosimilar rituximab)

- In January 2019, we and Allergan announced positive top-line results from a phase 1/phase 3 study evaluating the pharmacokinetics, efficacy and safety of ABP 798, a biosimilar candidate to RITUXAN® (rituximab), compared to rituximab in patients with moderate-to-severe rheumatoid arthritis. The results demonstrate that the study met its primary endpoint of pharmacokinetic similarity. Additionally, equivalent efficacy was established and a similar safety profile was demonstrated.

Next-generation biomanufacturing

- In April 2018, we announced plans to build a new next-generation biomanufacturing plant on our campus in West Greenwich, Rhode Island. The new plant will employ our next-generation biomanufacturing capabilities and manufacture products for the U.S. and global markets.

* 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 establishing our own affiliates, by acquiring existing third-party businesses or product rights or by partnering with third parties. Whether we use our own sales and marketing forces or 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 an opportunity and 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, which are the principal means of distributing our products to healthcare providers. We also market certain products through direct-to-consumer channels including, print, television and online media. For further discussion, see Government Regulation—Regulation in the United States—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 individually accounted for more than 10% of total revenues for each of the years ended December 31, 2018, 2017 and 2016. On a combined basis, these wholesalers accounted for 98%, 96% and 96% of our U.S. gross product sales for each of the years ended December 31, 2018, 2017 and 2016, respectively, and 84%, 81% and 81% of worldwide gross revenues for each of these years. 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 or obtaining credit insurance.

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 2018, 2017 and 2016.

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 patients with certain types of cancer (nonmyeloid) who receive anticancer medicines (chemotherapy) that can cause fever and a low blood cell count. In 2015, the Neulasta® Onpro® kit became available in the United States. The Neulasta® Onpro® kit provides physicians the opportunity to initiate the administration of Neulasta® on the same day as chemotherapy, with drug delivery of the recommended dose of Neulasta® at home the day after chemotherapy, thereby saving patients a trip back to the doctor.

Prolia® (denosumab)

We market Prolia® primarily in the United States and Europe. Prolia® contains the same active ingredient as XGEVA® (denosumab) 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 of 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.

Aranesp® (darbepoetin alfa)

We market Aranesp® primarily in the United States and Europe. It was launched in 2001 and is indicated to treat a lower-than-normal number of red blood cells (anemia) caused by chronic kidney disease (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 certain patients with nonmyeloid malignancies and when chemotherapy will be used for at least two months after starting Aranesp®.

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

XGEVA®

We market XGEVA® primarily in the United States and Europe. XGEVA® was launched in the United States in 2010 and is now 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 and multiple myeloma. XGEVA® was launched in Europe in 2011 and is used primarily in the indication for the prevention of SREs in patients with bone metastases from solid tumors. It was approved in January 2018 in the United States and April 2018 in Europe for the prevention of SREs in patients with multiple myeloma.

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 secondary hyperparathyroidism in adult patients with CKD who are on dialysis.

Sensipar® and our recently launched Parsabiv® (etelcalcetide) compete with each other.

EPOGEN®

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 in order to lessen the need for red blood cell transfusions. The majority of our sales are to a large dialysis provider.

Other Marketed Products

We also market a number of other products in various markets worldwide, including KYPROLIS® (carfilzomib), Nplate® (romiplostim), Vectibix® (panitumumab), Repatha® (evolocumab), NEUPOGEN® (filgrastim), Parsabiv®, BLINCYTO® (blinatumomab), Aimovig® (erenumab-aooe), IMLYGIC® (talimogene laherparepvec), Corlanor® (ivabradine), KANJINTI™ (biosimilar trastuzumab) and AMGEVITA™ (biosimilar adalimumab).

Patents

The following table lists our outstanding material patents for the indicated product by territory, general subject matter and latest expiry date. Certain of the European patents are the subjects of supplemental protection certificates that provide additional protection for the products 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 |
| Prolia®/ XGEVA® (denosumab) | U.S. | RANKL antibodies | 9/17/2021 |
| | 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 including epitope binding | 2/23/2021 |
| | Europe | RANKL antibodies including sequences[1] | 6/25/2022 |
| Aranesp® (darbepoetin alfa) | U.S. | Glycosylation analogs of erythropoietin proteins | 5/15/2024 |
| Sensipar®/ Mimpara® (cinacalcet) | U.S. | Formulation | 9/22/2026 |
| | Europe | Calcium receptor-active molecules[1] | 10/23/2015 |
| | Europe | Formulation | 9/10/2024 |
| KYPROLIS® (carfilzomib) | U.S. | Compositions and compounds | 12/7/2027 |
| | U.S. | Methods of treatment | 4/14/2025 |
| | U.S. | Methods of making | 5/8/2033 |
| | Europe | Compositions, compounds and methods of treatment[1] | 8/8/2025 |
| 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 |
| Vectibix® (panitumumab) | U.S. | Human monoclonal antibodies to epidermal growth factor receptor | 4/8/2020 |
| | Europe | Human monoclonal antibodies to epidermal growth factor receptor[1] | 5/5/2018 |
| Repatha® (evolocumab) | U.S. | Antibodies[2] | 10/25/2029 |
| | U.S. | Methods of treatment | 10/8/2030 |
| | Europe | Compositions and method of treatment | 8/22/2028 |
| Parsabiv® (etelcalcetide) | U.S. | Compound and pharmaceutical composition[2] | 7/29/2030 |
| | U.S. | Formulation | 6/27/2034 |
| | Europe | Compound and pharmaceutical composition | 7/29/2030 |
| | Europe | Formulation | 6/27/2034 |
| BLINCYTO® (blinatumomab) | U.S. | Bifunctional polypeptides[2] | 4/21/2019 |
| | U.S. | Method of administration | 9/28/2027 |
| | Europe | Bifunctional polypeptides[1] | 11/26/2024 |
| | Europe | Method of administration | 11/29/2026 |
| Aimovig® (erenumab-aooe) | U.S. | CGRP receptor antibodies[2] | 11/9/2031 |

| | | | |
|---|---|---|---|
| | U.S. | Methods of treatment | 12/18/2029 |
| | Europe | CGRP receptor antibodies and methods of treatment | 12/18/2029 |
| IMLYGIC® (talimogene laherparepvec) | U.S. | Compositions | 11/23/2025 |
| | U.S. | Method of treatment | 3/27/2022 |
| | Europe | Composition and uses[(1)] | 3/27/2022 |
| Corlanor® (ivabradine) | U.S. | Crystalline forms | 2/22/2026 |

(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:

•denosumab — France, Italy, Spain and the United Kingdom, expiring in 2025
•cinacalcet — Germany expiring in 2019; France, Italy, Spain and the United Kingdom, expiring in 2020
•carfilzomib — France, Germany, Italy and Spain, expiring in 2030
•romiplostim — France, Germany, Italy, Spain and the United Kingdom, expiring in 2024
•panitumumab — France, Germany, Italy, Spain and the United Kingdom, expiring in 2022
•evolocumab — France and Spain, expiring in 2030
•blinatumomab — France, Italy and Spain, expiring in 2029
•erenumab — Italy expiring in 2033
•talimogene laherparepvec — Spain, expiring in 2026; France, Germany, Italy and the United Kingdom, expiring in 2027

(2) 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. A number of our marketed products are indicated in disease areas in which other products or treatments are currently available or are being pursued by our competitors through research and development (R&D) activities. Additionally, some competitor-marketed products target the same genetic pathways as our recently launched marketed products or are being pursued currently. This competition could impact the pricing and market share of our products. We continue to pursue ways to increase the value of our medicines through innovations during their life cycles, which can include expanding the disease areas for which our products are indicated and finding new methods to make the delivery of our medicines easier and less costly. Such activities can offer important opportunities for differentiation. For example, in 2015, we launched the Neulasta® Onpro® kit, which provides physicians the opportunity to initiate the administration of the recommended dose of Neulasta® on the same day as chemotherapy, with drug delivery at home the day after chemotherapy, thereby saving patients a trip back to the doctor. We also launched in 2017 the AutoTouch® reusable auto-injector to be used with Enbrel Mini® single-dose prefilled cartridges (50 mg/mL). The Enbrel Mini® utilizes a new drug formulation of ENBREL that was associated with statistically significant lower mean injection site pain than the current formulation. We plan to continue pursuing innovation efforts to strengthen our competitive position. Such position 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 and generics. 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. We expect that the adverse impact on our product sales from biosimilar competition will be more like branded biologic competition than that seen when branded small molecules face generics, but we believe that when multiple biosimilar versions of one of our products get approved and launched, competition could intensify more rapidly, resulting in a greater impact on our product's sales. 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. In the United States, companies now have approved biosimilar versions of EPOGEN®, NEUPOGEN®, Neulasta® and ENBREL. See also Government Regulation—Regulation in the United States—Approval of Biosimilars. As biosimilar competitors come to market, we will leverage both the experience we have had in the United States versus branded competition and our experience in competing against epoetin alfa and filgrastim biosimilars in Europe. In addition, although most of our products are biologics, some of our products are small-molecule products. Because the FDA approval process allows generic manufacturers to rely on the safety and efficacy data of the innovator product rather than having to conduct their own costly and time-consuming clinical trials, generic manufacturers can often market their competing versions of our small-molecule products at much lower prices. As a result, upon the expiration or loss of patent protection for a small-molecule product, we can lose the majority of revenues for that product in a very short

period of time.

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, the term 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 from biosimilars and generics in the future.

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

| Product | Territory | Competitor-marketed product | Competitors |
|---|---|---|---|
| ENBREL | U.S. & Canada | REMICADE®* | Janssen Biotech, Inc. (Janssen)(1) |
| | U.S. & Canada | HUMIRA® | AbbVie Inc. |
| | U.S. & Canada | STELARA®(2) | Janssen(1) |
| | U.S. & Canada | Otezla®(2) | Celgene Corporation (Celgene) |
| Neulasta®(3) | U.S. | UDENYCA™ | Coherus BioSciences, Inc. |
| | U.S. | Fulphila® | Mylan Institutional Inc. |
| | U.S. & Europe | Filgrastim biosimilars | Various |
| Prolia® | U.S. & Europe | Alendronate, raloxifene and zoledronate generics | Various |
| Aranesp® | U.S. | PROCRIT®(4) | Janssen(1) |
| | U.S. | MIRCERA®(5) | Galenica Group (Galenica)/F. Hoffmann-La Roche Ltd. (Roche) |
| | U.S. & Europe | Epoetin alfa biosimilars | Various |
| XGEVA® | U.S. & Europe | Zoledronate generics | Various |
| Sensipar®(6)/ Mimpara® | U.S. & Europe | Active vitamin D analogs | Various |
| EPOGEN®(3) | U.S. | MIRCERA®(5) | Galenica/Roche |
| | U.S. | RETACRIT™ | Hospira(7) |
| KYPROLIS®(9) | U.S. | VELCADE® | Millennium Pharmaceuticals, Inc.(8) |
| | U.S. | REVLIMID® | Celgene |
| | U.S. | POMALYST® | Celgene |
| | U.S. | DARZALEX® | Janssen(1) |
| Repatha® | U.S. & Europe | PRALUENT® | Regeneron<br>Sanofi |
| Parsabiv® | U.S. & Europe | Active vitamin D analogs | Various |
| Aimovig® | U.S. | AJOVY™ | Teva Pharmaceuticals USA, Inc. |
| | U.S. | Emgality™ | Eli Lilly and Company |

* Approved biosimilars available.

