AMGEN INC
Form 10-K
February 28, 2008
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2007

OR

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

Commission file number 000-12477

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(g) of the Act:

Common stock, $0.0001 par value; preferred share purchase rights

(Title of class)

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 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 x No ¨

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

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

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

(Do not check if a smaller reporting company)

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

The approximate aggregate market value of voting and non-voting stock held by non-affiliates of the registrant was $60,164,451,325 as of June 30, 2007(A)

(A) Excludes 920,444 shares of common stock held by directors and officers, and any stockholders whose ownership exceeds five percent of the shares outstanding, at June 30, 2007. 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.

1,087,627,536

(Number of shares of common stock outstanding as of February 18, 2008)

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant s Proxy Statement with respect to the 2008 Annual Meeting of stockholders to be held May 7, 2008 are incorporated by reference into Part III of this annual report.

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PART I

Item 1. BUSINESS

Overview

Amgen Inc. (including its subsidiaries, referred to as Amgen, the Company, we, our and us) was incorporated in 1980 and is a global biotechnology company that discovers, develops, manufactures and markets human therapeutics based on advances in cellular and molecular biology. We operate in one business segment human therapeutics.

We market human therapeutic products in the areas of supportive cancer care, nephrology, inflammation and oncology. Our principal products include Aranesp® (darbepoetin alfa), EPOGEN® (Epoetin alfa), Neulasta® (pegfilgrastim), NEUPOGEN® (Filgrastim) and Enbrel® (etanercept). Aranesp® and EPOGEN® stimulate the production of red blood cells to treat anemia and belong to a class of drugs referred to as erythropoiesis-stimulating agents (ESAs). Aranesp® is used for the treatment of anemia both in supportive cancer care and in nephrology. EPOGEN® is used to treat anemia associated with chronic renal failure (CRF). Neulasta® and NEUPOGEN® selectively stimulate the production of neutrophils, one type of white blood cell that helps the body fight infections. ENBREL blocks the biologic activity of tumor necrosis factor (TNF) by inhibiting TNF, a substance induced in response to inflammatory and immunological responses, such as rheumatoid arthritis and psoriasis. For the years ended December 31, 2007, 2006 and 2005, our principal products represented 95%, 97% and 98% of total product sales, respectively.

We operate in a highly regulated industry and various U.S. and foreign regulatory bodies have substantial authority over how we conduct our business in those countries. Government authorities in the United States and in other countries regulate the manufacturing and marketing of our products and our ongoing research and development (R&D) activities. (See *Government Regulations.*) For example, prior to obtaining regulatory approval to market a product, we must conduct extensive clinical studies designed to establish the safety and effectiveness of the product candidate for use in humans in the indications sought. Furthermore, in order to maintain regulatory approval to market a product, we may be required to conduct further clinical trials and to provide additional information on safety and effectiveness. (See *Postmarketing and Safety Activities.*) The regulatory environment is evolving and there is increased scrutiny on drug safety and increased authority being granted to regulatory bodies, in particular the U.S. Food and Drug Administration (FDA), to assist in ensuring the safety of therapeutic products.

Most patients receiving our principal products for approved indications are covered by either government and/or private payer health care programs. The reimbursement environment is evolving with greater emphasis on cost containment. Therefore, sales of our products are and will continue to be affected by the availability and extent of reimbursement from third-party payers, including government and private insurance plans and administration of those programs. Governments may regulate access to, prices or reimbursement levels of our products to control costs or to affect levels of use of our products. Worldwide use of our products may be affected by these cost containment pressures and cost shifting from governments and private insurers to healthcare providers or patients in response to ongoing initiatives to reduce or reallocate healthcare expenditures. Further, safety signals or adverse events or results from clinical trials or studies performed by us or by others (including our licensees or independent investigators) or from the marketed use of our drugs may expand safety labeling or restrict the use for our approved products and may negatively impact worldwide reimbursement for our products. (See *Reimbursement.*)

We maintain sales and marketing forces primarily in the United States, Europe and Canada. We market our products to healthcare providers including physicians or their clinics, dialysis centers, hospitals and pharmacies. We market ENBREL under a co-promotion agreement with Wyeth in the United States and Canada (see *Joint Ventures and Business Relationships Wyeth*). In addition, we have entered into licensing and/or co-promotion agreements to market our principal products in certain geographic areas outside of the United States. In the United States, we sell primarily to wholesale distributors of pharmaceutical products. Outside the United States, we sell principally to hospitals and/or wholesalers depending upon the distribution practice in each country.

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We focus our R&D efforts on novel therapeutics for the treatment of grievous illness in the core areas of oncology, inflammation, bone and metabolic disorders. Our research takes a modality-independent approach to drug discovery in which we choose the best possible approach to block a specific disease process before considering the type of drug (modality) that may be required to pursue that approach. We study molecules in the areas of proteins (sometimes referred to as large molecules), including monoclonal antibodies and peptibodies, and small molecules. We have major R&D centers in several locations throughout the United States and in the United Kingdom, as well as, smaller R&D centers in certain other countries throughout the world. To augment our internal R&D efforts, we acquire companies, acquire and license certain product and technology rights and establish R&D collaborations with third parties.

Our manufacturing operations consist of bulk manufacturing, formulation, fill and finish activities which produce Aranesp®, Epoetin alfa, Neulasta®, NEUPOGEN®, ENBREL, Vectibix and other products and product candidates for both commercial and clinical purposes. We operate commercial and clinical manufacturing facilities in several locations throughout the United States and in Puerto Rico. Third-party contractors manufacture some or all of certain of our commercial products and/or product candidates.

Key Developments

The year of 2007 was defined by a number of key developments. During the past year, we faced various challenges on many fronts and, in particular, with respect to our marketed ESA products, Aranesp® and EPOGEN®, that resulted in a large unexpected reduction in revenues for these products, in particular Aranesp® sales in the U.S. supportive cancer care segment. These challenges necessitated that we restructure our worldwide operations and adapt to a new environment. Despite these adverse developments, we also achieved certain notable accomplishments. The following is a discussion of selected key developments in 2007 and early 2008.

ESA safety concerns resulted in regulatory and reimbursement changes

Late in 2006 and throughout 2007, adverse safety results involving ESA products were observed in various studies that were performed by us and by others (including our licensees or independent investigators) that culminated in significant regulatory and reimbursement developments affecting the class of ESA products, including Aranesp® and EPOGEN®. These developments were due to a combination of factors, particularly evident in the United States, that have increased the focus on exploring the safety risks associated with therapeutic products. As a result, there is increased focus on product safety and a greater urgency to act to ensure that safety concerns are quickly and fully disclosed, aggressively investigated and thoroughly considered in setting reimbursement and usage policies.

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The results of the following ESA studies were released in late 2006 or during 2007:

Sponsor	Study	Hb Target (g/dL)[1]	Disease	Study Results
Roche[2]	CREATE[3]	13-15	CKD[4]	Patients with CKD of stage 3 or 4 and mild-to-moderate anemia, the normalization of Hb levels to 13 g/dL to 15 g/dL did not reduce cardiovascular events as compared with the use of a lower target range (10.5 g/dL to 11.5 g/dL)
J&J[5]	CHOIR[6]	13.5	CKD	Increased risk of composite events in patients in the ESA group (death, myocardial infarction, congestive heart failure and stroke); No incremental improvement in quality of life
Amgen	Anemia of Cancer[7]	12-13	Non-myeloid malignancies	Higher mortality in ESA group
DAHANCA[8]	DAHANCA-10[9]	14-15.5	HNC[10]	5-year locoregional control poorer in ESA group; No significant difference in overall survival
AGO[11]	PREPARE[9][12]	12.5-13	Neoadjuvant breast cancer	No significant difference in pathologic complete remission between groups; Decreased 3-year relapse-free and overall survival
GOG[14]	GOG-191	12-14	Cervical cancer	Decreased 3-year PFS[13] and overall survival and locoregional control