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

(2) Dermatology only.

(3) Other biosimilars under regulatory review in the United States and Europe.

(4) PROCRIT® competes with Aranesp® in the supportive cancer care and predialysis settings.

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

(6) Our U.S. composition of matter patent for Sensipar® expired in March 2018. We are engaged in litigation with a number of companies seeking to market generic versions of Sensipar® surrounding our U.S. formulation patent that expires in September 2026. See Part IV—Note 20, Contingencies and commitments, to the Consolidated Financial Statements, for further information. Several of these generic versions of Sensipar® have been approved by the FDA.

(7) A subsidiary of Pfizer Inc. (Pfizer)

(8) A subsidiary of Takeda Pharmaceutical Company Limited.
(9) 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, remain focused on reducing the cost of healthcare, and 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 heavily scrutinized for cost containment. As a result, payers are becoming more restrictive regarding the use of biopharmaceutical products and scrutinizing the prices of these products, while requiring a higher level of clinical evidence to support the benefit such products bring to patients and the broader healthcare system. These pressures are intensified where our products are subject to increasing competition.

In the United States, healthcare providers and other entities such as pharmacies and Pharmacy Benefit Managers (PBMs) are reimbursed for covered services and products they deliver through Medicare, Medicaid and other government healthcare programs, as well as through private payers. We are required to provide rebates or discounts on our products that are reimbursed through certain government programs, including Medicare and Medicaid, and also provide discounts to qualifying healthcare providers under the Federal 340B Drug Pricing Program. In addition, we provide rebates to PBMs, as well as other entities (such as hospitals and pharmacies), which are payments by a biopharmaceutical manufacturer of a portion of the product's purchase price back to the PBMs or other entities. Biopharmaceutical-product pricing remains central to discussions on controlling healthcare costs in the United States. Policy makers from both of the major U.S. political parties are pursuing policies to lower drug costs for patients. In May 2018, U.S. president Donald Trump and his administration released a drug-pricing "blueprint" and requested public comment on an array of policy ideas intended to increase competition, improve the federal government's negotiating power, reduce drug prices and lower patients' out-of-pocket costs. The blueprint included a number of policy ideas with the potential to significantly affect, whether individually or collectively, the biopharmaceutical industry; and the U.S. presidential administration has already begun to implement certain elements described in the administration's drug-pricing blueprint, such as (i) seeking initial feedback on a potential program that would set the Medicare payment amount for Part B single-source drugs and biologics to be more closely aligned with international drug prices and rely on third-party vendors, (ii) issuing guidance to allow certain Medicare plans offered by private insurance companies to begin requiring that patients receiving Medicare Part B drugs first try a drug preferred by the plan before such plan will cover another therapy, (iii) lowering initial reimbursement rates for new Part B drugs launched beginning in 2019 and (iv) proposing new rules to require drug price information in direct-to-consumer drug television advertising. The blueprint also discussed (i) the potential removal of the safe-harbor protection under the federal anti-kickback statute for drug rebates paid to payers and (ii) changes to the Part D program. At the same time, value assessments of new technologies 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. In addition, continued consolidation of payers and integration of providers and payers (integrated delivery systems) increase the level of market power held by our customers. Such developments, particularly when taken in combination with increasing product competition, put greater pressure on access to, pricing of and sales of our products.

In addition, rebates and/or discount levels as well as the number of entities that are entitled to receive them since they are reimbursed through government programs have increased over time. For example, the Bipartisan Budget Act, enacted in 2018, requires biopharmaceutical manufacturers to pay greater discounts for patients in the Medicare Part D coverage gap beginning in 2019; and the Patient Protection and Affordable Care Act (ACA), enacted in 2010, increased many of the mandatory discounts and rebates required of us. The ACA also imposed a new Branded Prescription Pharmaceutical Manufacturers and Importers fee payable each year by us and other manufacturers. In the Tax Cuts and Jobs Act (2017 Tax Act) signed by President Trump in December 2017, Congress removed a key ACA provision by repealing the individual mandate penalty, which required every person to have health insurance or pay a penalty. Future changes to government programs such as the ACA, whether legislative or regulatory, could impact the

number of patient lives covered, could raise or lower the cost or quality of insurance, could affect Medicaid eligibility and could change levels of patient protections provided unless alternatives are put in place.

Other government 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 (ESRD); changes in the federal payment rate or new rebate requirements for covered drugs and policies for drug payment in Medicare or Medicaid; and changes to coverage and payment for biosimilars, such as policies that would facilitate easier substitution for, or provide reimbursement advantages over, the corresponding innovative products. In ESRD, the Centers for Medicare & Medicaid Services (CMS) uses a bundled-payment system and recently finalized changes allowing more new dialysis drugs to be eligible for temporary add-on payment adjustments starting in 2020. Sensipar® and Parsabiv® were already eligible for add-on payment adjustments beginning in 2018 and will continue to receive them in 2019. CMS has indicated interest in testing new models for drug payment in Medicare Part B and Part D. CMS also continues to test alternative payment models with providers, such as the

Oncology Care Model. These models provide financial incentives for providers who participate; under the models, providers take on greater risk for the overall cost and quality of care. In addition, in 2018 CMS implemented changes to Medicare payment to hospitals for Part B drugs acquired through the Federal 340B Drug Pricing Program but provided a financial incentive for hospitals to use biosimilar products over the corresponding innovative products. As described above, CMS is permitting Medicare Advantage plans to implement access controls for Part B drugs while also (i) considering a proposal that would set the Medicare payment amount for Part B single-source drugs and biologics to more closely align with international drug prices and rely on third-party vendors and (ii) considering changes to Medicare Part D and Medicare Advantage. These and/or other changes have the potential to impact prescribing and patient access to Amgen's therapies.

Additional efforts by state legislatures and government agencies in the United States could also affect us and our industry. For example, a California law requires manufacturers to provide payers advance notice of a price increase over a specified threshold, and laws in Oregon and Vermont require manufacturers to submit price increase justifications to a state attorney agency 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.

In the U.S. private sector, payers continue to institute cost reduction and containment measures that lower drug utilization and/or spending altogether and/or shift a greater portion of the costs to patients. Such measures include more limited benefit plan designs, higher patient co-pays or coinsurance obligations, limitations on patients' use of commercial manufacturer co-pay payment assistance programs (including through co-pay accumulator adjustment or maximization programs), stricter utilization management criteria before a patient may get access to a drug, and/or higher-tier formulary placement that increases the level of patient out-of-pocket costs. The use of such measures by PBMs and insurers that handle the majority of sales for ENBREL and Repatha® has continued to intensify and thereby limited Amgen product usage and sales. Consolidation has resulted in a smaller number of PBMs and insurers overseeing a large portion of total covered lives in the United States. As a result, PBMs and insurers have greater market power and negotiating leverage to mandate stricter utilization criteria and/or exclude drugs from their formularies in favor of competitor drugs or alternative treatments. Our past experience with Repatha® underscores that utilization management requirements, including the burdensome administrative processes required of physicians to demonstrate and document that patients meet such requirements, continue to be a significant challenge for patients and physicians, limiting access for appropriate usage. Formulary exclusion effectively encourages patients and providers to seek alternative treatments or pay 100% of the cost of a drug. A drug's inclusion and favorable positioning on formulary is essential to ensure patients have access. Even when access is available, some patients abandon their prescriptions due to economic reasons. In highly competitive treatment markets such as with ENBREL, Repatha® and Aimovig®, PBMs are also able to exert negotiating leverage by requiring incremental rebates from manufacturers in order to maintain their formulary position.

In many countries outside the United States, government-sponsored healthcare systems are the primary payers for drugs and biologics. With increasing budgetary constraints, and/or difficulty in understanding the value of medicines, governments and payers in many countries are applying a variety of measures to exert downward price pressure. These measures can include mandatory price controls; price referencing; therapeutic-reference pricing; increases in mandates; incentives for generic substitution and biosimilar usage; and government-mandated price cuts. In this regard, many countries have health technology assessment organizations that use formal economic metrics such as cost-effectiveness to determine prices, coverage and reimbursement of new therapies, and these organizations are expanding in established and emerging markets. We expect that countries will continue to take aggressive actions to seek to reduce expenditures on drugs and biologics. Similarly, fiscal constraints may also affect the extent to which countries are willing to approve new and innovative therapies and/or allow access to new technologies.

The dynamics and developments discussed above serve to create pressure on the pricing and potential usage of our products and the industry. 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 facilitate patient access to needed medicines. We do this by:

- investing billions of dollars annually in R&D;
- 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 policy makers, 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. Further, our expertise in manufacturing of biologics positions us well for leadership in the global biosimilars market. For additional information regarding manufacturing facilities, see Item 2. Properties.

Our internal manufacturing network has the commercial production capabilities of bulk manufacturing, formulation, fill, finish and device assembly. These activities are performed within the United States and its territories in our Puerto Rico, Rhode Island and California facilities as well as internationally in our Ireland, Netherlands and Singapore facilities. In addition, we utilize third-party contract manufacturers to supplement the capacity or capability of our commercial manufacturing network.

To support our clinical trials, we manufacture product candidates primarily at our California and, to a lesser extent, our Rhode Island facilities. 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 Puerto Rico, 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, each of our manufacturing locations also includes 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 risks while continuing to ensure adequate supply of our products.

In 2017, our next-generation biomanufacturing plant in Singapore was licensed by the FDA and the EMA for certain commercial-scale production. In 2018, we successfully completed additional bulk process qualification campaigns, which if approved, would permit the commercial production of an additional product at that site. A next-generation biomanufacturing plant incorporates multiple innovative technologies into a single facility and therefore can be built in half the construction time with approximately one-half of the operating cost of a traditional plant. Next-generation biomanufacturing plants require a smaller manufacturing footprint and offer greater environmental benefits, including reduced consumption of water and energy and lower levels of carbon emissions. Within the plant, the equipment is portable and smaller, and some components are disposable, which provides greater flexibility and speed when manufacturing different medicines simultaneously. This eliminates costly and complex retrofitting inherent in standard plants and allows Amgen to respond to changing demands for its medicines with increased agility, ultimately impacting the speed at which a medicine is available for patients. The Singapore site also has a plant with the capability to produce small-molecule drugs. When approved by relevant regulatory authorities this plant can be used for commercial manufacturing.

In July 2018, we announced the groundbreaking of our new next-generation biomanufacturing plant that will be constructed at our West Greenwich, Rhode Island, campus. The new plant is expected to be the first of its kind in the

United States and will use our next-generation biomanufacturing capabilities. After construction has been completed and upon approval by the FDA and other global regulatory authorities, this plant will expand our capacity to manufacture certain products for U.S. and global markets.

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 help authenticate 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, including global regulatory implications, that can adversely impact our development and marketing of commercial products.