(1) Hemoglobin (Hb) measured in grams per deciliter (g/dL)
(2) F. Hoffmann-La Roche Ltd. (Roche)
(3) Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta (CREATE)
(4) Chronic kidney disease (CKD)
(5) Johnson & Johnson (J&J)
(6) Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR)
(7) Anemia of Cancer (AoC 103 study)

(8) Danish Head and Neck Cancer (DAHANCA)
(9) Study included as part of Aranesp® pharmacovigilance program (see Postmarketing and Safety Activities).
(10) Head and neck cancer (HNC)
(11) German Gynecological Oncology Study Group (AGO)
(12) Preoperative Epirubicin Paclitaxel Aranesp® (PREPARE)
(13) Progression-free survival (PFS)
(14) Gynecologic Oncology Group (GOG)

The studies summarized in the table above explored the use of ESAs in settings different from those outlined in the FDA approved label, including targeting higher Hb levels and/or use in non-approved patient populations. As the results of these studies were reported, various regulatory and reimbursement agencies began to review the administration and reimbursement of ESA products resulting in certain key developments which

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have and will continue to materially adversely affect sales of our ESA products and, in particular, Aranesp® sales in the U.S. supportive cancer care segment.

Throughout 2007, we had ongoing discussions with the FDA and other regulatory authorities regarding the administration of our ESA products, which led to several key regulatory developments beginning with the FDA approval, on March 9, 2007, of updated safety information for the class of ESAs, including Aranesp® and EPOGEN®, including a boxed warning in the prescribing information.

Additionally, during 2007, certain of the FDA s advisory panels, including the Oncologic Drugs Advisory Committee (ODAC), the Cardiovascular-Renal Drug Advisory Committee (CRDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRMAC) held meetings to discuss the safety/efficacy profile of ESA use in certain settings. The ODAC is an advisory committee of external experts who advise the FDA about the safety and efficacy of drug products for use in treating cancer patients. The CRDAC is an advisory committee of external experts who advise the FDA about the safety and efficacy of drug products used in the treatment of cardiovascular and renal disorders. The DSaRMAC is an advisory committee of external experts who advise the FDA on, among other matters, risk management and communication. These committees are advisory only and FDA officials are not bound to or limited by their recommendations. However, the FDA commonly follows the recommendations of its advisory panels. On May 10, 2007, the ODAC held a panel meeting to discuss the safety/efficacy profile of ESAs in oncology. Responding to questions posed by the FDA, the ODAC recommended that more restrictions be added to ESA labels and that additional clinical trials be conducted by companies with currently approved ESAs, including us, although no specific restrictions or studies were recommended at the ODAC meeting (see *Postmarketing and Safety Activities*). Further, on September 11, 2007, the FDA held a joint meeting of the CRDAC and the DSaRMAC (referred to collectively as CRDAC/DSaRMAC), which evaluated the safety data on ESA use in renal disease. The CRDAC/DSaRMAC recommended against revising the ESA product labels to state that the target Hb level should not exceed 11 g/dL, recommended that the ESA dosages used to achieve the Hb levels in the lower target groups in the Normal Hematocrit Cardiac Trial and the CHOIR studies were sufficient to form the basis for ESA dosage recommendations and discussed potential clinical studies involving ESAs.

On November 8, 2007, in recognition of the input from the May 2007 ODAC and September 2007 joint CRDAC/DSaRMAC meetings, we announced additional updates to the Aranesp® and EPOGEN®/PROCRIT® package inserts in collaboration with the FDA and Johnson and Johnson Pharmaceutical Research & Development (J&JPRD), a subsidiary of J&J. J&J markets recombinant human erythropoietin under the trademark PROCRIT® in the United States (see *Joint Ventures and Business Relationships Johnson & Johnson*). The changes to the ESA labels included modifications to the boxed warnings, additional language in the INDICATIONS AND USAGE section, and the WARNINGS section and clarification of the Hb range for CRF patients was added in the DOSAGE AND ADMINISTRATION section. In addition, we discussed additional clinical study concepts with the FDA to address potential safety concerns in patients with specific tumor types to be added to our ongoing ESA pharmacovigilance program and are continuing to work with the FDA on this matter (see *Postmarketing and Safety Activities*).

We continue to work closely with the FDA to complete further labeling revisions to the class of ESAs, including Aranesp® and EPOGEN®. We are in discussions with the FDA regarding safety data from the PREPARE and GOG-191 studies including an updated box warning in the labeling information. These proposed labeling changes were submitted under the regulatory mechanism known as a changes being effected (CBE) process. We are also in discussions on proposed revisions to the labeling we submitted as part of our prior approval supplement (PAS) in December 2007, that addressed questions raised during the May 10, 2007 ODAC meeting regarding Hb initiation, Hb ceiling, discontinuance of ESA therapy after chemotherapy and data from additional clinical studies. Additionally, the FDA has scheduled an ODAC meeting on March 13, 2008 as part of the FDA s ongoing pharmacovigilance review of ESAs.

On October 29, 2007, the European Agency for the Evaluation of Medicinal Products (EMEA) issued a press release about upcoming changes to product information for ESAs stipulating a uniform target Hb range for all ESAs of 10 g/dL to 12 g/dL with a warning not to exceed a concentration of 12 g/dL. We continue to be in discussion with the EMEA to finalize updates to our ESA labels.

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Due to these regulatory developments, we and J&JPRD have taken further action since May 2007 in response to recommendations by the FDA and ODAC, including:

- Issued Dear Healthcare Provider letters to communicate labeling changes
- Submitted Medication Guide and Instructions for Use (currently under review by FDA) to further inform patients and enhance physician-patient discussion concerning the benefit:risk decision
- Along with Roche, engaged the Cochrane Collaboration, an independent international not-for-profit organization, to perform a patient-level combined analysis of all available controlled studies in ESAs in oncology patients
- Collaborating with the National Cancer Institute and FDA on research activities to evaluate ESA therapy in cancer
- Working with the FDA to design a large, definitive, well controlled study comparing the safety of ESAs administered to a maximum Hb target of 12 g/dL per the product labeling versus placebo in three major tumor types (non-small cell lung cancer (NSCLC), breast cancer and advanced colorectal cancer (CRC))

We and J&JPRD are continuing to develop and implement a risk management and risk minimization plan to address safety concerns regarding our ESA products. These activities include physician education, cancer patient/patient advocacy group communications, implementation of a Medication Guide, tracking of risk communication to patients, additional labeling changes and continuation of the ongoing pharmacovigilance and postmarketing commitment (PMC) studies (see *Postmarketing and Safety Activities*).

In addition to these regulatory developments, there have been a number of reimbursement and related developments during 2007. For example, in February 2007, following the reported results from our AoC 103 study, the United States Pharmacopoeia Dispensing Information (USP DI) Drug Reference Guides removed Aranesp® in the treatment of AoC. Thereafter, Aranesp® use in AoC decreased significantly throughout 2007.

Additionally, on July 30, 2007, the Centers for Medicare and Medicaid Services (CMS) issued its National Coverage Decision Memorandum for Use of Erythropoiesis Stimulating Agents in Cancer and Related Neoplastic Conditions (the Decision Memorandum). The Decision Memorandum establishes the ESA reimbursement policy for Medicare and other government beneficiaries who are treated for chemotherapy-induced anemia (CIA) and who all together accounted for approximately 50% of the U.S. cancer patients receiving Aranesp® prior to its issuance. We believe that the majority of CIA patients who received treatment with ESAs, including Aranesp®, were initiated at Hb levels above 10 g/dL and were maintained with Hb levels above 10 g/dL with continued therapy prior to the issuance of the Decision Memorandum. Given that the Decision Memorandum contains a coverage restriction for Hb levels greater than 10 g/dL, we believe that such restriction has and will continue to change the way ESAs are used in clinical practice, for example, by decreasing the number of treated patients, the average ESA dose and the duration of ESA therapy. We believe this restriction on reimbursement of ESAs in the Decision Memorandum has had and will continue to have a material adverse effect on the use, reimbursement and sales of Aranesp®. Additionally, based on our knowledge, although no private payers have implemented the Decision Memorandum to date, many private payers have implemented the Hb initiation restriction included in the Decision Memorandum. Further, due to difficulties in administering a two-tier medical practice, we believe many healthcare providers have reduced ESA utilization for all of their patients regardless of insurance coverage. On January 14, 2008, CMS issued changes to its Medicare National Coverage Determinations Manual, adding to the ESA Decision Memorandum, which provides instructions to local Medicare contractors with respect to the implementation of the Decision Memorandum. Local Medicare contractors have until April 7, 2008 to implement the instructions, although the effective date of the Decision Memorandum is for claims with dates of service on or after July 30, 2007. We continue to evaluate the Decision Memorandum s impact on use, reimbursement and sales of Aranesp®, and on our business and results of operations.