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, 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, reevaluate, 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 either a BLA for biologic products or a New Drug Application 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 nonclinical 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 initial 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 2018, 16 biosimilar applications have been approved by the FDA, including our products AMJEVITA™, a biosimilar candidate to HUMIRA® (adalimumab), and MVASI™, a biosimilar candidate to Avastin® (bevacizumab), as well as competitors to our products ENBREL, Aranesp®, EPOGEN®, NEUPOGEN® and Neulasta®. 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 drug products. Our product promotion for approved product indications must comply with the statutory standards of the FDCA and the FDA's implementing regulations and guidance. 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 reinspect 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 not authorized in any EU 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.

As a result of the United Kingdom’s vote to leave the EU in March 2019, the EMA announced that it will relocate its headquarters from London to Amsterdam by March 30, 2019. While negotiations continue regarding the terms of the United Kingdom’s withdrawal from the EU, the specific impact to the supervision, regulation and supply of medicines in the United Kingdom and Europe remain unclear.

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 can 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 time frames. 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 and product complaints reported following the use of our products through routine post-marketing 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 also proactively monitor product complaints through our quality systems, which includes assessing our drug delivery devices for device complaints, adverse events and malfunctions. 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®.

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 prescribing 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 entered into a corporate integrity agreement with the Office of Inspector General (OIG) of the U.S. Department of Health and Human Services, which was formally closed out in August 2018. 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 arguably 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. We capitalize on our strength in human genetics, novel biology and protein engineering. We leverage our biologic expertise and take a modality-independent approach to R&D. We use cutting-edge science and technology to study 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, other combination modalities or new modalities. Leveraging two decades of research at deCODE, a global leader in analyzing the human genome, we are reshaping our portfolio and increasingly focusing efforts on validated targets. Human genetic validation is used whenever possible in order to enhance the likelihood of success. For the years ended December 31, 2018, 2017 and 2016, our R&D expenses were $3.7 billion, $3.6 billion and $3.8 billion, respectively.

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

Our clinical trial activities are conducted by 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—Regulation in the United States—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 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 in which we have products or in which 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 greatly 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 shows a selection of certain of our product candidates by phase of development in our therapeutic areas of focus as of February 12, 2019, 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, nonregistrational 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 nonregistrational clinical trials for various reasons, including to evaluate real-world outcomes or to collect additional safety information with regard to the use of our products. In addition, the table does not include biosimilar products we are developing, which are discussed later in this section.

| Molecule | Disease/condition |
|---|---|
| Phase 3 Programs | |
| ENBREL | Rheumatoid arthritis remission |
| EVENITY™ | Postmenopausal osteoporosis; Male osteoporosis |
| IMLYGIC® | Metastatic melanoma |
| KYPROLIS® | Multiple myeloma |
| Omecamtiv mecarbil | Chronic heart failure |
| Tezepelumab | Severe asthma |
| AMG 520 / CNP520 | Alzheimer’s disease |
| Phase 2 Programs | |
| BLINCYTO® | Diffuse large B-cell lymphoma |
| Tezepelumab | Atopic dermatitis |
| AMG 714 / PRV-015 | Celiac disease |
| Phase 1 Programs | |
| IMLYGIC® | Various cancer types |
| AMG 119 | Small-cell lung cancer |
| AMG 160 | Prostate cancer |
| AMG 176 | Hematologic malignancies |
| AMG 212 | Prostate cancer |
| AMG 330 | Acute myeloid leukemia |
| AMG 397 | Hematologic malignancies |
| AMG 420 | Multiple myeloma |
| AMG 424 | Multiple myeloma |
| AMG 427 | Acute myeloid leukemia |
| AMG 510 | Solid tumors |
| AMG 562 | Non-Hodgkin’s lymphoma |
| AMG 570 | Systemic lupus erythematosus |
| AMG 592 | Inflammatory diseases |
| AMG 596 | Glioblastoma |
| AMG 598 | Obesity |
| AMG 673 | Acute myeloid leukemia |
| AMG 701 | Multiple myeloma |
| AMG 757 | Small-cell lung cancer |
| AMG 890 | Cardiovascular disease |
| AMG 966 | Inflammatory bowel diseases (Crohn’s and ulcerative colitis) |
| 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 the safety and proper dose ranges of product candidates in a small number of human subjects. |

Phase 3 Product Candidate Program Changes

As of February 12, 2018, we had 13 phase 3 programs. As of February 12, 2019, we had eight phase 3 programs, as regulatory approvals were received for three programs, and two programs concluded. These changes are set forth in the following table.

| Molecule | Disease/condition | Program change |
|---|---|---|
| Aimovig® | Migraine prevention | BLA approved by FDA |
| Aranesp® | Myelodysplastic syndromes | Concluded; no longer pursuing our marketing application with the EC |
| BLINCYTO® | ALL | sBLA approved by FDA |
| ENBREL | Psoriatic arthritis | Concluded; study achieved its primary endpoint |
| Prolia® | Glucocorticoid-induced osteoporosis | sBLA approved by FDA and EC |

Phase 3 Product Candidate Patent Information

The following table describes our outstanding composition of matter patents that have been issued thus far for our product candidates in phase 3 development that have yet to be approved for any indication in the United States or the EU. Patents for products already approved for one or more indications in the United States or the EU but that are 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* |
|---|---|---|---|
| EVENITY™ | U.S. | Polypeptides | 2026 |
| | Europe | Polypeptides | 2026 |
| Omecamtiv mecarbil | U.S. | Compound | 2027 |
| | Europe | Compound | 2025 |
| Tezepelumab | U.S. | Polypeptides | 2029 |
| | Europe | Polypeptides | 2028 |
| AMG 520 / CNP520 | U.S. | Compound | 2032 |
| | Europe | Compound | 2032 |

* 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 provides additional information about selected product candidates that have advanced into human clinical trials.

BLINCYTO®

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

A phase 2/3 study in patients with relapsed or refractory diffuse large B-cell lymphoma is ongoing.

ENBREL

ENBREL is a fusion protein that inhibits tumor necrosis factor.

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

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 January 2019, we and UCB announced support from the FDA BRUDAC for the approval of EVENITY™ for the treatment of postmenopausal women with osteoporosis at high risk for fracture. Also in January 2019, the Japanese Ministry of Health, Labor and Welfare granted a marketing authorization for EVENITY™ for the treatment of osteoporosis in men and postmenopausal women at high risk of fracture.

IMLYGIC®

IMLYGIC® is an oncolytic immunotherapy derived from herpes simplex virus type 1.

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

KYPROLIS®

KYPROLIS® is a proteasome inhibitor.

In April 2018, we announced that the CHMP of the EMA adopted a positive opinion recommending a label variation for KYPROLIS® to include the final overall survival data from the phase 3 ASPIRE study.

In June 2018, we announced that the FDA approved the sNDA to add the positive overall survival data from the phase 3 ASPIRE study to the U.S. Prescribing Information for KYPROLIS® in patients with relapsed or refractory multiple myeloma.

In October 2018, we announced that the FDA approved the sNDA to expand the Prescribing Information for KYPROLIS® to include a once-weekly dosing option in combination with dexamethasone for patients with relapsed or refractory multiple myeloma.

A phase 3 study comparing carfilzomib, dexamethasone, and daratumumab to carfilzomib and dexamethasone for the treatment of patients with relapsed or 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 collaboration with Servier for certain territories.

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

Tezepelumab

Tezepelumab is a human monoclonal antibody that inhibits the action of thymic stromal lymphopoietin. It is being evaluated as a treatment for severe asthma in an ongoing phase 3 study, as well as atopic dermatitis. Tezepelumab is being developed jointly in collaboration with AstraZeneca.

AMG 520 / CNP520

AMG 520 / CNP520 is a small-molecule inhibitor of beta-site amyloid precursor protein-cleaving enzyme-1 (BACE). It is being evaluated for the prevention of Alzheimer's disease, with phase 3 studies ongoing. AMG 520 / CNP520 is being developed jointly in collaboration with Novartis.

AMG 714 / PRV-015

AMG 714 / PRV-015 is a human monoclonal antibody that binds to Interleukin-15. It is being investigated for the treatment of celiac disease. In November 2017, Amgen reacquired the AMG 714 program from Celimmune LLC. AMG 714 / PRV-015 is being developed jointly in collaboration with Provention Bio.

Amgen Development of Biosimilars

We also develop and commercialize biosimilar medicines. Our biosimilar product candidates in late-stage clinical development are described in the following table:

| Program | Reference product | Status |
|---|---|---|
| ABP 710 | Infliximab (REMICADE®) | Filed BLA with the FDA and MAA with the EMA |
| ABP 798 | Rituximab (Rituxan® / Mabthera®) | Phase 3 rheumatoid arthritis study completed<br>Phase 3 non-Hodgkin's lymphoma study ongoing |
| ABP 959 | Eculizumab (Soliris®) | Phase 3 initiated |

In addition to the above programs, AMJEVITA™ / AMGEVITA™ and MVASI™ have been approved by the FDA and the EC. KANJINTI™ has been approved by the EC and we have refiled our BLA with the FDA. We are also pursuing other biosimilar product candidates in earlier-stage development.

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 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 nonrefundable, 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 commencement of a 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.

During the first quarter of 2018, we acquired the remaining 50% ownership interest of Kirin-Amgen, Inc. (K-A), from Kirin Holdings Company, Limited (Kirin), making K-A a wholly owned subsidiary of Amgen. Prior to the closing of the share acquisition, K-A was a 50-50 joint venture with Kirin. K-A develops and then licenses all product rights that have been transferred from Amgen and Kirin. See Part IV—Note 3, Business combinations and Note 10, Related party transactions, to the Consolidated Financial Statements.

Prior to the closing of the share acquisition, K-A had given us exclusive licenses to manufacture and market (i) filgrastim 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, filgrastim, darbepoetin alfa, recombinant human erythropoietin and romiplostim under the brand names Neulasta®, NEUPOGEN®/GRANULOKINE®, Aranesp®, EPOGEN® and Nplate®, respectively. Under these agreements, Amgen paid K-A royalties based on product sales. In addition, Amgen received payments from K-A for milestones earned and for conducting certain R&D activities on K-A's behalf.

K-A has also given and continues to grant Kirin exclusive licenses to manufacture and market (i) filgrastim and pegfilgrastim in Japan, Taiwan and South Korea; (ii) darbepoetin alfa, romiplostim and brodalumab in Japan, China, Taiwan, South Korea and 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 filgrastim, pegfilgrastim and recombinant human erythropoietin in China, which Amgen subsequently assigned to Kirin, and as a result, Kirin now manufactures and markets filgrastim and recombinant human erythropoietin exclusively in China. Kirin markets filgrastim, 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

receives payments from K-A for conducting certain R&D activities on K-A's behalf.

Novartis

In April 2017, we expanded our existing migraine collaboration with Novartis. In the United States, Amgen and Novartis jointly develop and collaborate on the commercialization of Aimovig®. Amgen, as the principal, recognizes product sales of Aimovig® in the United States, shares U.S. commercialization costs with Novartis and pays Novartis a significant royalty on net sales in the United States. Novartis holds global co-development rights and exclusive commercial rights outside the United States and Japan for Aimovig® and other specified migraine programs. Novartis pays Amgen double-digit royalties on net sales of the products in the Novartis exclusive territories and funds a portion of global R&D expenses. In addition, Novartis will make a payment to Amgen of up to $100 million if certain commercial and expenditure thresholds are achieved with respect to Aimovig® in the United States. Amgen manufactures and supplies Aimovig® worldwide.

UCB

We are in a collaboration with UCB for the development and commercialization of EVENITY™. Under our collaboration, UCB has the rights to lead commercialization for EVENITY™ for all indications in Europe, China (excluding Hong Kong) and Brazil. All other territories 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 the United States and Japan, Bayer manages all commercialization activities and incurs all sales and marketing expenditures and mutually agreed R&D expenses, and we reimburse Bayer for half of those expenditures. In all countries outside the United States and 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 six-year supply agreement with DaVita Inc. (DaVita), which superseded the previously existing seven-year supply agreement that commenced in 2012. Pursuant to the 2017 agreement, we supply EPOGEN® and Aranesp® in amounts necessary to meet specified annual percentages of DaVita's and its affiliates' requirements for erythropoiesis-stimulating agents (ESAs) used in providing dialysis services in the United States and Puerto Rico. Such percentage varies during the term of the agreement, but in each year is at least 90%. The 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, 2018, Amgen had approximately 21,500 staff members. We consider our staff relations to be good.

Executive Officers of the Registrant

Mr. Robert A. Bradway, age 56, has served as a director of the Company since 2011 and Chairman of the Board of Directors since 2013. Mr. Bradway has been the Company's President since 2010 and Chief Executive Officer since 2012. From 2010 to 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 2007 to 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 The Boeing Company, an aerospace company and manufacturer of commercial airplanes, defense, space and securities systems, since 2016. He has served on the board of trustees of the University of Southern California since 2014 and on the advisory board of the Leonard D. Schaeffer Center for Health Policy and Economics at that university since 2012. From 2011 to 2017, Mr. Bradway was a director of Norfolk Southern Corporation, a transportation company.

Mr. Murdo Gordon, age 52, became Executive Vice President, Global Commercial Operations in 2018. Prior to joining the Company, Mr. Gordon was the Chief Commercial Officer at Bristol-Myers Squibb Company (BMS) from 2016 to July 2018. Mr. Gordon served as Head of Worldwide Markets at BMS from 2015 to 2016. Prior to this, Mr. Gordon served in a variety of leadership roles at BMS for over 25 years.

Mr. Jonathan P. Graham, age 58, became Senior Vice President, General Counsel and Secretary in 2015. From 2006 to 2015, Mr. Graham was Senior Vice President and General Counsel at Danaher Corporation. From 2004 to 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.

Ms. Lori A. Johnston, age 54, became Senior Vice President, Human Resources in 2016. From 2012 to 2016, Ms. Johnston was Executive Vice President and Chief Administrative Officer of Celanese Corporation. From 2006 to 2012, Ms. Johnston served in a series of progressive leadership roles at the Company, 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. David W. Meline, age 61, became Executive Vice President and Chief Financial Officer in 2014. From 2011 to 2014, Mr. Meline served as Senior Vice President and Chief Financial Officer at 3M Company (3M). From 2008 to 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 at 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 2016, currently serving as the chairman 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 2014 until its acquisition by ZF Friedrichshafen AG in 2015.

Ms. Cynthia M. Patton, age 57, became Senior Vice President and Chief Compliance Officer in 2012. Ms. Patton joined the Company in 2005. From 2005 to 2010, Ms. Patton was Associate General Counsel. From 2010 to 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 62, became Senior Vice President, Business Development, in 2014. Mr. Piacquad joined the Company in 2010 and served as Vice President, Strategy and Corporate Development, until 2014. Mr. Piacquad served as Vice President, Business Development in 2014. Prior to joining the Company, from 2009 to 2010 Mr. Piacquad was Principal of David A. Piacquad Consulting LLC. From 2006 to 2009, Mr. Piacquad served as Senior Vice President, Business Development and Licensing at Schering-Plough Corporation (Schering-Plough). 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.

Dr. David M. Reese, age 56, became Executive Vice President, Research and Development in 2018. Dr. Reese joined the Company in 2005 and has held leadership roles in development, medical sciences and discovery research. Dr. Reese was Senior Vice President, Translational Sciences and Oncology, from 2017 to 2018 and Senior Vice President, Translational Sciences, from 2015 to 2017. Prior to joining Amgen, Dr. Reese was director of Clinical Research for

the Breast Cancer International Research Group from 2001 to 2003 and a co-founder, president and chief medical officer of Translational Oncology Research International, a not-for-profit academic clinical research organization from 2003 to 2005. Dr. Reese previously served on the faculty at University of California, Los Angeles and the University of California, San Francisco.

Mr. Esteban Santos, age 51, became Executive Vice President, Operations, in 2016. Mr. Santos joined the Company in 2007 as Executive Director, Manufacturing Technologies. From 2008 to 2013, Mr. Santos held a number of Vice President roles at the Company in engineering, manufacturing, site operations and drug product. From 2013 to 2016, Mr. Santos was Senior Vice President, Manufacturing. Prior to joining the Company, Mr. Santos served as Site General Manager of 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 4, Revenues and Note 13, Property, plant and equipment, 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 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.)

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. These 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 initiatives to contain costs and manage drug utilization. These payers are increasingly focused on the effectiveness, benefits and costs of similar treatments, which could result for our products in lower reimbursement rates or narrower populations for whom payers will reimburse. Continued intense public scrutiny of the price of drugs and other healthcare costs, together with payer dynamics, may limit our ability to set or adjust the price of our products based on their value, which could have a material adverse effect on our business. In the United States, the public discussions of drug pricing issues are likely to continue.

—Changing federal coverage and reimbursement policies and practices have impacted and may continue to impact access to and sales of our products

A substantial portion of our U.S. business relies on reimbursement from U.S. federal government healthcare programs and commercial insurance plans regulated by the U.S. federal and state governments. See Item 1. Business—Reimbursement. Our business has and will continue to be impacted by legislative actions changing U.S. federal reimbursement policy. For example, in February 2018, the U.S. Congress passed legislation requiring biopharmaceutical manufacturers to provide greater discounts beginning in 2019 on products dispensed to patients in the coverage gap between the initial coverage limit of Medicare Part D and the program's catastrophic-coverage threshold, which will reduce our net product sales relating to such patients. Additional legislative proposals have been introduced by members of Congress to overhaul provisions of the Patient Protection and ACA, to allow commercial-level re-importation of prescription medications from Canada or other countries and to enable Medicare to negotiate drug prices with biopharmaceutical manufacturers. Congressional focus on drug pricing has increased since the Democrats took control of the U.S. House of Representatives in November 2018. For example, in January 2019, the chair of the House Oversight and Reform Committee sent letters to twelve different biopharmaceutical manufacturers, including Amgen, seeking documents and detailed information about such companies' drug pricing. Both that committee and the Senate Finance Committee held committee hearings in January 2019 on the topic of drug pricing and have indicated that further committee hearings on the topic are likely.

Also our business has been and is expected to continue to be impacted by changes in U.S. federal reimbursement policy resulting from executive actions, federal regulations, or federal demonstration projects. For example, in May 2018, the U.S. presidential administration released a drug pricing “blueprint” and requested public comment on an array of policy ideas intended to increase competition, improve the negotiating power of the federal government, reduce drug prices and lower patient out-of-pocket costs. This blueprint includes a number of policy ideas with the potential to significantly impact, whether individually or collectively, our industry. Such proposals include moving coverage and reimbursement for Medicare Part B drugs into Medicare

Part D, instituting a competitive acquisition program for Part B drugs in which competing third-party vendors take on the financial risk of acquiring drugs and billing Medicare, removing the safe harbor protection under the federal anti-kickback statute for drug rebates paid to payers, and requiring the inclusion of drug price information in direct-to-consumer drug advertising.

Since that time, the president and/or federal agencies, such as CMS, have announced a number of demonstration projects, recommendations and proposals to implement various elements described in the drug pricing blueprint. CMS, the federal agency responsible for administering Medicare and overseeing state Medicaid programs and Health Insurance Marketplaces, has substantial power to implement policy changes or demonstration projects that can quickly and significantly affect how drugs, including our products, are covered and reimbursed. For example, in October 2018, President Trump announced that CMS was evaluating a pilot program proposed to initially cover fifty percent of spending on Part B single-source drugs referred to as the "International Price Index" that would, among other things, set the Medicare payment amount for such single-source drugs to more closely align with international drug prices. CMS has taken additional actions to implement other elements described in the administration's drug-pricing blueprint, including issuing guidance to allow certain Medicare plans offered by private insurance companies to require that patients receiving Medicare Part B drugs first try a drug preferred by the plan before such plan will cover another therapy and proposing lower reimbursement rates for new Part B drugs. And on January 31, 2019, the U.S. Department of Health and Human Services released a proposal to revise the federal anti-kickback statute safe harbor regulations to exclude from safe harbor protection certain rebates and other forms of remuneration paid by a manufacturer of prescription drugs to Medicaid managed care organizations or plan sponsors under Medicare Part D, either directly or through PBMs.

Further, CMS has undertaken demonstration projects to test care models, such as the CMS Oncology Care Model, which provides participating physician practices with performance-based financial incentives that aim to manage or reduce Medicare costs without negatively impacting the efficacy of care. We believe the Oncology Care Model has reduced utilization of certain of our oncology products by participating physician practices and may continue to do so in the future. In addition, CMS has solicited suggestions regarding other potential care models.

In this dynamic environment, we are unable to predict which or how many of these various federal policy, legislative or regulatory changes may ultimately be enacted, to the extent that these or other federal government initiatives decrease or modify the coverage or reimbursement available for our products, limit our ability to offer co-pay payment assistance to commercial patients, require that we pay increased rebates or shift other costs to us, limit or impact our decisions regarding the pricing of biopharmaceutical products or otherwise reduce the use of our U.S. products, such actions could have a material adverse effect on our business and results of operations.

We also face risks relating to the reporting of pricing data that affects the reimbursement of and discounts provided for our products. Government price reporting regulations are complex and may require a manufacturer to update certain previously submitted 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.

—Changing state reimbursement and pricing actions may impact access to and have impacted and may continue to impact sales of our products

At the state level, government actions or ballot initiatives can also affect how our products are covered and reimbursed and/or create additional pressure on our pricing decisions. A number of states have adopted, and many other states have discussed and debated and are considering, new pricing actions, including proposals designed to require biopharmaceutical manufacturers to publicly report proprietary pricing information, limit price increases or to place a maximum price ceiling or cap on biopharmaceutical products. Existing and proposed state pricing laws have added complexity to the pricing of drugs and may already be impacting industry pricing decisions. For example, in October 2017, California enacted a drug-pricing transparency bill that requires biopharmaceutical manufacturers to notify health insurers and government health plans at least 60 days before scheduled prescription drug price increases that exceed certain thresholds. Other states are seeking to change the way their states pay for drugs for patients covered by state programs. For example, in August 2018 the Ohio Department of Medicaid ordered that all the state's Medicaid

managed care plans terminate and renegotiate contracts with PBMs to eliminate the drug purchasing model in which PBMs bill the state more than they reimburse pharmacists for filling Medicaid patient prescriptions. In January 2019, California's governor issued an executive order expanding state Medicaid coverage and directing state agencies and programs to consolidate drug purchases and to negotiate drug prices with manufacturers. Other states could adopt similar approaches or could pursue different policy changes in a continuing effort to reduce their costs. Ultimately, as with U.S. federal government actions, existing or future state government actions or ballot initiatives may also have a material adverse effect on our product sales, business and results of operations.