On November 13, 2007, we submitted new evidence to the CMS to support a formal request for reconsideration of their Decision Memorandum on ESAs. In this request, we stated that we are supportive of most aspects of the Decision Memorandum and are requesting a very narrow reconsideration of a specific provision in the policy.

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In particular, we indicated that we share the serious concerns voiced by physicians and their patients that one aspect of the Decision Memorandum, namely the restriction on reimbursement for ESAs when Hb is greater than 10 g/dL, should be reconsidered. We believe that this restriction prevents physicians from using their discretion in appropriately managing CIA with ESAs in individual Medicare patients, subjects Medicare beneficiaries to an untested treatment regimen and may subject them to receive otherwise avoidable blood transfusions. On December 22, 2007, we submitted to CMS a supplement to the November 13, 2007 reconsideration request to reflect updated clinical data.

In addition to the above, further developments occurred in 2007 that have and will continue to affect the administration and reimbursement of our ESA products. For example, on July 20, 2007, the CMS published revisions to its Claims Monitoring Policy: Erythropoietin/darbepoetin alfa usage for beneficiaries with end stage renal disease (EMP), effective January 1, 2008, requiring a 50% reduction in Medicare reimbursement if a patient s Hb is above 13 g/dL for three or more consecutive months. In addition, the EMP reduces the monthly dosing limits to 400,000 international units (IUs) of EPOGEN®, from 500,000 IUs, and to 1,200 micrograms (mcgs) of Aranesp®, from 1,500 mcgs. Also, on August 30, 2007, the National Kidney Foundation (NKF) distributed to the nephrology community final Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines and recommendations for anemia in CKD. Based on this review, the NKF-KDOQI Anemia Work Group recommended in their 2007 Update to the NKF-KDOQI Anemia Management Guidelines that physicians target Hb in the range of 11 g/dL to 12 g/dL, and also stipulated that the target not be above 13 g/dL.

Restructuring

As a result of certain of the above regulatory and reimbursement developments affecting ESAs, including our marketed ESA products Aranesp® and EPOGEN®, and the resulting impact on our operations, on August 15, 2007, we announced a plan to restructure our worldwide operations in order to improve our cost structure while continuing to make significant R&D investments and build the framework for our future growth. The restructuring plan is also, to a lesser degree, the result of various challenges facing certain of our other products discussed further below.

Key components of our restructuring plan include: i) staff reductions aggregating approximately 2,200 to 2,600 positions or approximately 12% to 14% of our worldwide staff, ii) rationalization of our worldwide network of manufacturing facilities in order to gain cost efficiencies while continuing to meet future commercial and clinical demand for our products and product candidates and, to a lesser degree, changes to certain R&D capital projects and iii) abandoning leases for certain R&D facilities that will not be used in our operations. We currently anticipate that we will incur approximately $775 million to $825 million of restructuring charges in connection with these actions, of which $739 million was incurred through December 31, 2007.

Other regulatory developments

In addition to the developments affecting ESAs that largely led to our restructuring, there were other developments in 2007 that have negatively impacted and potentially could further impact certain of our other products. For example, we are in discussions with the FDA with respect to the class of TNF inhibitor agents around several safety issues, which may result in additional patient safety information in the form of a boxed warning that will apply to the ENBREL label as has been the case with other TNF inhibitor agents.