—U.S. commercial payer actions have impacted and may continue to impact access to and sales of our products
Payers, including healthcare insurers, PBMs and group purchasing organizations, increasingly seek ways to reduce their and their respective members' costs. With increasing frequency, payers are adopting benefit plan changes that shift a greater portion of drug costs to patients. Such measures include more limited benefit plan designs, high deductible plans, higher patient co-pay or coinsurance obligations and limitations on patients' use of manufacturer commercial co-pay payment assistance programs (including through co-pay accumulator adjustment or maximization programs). Payers have sought and will likely continue to seek price discounts or rebates in connection with the placement of our products on their formularies or those they manage, particularly in treatment areas where the payer has taken the position that multiple branded products are therapeutically comparable. Payers also control costs by imposing restrictions on access to or usage of our products, such as requiring that patients first try a drug preferred by the payer or receive the payer's prior authorization before covering the product, or that patients use a mail-order pharmacy or mail-order pharmacy or a limited network of fully-owned specialty pharmacies; payers may also choose to exclude certain indications for which our products are approved or even choose to exclude coverage entirely. For example, the burdensome administrative processes required for physicians to demonstrate or document that the patients for whom Repatha® has been prescribed meet payer utilization management criteria has limited and may continue to limit patient access to Repatha® treatment. In an effort to reduce barriers to access, we reduced the net price of Repatha® by providing greater discounts and rebates to payers, including PBMs that administer Medicare Part D prescription drug plans. However, affordability of patient out-of-pocket co-pay cost has and may continue to limit patient use. For example, a very high percentage of Medicare patients have abandoned their Repatha® prescriptions rather than pay their co-pay payment. In late 2018 and early 2019, we introduced a set of new NDCs to make Repatha® available at a lower list price to attempt to address affordability for patients, particularly those on Medicare. Despite the recent net and list price reductions, payers may continue to restrict patient access, change formulary coverage for Repatha®, seek further discounts or rebates or take other actions that could reduce our sales of Repatha®. Further, our introduction of the new NDCs may not be rapidly adopted by payers, which could continue to limit patient use and could also reduce our sales of Repatha®.
Significant 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 discounts and rebates required of manufacturers and limiting patient access and usage. For example, in the United States, the top three PBMs now oversee greater than two-thirds of prescription claims as well as government and commercial covered lives. The consolidation among insurers, PBMs and other payers, including through integrated delivery systems and/or with specialty or mail-order pharmacies and pharmacy retailers, has increased the negotiating leverage such entities have over us and other drug manufacturers and has resulted in greater price discounts, rebates and fees for other services being realized by those payers. For example, during the fourth quarter of 2018, two of the nation's largest PBMs, Express Scripts and CVS Health, completed their combinations with major insurance companies Cigna and Aetna, respectively. Additional consolidation would further increase the leverage of such entities. Ultimately, additional discounts, rebates, coverage or plan changes, restrictions or exclusions imposed by these commercial payers could have a material adverse effect on our product sales, business and results of operations.
—Government and commercial payer actions outside the United States have impacted and will continue to impact access to and sales of our products
Outside the United States, we expect countries will continue to take actions to reduce their drug expenditures. See Item 1. Business—Reimbursement. International reference pricing (IRP) has been widely used by many countries outside the United States 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. In addition, countries may refuse to reimburse or may restrict the reimbursed population for a product when their national health technology assessments do not consider a medicine to demonstrate sufficient clinical benefit beyond existing therapies or that it does not meet certain cost effectiveness thresholds. For example, despite the EMA's May 2018 approval of Repatha® for the treatment of patients with established atherosclerotic disease, reimbursement for Repatha® in France and Germany has remained limited to narrower patient populations (such as those with homozygous familial hypercholesterolemia)

following national health technology assessments in mid-2018. While the pricing and reimbursement process in those countries remains ongoing, these assessments currently limit our efforts in France and Germany to expand Repatha® access to the broader patient population covered by the approved label. Failure to obtain coverage and reimbursement for our products, a deterioration in their existing coverage and reimbursement, or a decline 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.

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

We currently face competition from biosimilars in both Europe and the United States, and we expect to face increasing biosimilar and/or generics competition this year and beyond. Expiration or successful challenge of applicable patent rights or

expiration of an applicable exclusivity period would accelerate such competition, and we expect to 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 and generics, the rate of increased competition for our products could accelerate.

In the EU, biosimilars are evaluated for marketing authorization 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 and others 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 impose automatic price reductions upon market entry of one or more biosimilar competitors. While the degree of competitive impact of biosimilar competition differs between EU countries and between products, in the EU the overall use of biosimilars and the rate at which product sales of innovative products are being impacted by biosimilar competition is increasing.

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 biosimilar versions of ENBREL, Neulasta® and EPOGEN®, and a growing number of companies have announced that they are also developing biosimilar versions of our products. Two biosimilar versions of Neulasta® are now marketed in the United States and others may receive approval in 2019. Impact to our Neulasta® sales could accelerate as additional competitors are launched. See Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition. The approved biosimilar version of EPOGEN® has also launched in the United States, and we are currently involved in patent litigation with the manufacturer of the approved version of ENBREL. Manufacturers of biosimilars may attempt to compete with our products by offering lower list prices, greater discounts or rebates, or contracts that offer longer-term pricing or a broader portfolio of other 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 and generics patent litigation, see Part IV—Note 20, Contingencies and commitments, to the Consolidated Financial Statements. See 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 or already marketing biosimilars may seek to register their products as interchangeable biosimilars, which could make it easier for pharmacists to substitute those biosimilars for our reference products or could encourage prescribers or payers who are inclined to select the interchangeable biosimilar over our innovative products or our biosimilars. 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. For example, the FDA is considering whether subsequent changes to a licensed biologic would be protected by the remainder of the reference product's original 12-year exclusivity period (a concept known in the generic drug context as "umbrella exclusivity"). If the FDA were to decide that umbrella exclusivity does not apply to biological reference products or were to make other changes to the exclusivity period, this could expose us to biosimilar competition at an earlier time. There also have been, and may continue to be, public, legislative, and FDA efforts to promote price competition through policies enabling easier generic and biosimilar entry, including efforts to lower standards for demonstrating biosimilarity or interchangeability and provide greater clarity for how to do so, and through changes to the reimbursement policies for biologics.

Upon the expiration or loss of patent protection for one of our small-molecule products, we can lose the majority of revenues for that product in a very short period of time. See Item 1. Business—Marketing, Distribution and Selected Marketed Products—Competition. Our U.S. composition of matter patent for Sensipar®, a small-molecule product, expired in March 2018. We are engaged in litigation with a number of companies seeking to market generic versions

of Sensipar® surrounding our U.S. formulation patent that expires in September 2026. Several of these generic versions of Sensipar® have been approved by the FDA, and the manufacturer of one of the approved generic versions began selling its product in late 2018 before reaching a settlement agreement with us in early January 2019. We were subsequently sued by a manufacturer of another approved generic version of Sensipar® who is contending that provisions of its own settlement agreement with Amgen have been triggered by the first manufacturer's at-risk launch, giving this second manufacturer a right to market its own generic version under its settlement agreement. See Part IV—Note 20, Contingencies and commitments, to the Consolidated Financial Statements. While no generic versions of Sensipar® are currently available for sale, one or more other companies may elect to launch their approved generic versions at-risk prior to the conclusion of our ongoing litigation, or may seek and obtain a judicial declaration that they are permitted to launch their generic versions. If this happens, our product sales for Sensipar® could be materially and adversely affected.

While we are unable to predict the precise impact of biosimilars and generics on our products, we are currently facing and expect to face greater competition in the United States, Europe and elsewhere this year and beyond as a result of biosimilar and

generic competition and downward pressure on our product prices and sales. This competition has had and could increasingly 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 offer higher rebates or discounts, 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.

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. Driven by cost pressures, efforts to limit or weaken patent protection for our industry are increasing. 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 expect to 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. 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 recover fully 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 are facing 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. For example, we are currently engaged in litigation in the United States regarding MVASI™, KANJINTI™ and AMJEVITA™, and in Europe we are engaged in litigation regarding AMGEVITA™. While we may attempt to challenge the patents held by the companies manufacturing, marketing or selling the applicable reference products, our efforts may be unsuccessful. Alternatively, such patents may contribute to a decision by us to not pursue all of the same labeled indications as are held by these companies. For information related to our patent litigation, see Part IV—Note 20, Contingencies and commitments, to the Consolidated Financial Statements.

Certain of the existing patents on our products have 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. 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. In addition, a growing number of organizations are providing assessments of the value and pricing of biopharmaceutical products, and even organizations whose guidelines have historically been focused on clinical matters have begun to incorporate analyses of the cost effectiveness of various treatments into their treatment guidelines and recommendations. Value assessments may come from private organizations that publish their findings and offer recommendations relating to the products' reimbursement by government and private payers. Some companies and payers have announced pricing and payment decisions based in part on the assessments of private organizations. For example, CVS Caremark indicated in August 2018 that it will begin utilizing third-party cost effectiveness analyses to make formulary and coverage determinations for newly-approved drugs. In addition, government health technology assessment organizations in many countries 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 health technology assessment 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.

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 approvals 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 laws or regulations governing manufacturer communications concerning drug products and drug product candidates, and whether such changes could have a material adverse effect on our product sales, business and results of operations. In the United States, a partial federal government shutdown halted the work of many federal agencies and their employees from late December 2018

through late January 2019. While federal employees have since returned to work, a subsequent extended shutdown could result in reductions or delays of FDA's activities, including with respect to our ongoing clinical programs, our manufacturing of our products and product candidates, and our product approvals.

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, measured by progression-free survival (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 initially approved Repatha® in 2015 only for a subset of those patients, citing among other things the absence of positive outcomes data showing that Repatha® prevents cardiovascular events. In December 2017, the FDA granted broader approval of Repatha® to reduce the risk of certain cardiovascular events, and also to be used, alone or in combination with other lipid-lowering therapies, for the treatment of adults with primary hyperlipidemia to reduce LDL-C, only after our large phase 3 outcomes study evaluating the ability of Repatha® to prevent cardiovascular events met its primary composite endpoint and key secondary composite endpoint. 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 other existing treatment options 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 an accelerated or conditional basis with full approval conditioned upon fulfilling the requirements of regulators. For example, in March 2018, we announced that the FDA approved BLINCYTO® under accelerated approval for the treatment of adults and children with B-cell precursor ALL in first or second complete remission with minimal residual disease greater than or equal to 0.1 percent. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. 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 the United States, 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. 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. The drug delivery devices approved for use in combination with our products are also subject to regulatory oversight and review for safety and malfunctions. 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, other pharmacovigilance or other safety or quality assessment 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 or 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;

- required changes to the processes used in the manufacture of our products, which could increase our manufacturing costs and affect the availability of contract manufacturers we may utilize to assist in such manufacturing;
- 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, the FDA is currently evaluating our BLA for EVENITY™ for the treatment of postmenopausal women with osteoporosis at high risk of fracture. In January 2018, the FDA's BRUDAC recommended that the FDA approve EVENITY™, but also suggested that the FDA require appropriate post-marketing review to evaluate a potential cardiovascular risk seen in one of the EVENITY™ pivotal clinical trials. See Item 1. Business—Significant Developments. While the FDA is not bound to follow the recommendations of its advisory committees, it often does; if the FDA approves EVENITY™ it may require that we complete a post-marketing study, which could be time consuming and costly.

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, discussions continue as to the evidence needed to demonstrate biosimilarity or interchangeability for specific products. See We currently face competition from biosimilars and expect to face increasing competition from biosimilars and generics in the future. Delays or uncertainties in the development or implementation 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 or on our marketed biosimilars. In addition, if we are unable to bring our biosimilar products to market on a timely basis, and secure "first-to-market" or other advantageous 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 animals or humans;
- 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;
- 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, contracted organizations or independent investigators may have failed to effectively conduct clinical development or clinical manufacturing activities;
- the pathway to regulatory approval or reimbursement for product candidates was uncertain or not well-defined; and
- 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.

We have spent considerable time, energy and resources developing our expertise in human genetics with the belief that genetics could meaningfully aid our search for new medicines and help guide our research and development decisions and investments. We have focused our R&D strategy on drug targets validated by genetic or other

compelling human evidence. However,

product candidates based on genetically validated targets remain subject to the uncertainties of the drug development process and may not reach the market for a number of reasons, including the factors listed above.

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 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 more 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. In some circumstances, we enter into co-development arrangements with other pharmaceutical and medical devices companies that provide for the other company to conduct certain clinical trials for the product we are co-developing or to develop a diagnostic test used in screening patients for our clinical trials. See Some of our pharmaceutical pipeline and of our commercial product sales relies on collaborations with third parties, which may adversely affect the development and sale of our products. We also may acquire companies that have past or ongoing clinical trials or rights to products or product candidates for which clinical trials have been or are being conducted. 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 co-development partners, or the independent investigators or vendors selected by us, our co-development partners or by a company we have acquired or from which we have acquired rights to a product or product candidate, 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 delay or otherwise negatively impact our ability to obtain or maintain marketing approval of the product or indication. In addition, delays or failures to develop diagnostic tests for our clinical trials can affect the timely enrollment of such trials and lead to delays or inability to obtain marketing approval. 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 utilize 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 product 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, such quality or supply problems 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 and conducted 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 product sales, 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. For example, Neulasta® is available as part of the Neulasta® Onpro® kit, and our AutoTouch® reusable auto-injector is used with Enbrel Mini® single-dose prefilled cartridges. In addition, some of our products or product candidates may also require the use of a companion diagnostic device such as a device that determines whether the patient is eligible to use our drug or that helps ensure its safe and effective use. 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 development of such devices is delayed, such devices do not also gain or maintain regulatory approval or clearance, or if such devices do not remain commercially available. 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, modify, 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 or maintain, regulatory approval; and/or associated delays in a product candidate reaching the market or in the addition of new indications for existing products. We are also required to collect and assess user complaints, adverse events, and malfunctions regarding our devices, and 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. Additionally, regulatory agencies conduct routine monitoring and conduct inspections to identify and evaluate potential issues with our devices. For example, in 2017 the FDA reported on its adverse event reporting system that it is evaluating our Neulasta® Onpro® kit. 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.

Some of our pharmaceutical pipeline and of our commercial product sales relies on collaborations with third parties, which may adversely affect the development and sale of our products.

We depend on alliances with other companies, including pharmaceutical and biotechnology companies, vendors and service providers, for the development of a portion of the products in our pharmaceutical pipeline and for the commercialization and sales of certain of our commercial products. For example, we have collaborations with third parties under which we share development rights, obligations and costs and/or commercial rights and obligations. See Item 1. Business—Business Relationships.

Failures by these parties to meet their contractual, regulatory, or other obligations to us, or any disruption in the relationships between us and these third parties, could have a material adverse effect on our pharmaceutical pipeline and business. In addition, our collaborative relationships for research and development and/or commercialization and sales often extend for many years and

may give rise to disputes regarding the relative rights, obligations and revenues of us and our collaboration partners, including the ownership or prosecution of intellectual property and associated rights and obligations. This could result in the loss of intellectual property rights or protection, delay the development and sale of potential pharmaceutical products, impact the effective sale and delivery of our commercialized products and lead to lengthy and expensive litigation, administrative proceedings or arbitration.

The adoption and interpretation 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, including the Internal Revenue Service (IRS), are becoming more aggressive in their audits and are particularly focused on the allocations of income and expense among tax jurisdictions. As previously disclosed, we received a Revenue Agent Report (RAR) from the IRS for the years 2010, 2011 and 2012. The RAR proposes to make significant adjustments that relate primarily to the allocation of profits between certain of our entities in the United States and the U.S. territory of Puerto Rico. In November 2017, we received a modified RAR that revised the IRS's calculation but continued to propose substantial adjustments. We disagree with the proposed adjustments and are pursuing resolution with the IRS administrative appeals office, which currently has jurisdiction over the matter. If we deem necessary, we will vigorously contest the proposed adjustments through the judicial process. Although final resolution of this complex matter is not likely within the next 12 months, such resolution could have a material negative impact on our consolidated financial statements. 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.

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. The 2017 Tax Act is complex and further regulations and interpretations are still being issued. We could face audit challenges on how we apply the new law that could have a negative impact on our provision for income taxes. A change to the U.S. tax system, such as a repeal or modification of the 2017 Tax Act, a change to the tax system in a jurisdiction where we have significant operations, such as the U.S. territory of Puerto Rico, or changes in tax law in the United States or other jurisdictions where we do business, could have a material and adverse effect on our business and on the results of our operations.

We perform a substantial majority of our commercial manufacturing activities at our facility in the U.S. territory of Puerto Rico and a substantial majority of our clinical manufacturing activities at our facility in Thousand Oaks, California; significant disruptions or production failures at these facilities could significantly impair our ability to supply our products or continue our clinical trials.

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 our manufacturing facilities, in particular those in the U.S. territory of Puerto Rico and Thousand Oaks, California. See Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales.

We currently perform a substantial majority of our clinical manufacturing activities at our facility in Thousand Oaks, California. A substantial disruption in our ability to operate our Thousand Oaks, California manufacturing facility could materially and adversely affect our ability to supply our product candidates for use in our clinical trials, leading to delays in development of our product candidates.

In addition, we currently perform a substantial majority of our commercial manufacturing activities at our facility in the U.S. territory of Puerto Rico. In late September 2017, Hurricane Maria made landfall on the island of Puerto Rico. The hurricane destroyed residential and commercial buildings, agriculture, communications networks and most of Puerto Rico's electric grid. While the critical manufacturing areas of our commercial manufacturing facility were not

significantly impacted by the storm, the restoration of electrical service on the island was a slow process, and our facility operated with electrical power from back-up diesel powered generators for some time. In January 2018, we reconnected to the Puerto Rico electric grid but have continued to use diesel generators as needed when sufficient electric power has not been reliably available. Further instability of the electric grid could require us to increase the use of our generators or even return to using them exclusively. In addition, future storms or other disasters or events could cause a more significant impact to our manufacturing operations. A substantial disruption in our ability to operate our Puerto Rico manufacturing facility (whether due to problems with the facility itself, the infrastructure and services available on the island, the unavailability of raw materials or supplies from vendors, the unavailability of key staff or otherwise) or get supplies and manufactured products transported to and from that location could materially and adversely affect

our ability to supply our products and affect our product sales. See Manufacturing difficulties, disruptions or delays could limit supply of our products and limit our product sales.

The impact of Hurricane Maria placed greater stress on the island's already challenged economy. Prior to Hurricane Maria, the government of Puerto Rico was unable to pay its roughly $72 billion in debt. In June 2016, the U.S. Congress passed the Puerto Rico Oversight, Management, and Economic Stability Act (PROMESA), which established a 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 its debt restructuring. In May 2017, after negotiations for debt restructuring with creditors were unsuccessful, the Oversight Board approved and certified the filing in the U.S. District Court for the District of Puerto Rico of a voluntary petition under Title III of PROMESA for the government of Puerto Rico and certain of its governmental entities, including the Puerto Rico Electric Power Authority (PREPA). Title III of PROMESA provides Puerto Rico with a judicial process for restructuring its debt similar to, but not identical to, Chapter 9 of the U.S. Bankruptcy Code. The Governor of Puerto Rico declared a state of emergency and authorized a moratorium on the payment of general obligation bonds and other debts issued by certain instrumentalities, which moratorium has been extended and may continue to be extended while the Oversight Board is in effect. Given the severe conditions in Puerto Rico after Hurricane Maria, resolution of Puerto Rico's debt situation through the PROMESA judicial process has been delayed. In the case of PREPA, the effects of Hurricane Maria and several changes in PREPA's management have delayed reconstruction efforts.

In June 2018, the Oversight Board certified a budget for Puerto Rico's fiscal year 2019 that imposes significant expense reductions across the government. The Title III Court upheld government challenges to the budget, and the Governor and Legislature of Puerto Rico have now filed appeals before the U.S. Court of Appeals for the First Circuit. In addition, certain non-governmental entities have brought suit claiming the appointment process of the Oversight Board members set forth in PROMESA conflicts with the appointments clause of the U.S. Constitution. If the First Circuit were to hold that PROMESA has a constitutional infirmity and that actions taken by the Oversight Board are invalid, the commencement of all Title III proceedings could be invalid. In such event, the current debt restructuring process and the debtholder litigation stay under Title III of PROMESA could be in jeopardy.

In October 2018, the fiscal plan for Puerto Rico was updated, including a projected increase in federal disaster funding and projected material deficits once the stimulus effects of the disaster recovery dissipate. The fiscal plan stresses the importance of structural reforms to address Puerto Rico's challenging economic and demographic trends that may be difficult to implement as well as have a material adverse impact on our consolidated financial statements.

In addition, the 2017 Tax Act will no longer permit deferral of U.S. taxation on Puerto Rico earnings of U.S. companies (or their foreign subsidiaries), although these earnings generally will be taxed in the United States at a reduced 10.5% rate. Given Puerto Rico's challenged economy and hurricane recovery needs, it may be difficult for Puerto Rico to sustain or grow its manufacturing base due to competition from other foreign locations subject to a similar level of U.S. taxation, or U.S. locations due to the reduction in the U.S. corporate tax rate from 35% to 21%. The manufacturing sector contributes more than 45% of Puerto Rico's gross domestic product, and multinational companies with Puerto Rico operations contribute approximately 30% of Puerto Rico's revenue base.

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 ongoing economic challenges, the effects of Hurricane Maria and the potential impact of the 2017 Tax Act could negatively affect 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, or make it more expensive or difficult for us to operate in Puerto Rico, which could materially and adversely affect our ability to supply our products and affect our product sales.

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.

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 similar or other shortages in the future resulting in delayed shipments, supply constraints, clinical trial delays, contract disputes and/or stock-outs of our products. These or other similar 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 sales, business and results of operations.

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 to support our clinical trials) 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;
- breakdown, failure, substandard performance or improper installation or operation of equipment; and/or
- delays in the ability of the FDA or foreign regulatory agencies to provide us necessary reviews, inspections and approvals, including as a result of a subsequent extended U.S. federal government shutdown.