Additionally, on March 22, 2007, as a result of safety concerns related to patient survival, we announced that we had discontinued Vectibix treatment in our Panitumumab Advanced Colorectal Cancer Evaluation (PACCE) trial, a non-registration-enabling trial evaluating the addition of Vectibix to standard chemotherapy and Avastin® (bevacizumab) for the treatment of first-line metastatic colorectal cancer (mCRC). On October 24, 2007, we announced that we and the FDA adopted changes to the U.S. prescribing information for Vectibix based on the results of the PACCE trial highlighting to clinicians the greater risk seen when Vectibix is combined with Avastin® and the specific chemotherapy used in the PACCE trial to treat patients with first-line mCRC. Vectibix is not indicated for the first-line treatment of mCRC and the new safety information applies to an unapproved use of Vectibix . Avastin® is the registered trademark for Genentech, Inc. s (Genentech) recombinant humanized monoclonal IgG1 antibody.

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Accomplishments

Despite these significant challenges, we were encouraged by certain notable accomplishments in 2007 and early 2008. For example, we successfully defended our intellectual property in 2007 with the October 23, 2007, jury verdict in the U.S. Federal District Court in Boston and the Court s rulings on various pre-trial and post-trial motions whereby Roche was found to infringe a total of 10 claims from four of Amgen s erythropoietin product (EPO) patents.

Furthermore, our pipeline continued to advance in 2007. Our early stage pipeline achieved significant expansion and our late-stage clinical programs, including denosumab, continued to progress. In January 2008, we announced that our one-year, head-to-head study of denosumab versus alendronate met primary and all secondary endpoints. In addition, we submitted a Biologics License Application (BLA) with the FDA for Nplate (Romiplostim) for the treatment of thrombocytopenia in adult patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) in October 2007 and also completed regulatory filings for this indication in Europe, Canada and Australia. The FDA has granted priority review of Nplate , which will be discussed at the March 12, 2008 ODAC meeting, and we expect a regulatory decision in the first half of 2008. Further, on December 5, 2007, the European Commission granted a conditional marketing authorization for Vectibix as monotherapy for the treatment of patients with epidermal growth factor receptors (EGFr) expressing mCRC with non-mutated (wild-type) KRAS genes after failure of standard chemotherapy regimens. On January 24, 2008, we announced the results of a biomarker analysis which indicated that in mCRC patients who have failed all other chemotherapeutic regimens, the efficacy of Vectibix monotherapy is confined to patients with non-mutated (wild-type) KRAS tumors. Specifically, in patients with non-mutated KRAS tumors, Vectibix significantly increased PFS and had an impact on quality of life and disease-related symptoms, compared to best supportive care alone.

We also entered into partnering agreements, including a collaboration and license agreement with Daiichi Sankyo Company, Limited (Daiichi Sankyo) in July 2007, which provided them the exclusive rights to develop and commercialize denosumab in Japan in postmenopausal osteoporosis (PMO) and oncology with the potential for additional indications. In February 2008, we entered into a license agreement with Takeda Pharmaceutical Company Limited (Takeda), which provided them the exclusive rights to develop and commercialize for the Japanese market up to 13 early to mid-stage molecules from our pipeline across a range of therapeutic areas, including oncology and inflammation. The molecules covered by the license agreement primarily include: AMG 108, AMG 317, AMG 386, AMG 479, AMG 655 and Vectibix (panitumumab). Amgen has the right to participate in the promotion of these products in Japan. In addition, we entered into a collaboration agreement with Takeda for the worldwide development and commercialization of motesanib diphosphate (AMG 706). Each party has the right to participate in the commercialization of motesanib diphosphate in the other party s territory. In connection with these agreements, Takeda has agreed to acquire our subsidiary in Japan, Amgen K.K.

During 2007, we acquired Alantos Pharmaceuticals Holding, Inc. (Alantos), which was a privately held company that specialized in the development of drugs for the treatment of diabetes and inflammatory diseases, and Ilypsa, Inc. (Ilypsa), which was a privately held company that specialized in the development of non-absorbed drugs for renal disorders.