If any of these or other problems affect production in one or more of our facilities or those of our third-party contract manufacturers, or if we do not accurately forecast demand for our products or the amount of our product candidates required in clinical trials, we may be unable to increase production in our unaffected facilities to meet demand. 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 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, and in April 2018 we initiated a precautionary recall of two batches of Vectibix® distributed in Switzerland after potential crimping defects were discovered in the metal seals on the product vials. 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, those of our third-party contract manufacturers and those of certain of our third-party service providers 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 or service provider. If we elect or are required to make changes to our manufacturing processes because of new regulatory requirements, new interpretations of existing requirements or other reasons, this could increase our manufacturing costs and result in delayed shipments, delays in our clinical trials, supply constraints, stock-outs, adverse event trends or contract negotiations or disputes. Such manufacturing challenges may also occur if our existing contract manufacturers are unable or unwilling to implement such changes.

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, delays in our clinical trials, supply constraints, contract disputes, 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 and sea freight, for the distribution of our products to our customers, which may be negatively impacted by natural disasters or security threats.

Concentration of sales at certain of our wholesaler distributors and at one free-standing dialysis clinic business 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. DaVita owns or manages a large number of the outpatient dialysis facilities located in the United States and accounts for approximately 70% of all EPOGEN® sales. Similarly, as discussed above, there has been significant consolidation in the health insurance industry, including that a small number of PBMs now oversee a substantial percentage of total covered lives in the United States. See Our sales depend on coverage and reimbursement from third-party payers, and pricing and reimbursement pressures may affect our profitability. The three largest PBMs in the United States are now part of major health insurance providers. The growing 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 product sales, business and results of operations due to their purchasing volume. Further, if one of our significant wholesale distributors encounters financial or other difficulties and becomes unable or unwilling to pay us all amounts that

such distributor owes us on a timely basis or at all, it could negatively impact our business and results of operations. In addition, if one of our significant wholesale distributors becomes insolvent or otherwise unable to continue its commercial relationship with us in its present form, it could significantly disrupt our business and adversely affect our product sales, our business and results of operations unless suitable alternatives are timely found or lost sales are absorbed by another distributor.

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 seek innovation through significant investment in both internal R&D and external transactions including collaborations, partnering, alliances, licenses, joint ventures, mergers and acquisitions (acquisition activity). We have an ongoing process of evaluating such potential acquisition activity opportunities that we expect will contribute to our future growth and expand our geographic footprint, product offerings and/or our R&D pipeline. Acquisitions or similar arrangements may be complex, time

consuming and expensive and 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. We may pay substantial amounts of cash, incur debt or issue equity securities to pay for acquisition activities, which could adversely affect our liquidity or result in dilution to our stockholders, respectively. 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.

Our sales and operations are subject to the risks of doing business internationally, including 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 and local political, legal, regulatory and financial instability, including sovereign debt issues and/or the imposition of international sanctions in response to certain state actions. 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. 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. 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, trade restrictions or other barriers designed to protect industry in the home country against foreign competition, 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 20, 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 product sales, 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. We cannot ensure that all our employees, agents, contractors, vendors, licensees, partners or collaborators will comply with all applicable laws and regulations. In 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 and agreed to operate under a corporate integrity agreement with the OIG of the U.S. Department of Health and Human Services, which was formally closed out in August 2018. 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.

A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our information technology systems and network-connected control systems and our data, interrupt the operation of our business and affect our reputation.

To achieve our business objectives, we rely to a large extent upon sophisticated information technology systems and network-connected control systems, some of which are managed, hosted, provided or serviced by third parties. Internal or external events that compromise the confidentiality, integrity and availability of our systems and data may significantly interrupt the operation of our business, result in significant costs and/or affect our reputation.

Our information technology systems are highly integrated into our business, including our R&D efforts, our clinical and commercial manufacturing processes and our product sales and distribution processes. The complexity and interconnected nature of our systems makes them potentially vulnerable to breakdown or other service interruptions. Our systems are also subject to frequent cyberattacks. As the cyber-threat landscape evolves, these attacks are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect. Such attacks could include the use of key loggers or other harmful and virulent malware, including ransomware or other denials of service, and can be deployed through malicious websites, the use of social engineering and/or other means. Attacks such as those seen with other multi-national companies, including some of our peers, could leave us unable to utilize key business systems or access important data needed to operate our business, including developing, gaining regulatory approval for, manufacturing, selling and distributing our products. For example, in 2017, a pharmaceutical company experienced a cyberattack involving virulent malware that significantly disrupted its operations, including its research and sales operations and the production of some of its medicines and vaccines. As a result of the cyberattack, its orders and sales for certain products in certain markets were negatively impacted. Our systems also contain and utilize a high volume of sensitive data, including intellectual property, trade secrets, financial information, regulatory information, strategic plans, sales trends and forecasts, litigation materials or personal information belonging to us, our staff, our patients, customers and/or other business partners. In some cases, we utilize third-party service providers to process, store, manage or transmit such data, which may increase our risk. Intentional or inadvertent data privacy or security breaches (including cyberattacks) by employees, service providers, nation states, organized crime organizations, “hacktivists” or others, pose risks that our sensitive data may be exposed to unauthorized persons, our competitors, or the public. Finally, domestic and global government regulators, our key business partners, suppliers with whom we do business, companies that provide us or our partners with important business services and companies we may acquire may face similar risks, and security breaches of their systems could adversely affect our security, leave us without access to important systems, products, raw materials, components, services or information or expose our confidential data. For example, we distribute our products in the United States primarily through three pharmaceutical wholesalers, and a security breach that impairs the distribution operations of our wholesalers could significantly impair our ability to deliver our products to healthcare providers.

Although in the past we have experienced system breakdowns, attacks and information security breaches, we do not believe such breakdowns, attacks and breaches have had a material adverse effect on our business or results of operations. We continue to invest in the monitoring, protection, and resilience of our critical or sensitive data and systems. However, there can be no assurance that our efforts will detect, prevent or fully recover systems or data from all breakdowns, service interruptions, attacks, or breaches of our systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive data, which could result in financial, legal, business or reputational harm to us or impact our stock price. While we maintain cyber-liability insurance, our insurance is not sufficient to cover us against all losses that could potentially result from a service interruption, breach of our systems or loss of our critical or sensitive data.

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, including via social media channels, 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.

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.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

As of December 31, 2018, we owned or leased approximately 190 properties. The locations and primary functions of significant properties are summarized in the following tables:

Excluded from the information above are (i) undeveloped land and leased properties that have been abandoned and (ii) 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 uses 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 of 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 20, 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 7, 2019, there were approximately 5,760 holders of record of our common stock.

Performance graph

The following graph shows the value of an investment of $100 on December 31, 2013, 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, 2013

| | 12/31/2013 | 12/31/2014 | 12/31/2015 | 12/31/2016 | 12/31/2017 | 12/31/2018 |
|---|---|---|---|---|---|---|
| Amgen (AMGN) | $100.00 | $142.32 | $147.97 | $136.80 | $167.33 | $192.57 |
| Amex Biotech (BTK) | $100.00 | $147.91 | $164.76 | $133.21 | $183.58 | $184.07 |
| Amex Pharmaceutical (DRG) | $100.00 | $116.58 | $121.45 | $111.32 | $129.83 | $139.50 |
| S&P 500 (SPX) | $100.00 | $113.68 | $115.24 | $129.02 | $157.26 | $150.39 |

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, 2018, 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 | 4,151,700 | $ 198.37 | 4,151,700 | $2,855,891,358 |
| November 1 - November 30 | 2,461,000 | $ 195.19 | 2,461,000 | $2,375,524,842 |
| December 1 - December 31 | 4,508,700 | $ 190.99 | 4,508,700 | $5,114,429,813 |
| | 11,121,400 | $ 194.67 | 11,121,400 | |
| January 1 - December 31 | 94,473,223 | $ 189.00 | 94,473,223 | |

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

(2) In December 2018, our Board of Directors increased the amount authorized under our stock repurchase program by an additional $3.6 billion.

Dividends

For the years ended December 31, 2018 and 2017, 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 17, 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 Statements of Income Data: | 2018 | 2017 | 2016 | 2015 | 2014 |
| | (In millions, except per-share data) | | | | |
| Revenues: | | | | | |
| Product sales | $22,533 | $21,795 | $21,892 | $20,944 | $19,327 |
| Other revenues | 1,214 | 1,054 | 1,099 | 718 | 736 |
| Total revenues | $23,747 | $22,849 | $22,991 | $21,662 | $20,063 |
| Operating expenses: | | | | | |
| Cost of sales | $4,101 | $4,069 | $4,162 | $4,227 | $4,422 |
| Research and development | $3,737 | $3,562 | $3,840 | $4,070 | $4,297 |
| Selling, general and administrative | $5,332 | $4,870 | $5,062 | $4,846 | $4,699 |
| Net income[1] | $8,394 | $1,979 | $7,722 | $6,939 | $5,158 |
| Diluted earnings per share[1] | $12.62 | $2.69 | $10.24 | $9.06 | $6.70 |
| Dividends paid per share | $5.28 | $4.60 | $4.00 | $3.16 | $2.44 |

| | As of December 31, | | | | |
|---|---|---|---|---|---|
| Consolidated Balance Sheets Data: | 2018 | 2017 | 2016 | 2015 | 2014 |
| | (In millions) | | | | |
| Total assets | $66,416 | $79,954 | $77,626 | $71,449 | $68,882 |
| Total debt[2] | $33,929 | $35,342 | $34,596 | $31,429 | $30,588 |
| Total stockholders' equity[3] | $12,500 | $25,241 | $29,875 | $28,083 | $25,778 |

In addition to the following notes, see Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations, Part IV—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 affect the comparability of future results. Also see Part IV—Note 17, 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 2018, 2017 and 2016. In addition, our Board of Directors declared dividends per share of $0.79 and $0.61 that were paid in each of the four quarters of 2015 and 2014, respectively.

(1) In 2017, we recorded a net charge of $6.1 billion as a result of the 2017 Tax Act. See Part IV—Note 7, Income taxes, to the Consolidated Financial Statements.

(2) See Part IV—Note 16, Financing arrangements, to the Consolidated Financial Statements, for discussion of our financing arrangements. In 2015, we issued $3.5 billion of debt and repaid $2.4 billion of debt. In 2014, we issued $4.5 billion of debt and repaid $5.6 billion of debt.

(3) Throughout the five years ended December 31, 2018, we had a stock repurchase program authorized by the Board of Directors, through which we repurchased $17.9 billion, $3.1 billion, $3.0 billion, $1.9 billion and $0.2 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 Part I, 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 forecasted 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 a highly focused biotechnology company committed to unlocking the potential of biology for patients suffering from serious illnesses. 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 principal products—those with the most significant annual commercial sales—are ENBREL, Neulasta®, Prolia®, Aranesp®, XGEVA®, Sensipar®/Mimpara® and EPOGEN®. We also market a number of other products, including KYPROLIS®, Nplate®, Vectibix®, Repatha®, NEUPOGEN®, Parsabiv®, BLINCYTO®, Aimovig®, IMLYGIC®, Corlanor®, KANJINTI™ and AMGEVITA™. For additional information about our products, see Part I, Item 1. Business—Marketing, Distribution and Selected Marketed Products.

Our strategy includes a set of integrated activities intended to maintain and strengthen our competitive position in the industry. In 2018, we advanced our strategy while delivering strong financial performance and returning capital to shareholders, advancing our innovative pipeline and branded biosimilar programs, increasing our global geographic reach and expanding our next-generation manufacturing capabilities.

In 2018, total product sales increased 3% driven primarily by Prolia®, XGEVA®, Repatha® and KYPROLIS®, along with our recently launched products Aimovig® and Parsabiv®. Product sales grew 2% in the United States and 9% in the rest of the world. Total operating expenses increased 5% as we supported our recently launched products and R&D pipeline, including early oncology assets. Cash inflows from operating activities were $11.3 billion, enabling us to invest in our business while returning capital to shareholders through the payment of cash dividends and stock repurchases. We increased our quarterly cash dividend by 15% to $1.32 per share of common stock. In December 2018, we declared a cash dividend of $1.45 per share of common stock for the first quarter of 2019, an increase of 10% for this period, to be paid in March 2019. We also repurchased 94.5 million shares of our common stock throughout 2018 at an aggregate cost of $17.9 billion.

In addition to launching Aimovig® in the United States and Parsabiv® in the United States and the EU, we received approvals for new indications for Repatha® and Prolia®, along with KYPROLIS®, BLINCYTO®, XGEVA® and Nplate® within our oncology/hematology portfolio. We continued to strengthen our international footprint with the approvals of Repatha® in China, and in early 2019, EVENITY™ in Japan. In addition to these commercial products, we continue to advance our pipeline of innovative first-in-class molecules, including our phase 3 molecule, tezepelumab. The FDA granted Breakthrough Therapy Designation for tezepelumab in patients with severe asthma without an eosinophilic phenotype. We have also continued to invest in external innovation to augment our internal innovation with a focus when possible, on genetic related investments and genetically validated targets.

We also continued to advance our biosimilar program with the approval of MVASI™ for the treatment of five types of cancer in the United States and the EU, and the launches of KANJINTI™ and AMGEVITA™ in Europe. Lastly, we made regulatory submissions for ABP 710 in the United States and the EU.

We broke ground on our new next-generation biomanufacturing plant in Rhode Island in 2018. This new plant will be the first of its kind in the United States and will use our proven next-generation biomanufacturing capabilities to manufacture our products while maintaining a reliable, high-quality, compliant supply of medicines. Next-generation biomanufacturing plants require a smaller manufacturing footprint and offer greater environmental benefits, including reduced consumption of water and energy and lower levels of carbon emissions. Our first next-generation biomanufacturing facility located in Singapore is already in use for certain commercial-scale production for multiple countries.

While 2018 execution was strong, we face competition on our more mature products. We have established productivity initiatives to enable investment in new products and the defense of existing products to optimize long- and short-term growth.

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 face increasing pressure from competition, including biosimilars and generics. 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.

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, 2018 | Change | | Year ended December 31, 2017 |
|---|---|---|---|---|
| Product sales: | | | | |
| U.S. | $ 17,429 | 2 | % | $ 17,131 |
| Rest of world (ROW) | 5,104 | 9 | % | 4,664 |
| Total product sales | 22,533 | 3 | % | 21,795 |
| Other revenues | 1,214 | 15 | % | 1,054 |
| Total revenues | $ 23,747 | 4 | % | $ 22,849 |
| Operating expenses | $ 13,484 | 5 | % | $ 12,876 |
| Operating income | $ 10,263 | 3 | % | $ 9,973 |
| Net income | $ 8,394 | * | | $ 1,979 |
| Diluted EPS | $ 12.62 | * | | $ 2.69 |
| Diluted shares | 665 | (10 | )% | 735 |

* Change in excess of 100%

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. In addition, any reference to increases or decreases in inventory refers to changes in inventory held at wholesaler customers and end-users (such as pharmacies).

Total product sales increased for 2018, driven primarily by higher unit demand, offset partially by a decline in net selling price. For 2019, we expect net selling price to continue to decline.

Other revenues increased for 2018, driven primarily by higher milestone payments and royalties.

Operating expenses increased for 2018, driven primarily by investments in product launches and increased spend in R&D, including support of our early pipeline. All expense categories continued to benefit from our transformation and process improvement efforts, which enabled investment in newer and recently launched 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 2018, 2017 or 2016.

Results of Operations

Product sales

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

| | Year ended December 31, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| ENBREL | $ 5,014 | (8)% | $ 5,433 | (9)% | $ 5,965 |
| Neulasta® | 4,475 | (1)% | 4,534 | (2)% | 4,648 |
| Prolia® | 2,291 | 16 % | 1,968 | 20 % | 1,635 |
| Aranesp® | 1,877 | (9)% | 2,053 | (2)% | 2,093 |
| XGEVA® | 1,786 | 13 % | 1,575 | 3 % | 1,529 |
| Sensipar®/Mimpara® | 1,774 | 3 % | 1,718 | 9 % | 1,582 |
| EPOGEN® | 1,010 | (8)% | 1,096 | (15)% | 1,282 |
| Other products | 4,306 | 26 % | 3,418 | 8 % | 3,158 |
| Total product sales | $ 22,533 | 3 % | $ 21,795 | — % | $ 21,892 |
| Total U.S. | $ 17,429 | 2 % | $ 17,131 | (1)% | $ 17,325 |
| Total ROW | 5,104 | 9 % | 4,664 | 2 % | 4,567 |
| Total product sales | $ 22,533 | 3 % | $ 21,795 | — % | $ 21,892 |

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, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| ENBREL — U.S. | $ 4,807 | (8)% | $ 5,206 | (9)% | $ 5,719 |
| ENBREL — Canada | 207 | (9)% | 227 | (8)% | 246 |
| Total ENBREL | $ 5,014 | (8)% | $ 5,433 | (9)% | $ 5,965 |

The decrease in ENBREL sales for 2018 was driven primarily by lower unit demand and net selling price.

The decrease in ENBREL sales for 2017 was driven primarily by lower unit demand and net selling price, offset partially by an increase in inventory.

For 2019, we expect the trend of lower unit demand to continue.

Multiple companies are developing proposed biosimilar versions of ENBREL, and we are involved in patent litigation with the company seeking to market the biosimilar version of ENBREL approved by the FDA in 2016. See Part IV—Note 20, Contingencies and commitments, to the Consolidated Financial Statements.

Neulasta®

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

| | Year ended December 31, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| Neulasta® — U.S. | $ 3,866 | (2)% | $ 3,931 | — % | $ 3,925 |
| Neulasta® — ROW | 609 | 1 % | 603 | (17)% | 723 |
| Total Neulasta® | $ 4,475 | (1)% | $ 4,534 | (2)% | $ 4,648 |

The decrease in global Neulasta® sales for 2018 was driven primarily by favorable changes in accounting estimates of product returns in 2017, offset partially by favorable changes in inventory. Neulasta® sales for 2018 included a $55 million order in the fourth quarter from the U.S. government.

The decrease in global Neulasta® sales for 2017 was driven primarily by lower unit demand, offset partially by an increase in net selling price in the United States.

Neulasta® sales have been and will continue to be affected by the development of new protocols, tests and/or treatments for cancer and/or new treatment alternatives, including those that have reduced and may continue to reduce the use of myelosuppressive regimens in some patients.

Our final material U.S. patent for Neulasta® expired in October 2015. Therefore, we face competition in the United States, which over time may have a material adverse impact on future sales of Neulasta®. A biosimilar version of Neulasta® was approved in the second quarter of 2018 and launched in July 2018, and another biosimilar version was approved in the fourth quarter of 2018 and launched in January 2019. Other biosimilar versions of Neulasta® may also receive approval in the near future. For a discussion of ongoing patent litigations with these and other companies that are developing proposed biosimilar versions of Neulasta®, see Part IV—Note 20, 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, that are related to our European patent for Neulasta® expired in August 2017. In 2019, we expect European sales to decline with the launch of multiple long-acting biosimilar competitors.

Prolia®

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

| | Year ended December 31, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| Prolia® — U.S. | $ 1,500 | 18 % | $ 1,272 | 21 % | $ 1,049 |
| Prolia® — ROW | 791 | 14 % | 696 | 19 % | 586 |
| Total Prolia® | $ 2,291 | 16 % | $ 1,968 | 20 % | $ 1,635 |

The increases in global Prolia® sales for 2018 and 2017 were driven primarily by higher unit demand.

Aranesp®

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

| | Year ended December 31, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| Aranesp® — U.S. | $ 942 | (15)% | $ 1,114 | 3 % | $ 1,082 |
| Aranesp® — ROW | 935 | — % | 939 | (7)% | 1,011 |
| Total Aranesp® | $ 1,877 | (9)% | $ 2,053 | (2)% | $ 2,093 |

The decrease in global Aranesp® sales for 2018 was driven primarily by the impact of competition on unit demand.

The decrease in global Aranesp® sales for 2017 was driven primarily by unfavorable changes in foreign currency exchange rates, offset partially by higher unit demand, including a shift of some U.S. dialysis centers from

EPOGEN®.

Aranesp® faces competition from a long-acting product. Aranesp® also faces competition from a biosimilar version of EPOGEN®, which was approved in the second quarter of 2018 and launched in the fourth quarter of 2018. Other biosimilar versions of EPOGEN ® may also receive approval. In 2019, we expect sales in the United States to decline at a faster rate than 2018 due to short- and long- acting competition.

XGEVA®

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

| | Year ended December 31, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| XGEVA® — U.S. | $ 1,338 | 16 % | $ 1,157 | 4 % | $ 1,115 |
| XGEVA® — ROW | 448 | 7 % | 418 | 1 % | 414 |
| Total XGEVA® | $ 1,786 | 13 % | $ 1,575 | 3 % | $ 1,529 |

The increases in global XGEVA® sales for 2018 and 2017 were driven primarily by higher unit demand.

Sensipar®/Mimpara®

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

| | Year ended December 31, 2018 | Change | Year ended December 31, 2017 | Change | Year ended December 31, 2016 |
|---|---|---|---|---|---|
| Sensipar® — U.S. | $ 1,436 | 5 % | $ 1,374 | 11 % | $ 1,240 |
| Sensipar®/Mimpara® — ROW | 338 | (2 )% | 344 | 1 % | 342 |
| Total Sensipar®/Mimpara® | $ 1,774 | 3 % | $ 1,718 | 9 % | $ 1,582 |

The increase in global Sensipar®/Mimpara® sales for 2018 was driven primarily by an increase in net selling price in the United States, offset partially by lower unit demand.

The increase in global Sensipar®/Mimpara® sales for 2017 was driven primarily by an increase in net selling price in the United States and, to a lesser extent, higher unit demand.

Our U.S. composition of matter patent related to Sensipar®, a small molecule, expired in March 2018. We are involved in patent litigation with a number of companies seeking to market generic versions of Sensipar®, one of which began selling its generic version in late December 2018 until reaching a settlement agreement with us in early January 2019. In a separate litigation, we have been sued by the manufacturer of another approved generic version of Sensipar