Principal Products

We market our principal products in the areas of supportive cancer care, nephrology and inflammation. Our principal products include Aranesp®, EPOGEN®, Neulasta®, NEUPOGEN® and ENBREL. As discussed above, certain of our products, principally our marketed ESA products, Aranesp® and EPOGEN®, have and will continue to face various challenges arising primarily from regulatory and reimbursement developments that began in 2007. The developments involving our marketed ESA products have and will continue to materially adversely affect product sales, particularly Aranesp® sales in the U.S. supportive cancer care segment, as physicians conform to label and reimbursement changes. EPOGEN® sales have also, to a lesser degree, been negatively affected as physician behavior in making treatment and dosing decisions has reflected the issuance by the NKF of the final

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KDOQI guidelines, revised labeling and anticipation of CMS announced revisions to its EMP, effective January 1, 2008. In addition, we continue to work closely with the FDA and the EMEA to complete further revisions to labeling for our marketed ESA products, as previously discussed. Further, Aranesp® continues to face competitive pressures associated with the emergence of biosimilar and other products in the European Union (EU).

Aranesp® (darbepoetin alfa)

Aranesp® is our registered trademark for one of our erythropoiesis-stimulating proteins, a protein that stimulates red blood cell production. Red blood cells transport oxygen to all cells of the body. Without adequate amounts of erythropoietin, the red blood cell count is reduced. A deficient red blood cell count can result in anemia, a condition where insufficient oxygen is delivered to the body s organs and tissues. Anemia can be associated with CRF, both in patients on dialysis and not on dialysis. Anemia can also result from chemotherapy treatments for patients with non-myeloid malignancies.

We were granted an exclusive license by Kirin-Amgen, Inc. (KA), a joint venture between Kirin Holdings Company, Limited (Kirin) (formerly named Kirin Brewery Company, Limited) and Amgen (see *Joint Ventures and Business Relationships Kirin Holdings Company, Limited*), to manufacture and market darbepoetin alfa in the United States, all European countries, Canada, Australia, New Zealand, Mexico, all Central and South American countries and certain countries in Central Asia, North Africa and the Middle East.

We market Aranesp® primarily in the United States, Europe and Canada. Darbepoetin alfa is also marketed under the brand name Nespo® in Italy. Aranesp® was initially launched in 2001 in the United States and Europe for the treatment of anemia associated with CRF (both in patients on dialysis and patients not on dialysis) and is also indicated for the treatment of CIA in patients with non-myeloid malignancies.

Worldwide Aranesp® sales for the years ended December 31, 2007, 2006 and 2005 were $3.6 billion, $4.1 billion and $3.3 billion, respectively. As a result of certain of the regulatory and reimbursement developments discussed above in the *Key Developments* section, worldwide Aranesp® sales and, in particular, sales in the U.S. supportive cancer care setting have been and will continue to be materially adversely affected.

EPOGEN® (Epoetin alfa)

EPOGEN® is our registered trademark for our recombinant human erythropoietin product, a protein that stimulates red blood cell production. A reduced red blood cell count can result in anemia (see *Aranesp® (darbepoetin alfa)*). People with CRF suffer from anemia because they do not produce sufficient amounts of erythropoietin, which is normally produced in healthy kidneys.

We were granted an exclusive license to manufacture and market recombinant human erythropoietin in the United States under a licensing agreement with KA. We have retained exclusive rights to market EPOGEN® in the United States for dialysis patients. We granted Ortho Pharmaceutical Corporation (which has assigned its rights under the Product License Agreement to Ortho Biotech Products, L.P., a subsidiary of J&J, hereafter referred to as Ortho Biotech Products, L.P. or J&J) a license to commercialize recombinant human erythropoietin as a human therapeutic in the United States in all markets other than dialysis (see *Joint Ventures and Business Relationships Johnson & Johnson*).

We launched EPOGEN® in the United States in 1989 for the treatment of anemia associated with CRF for patients who are on dialysis. We market EPOGEN® for the treatment of anemic adult and pediatric patients with CRF who are on dialysis. EPOGEN® is indicated for elevating or maintaining the red blood cell level (as determined by hematocrit or Hb measurements) and decreasing the need for blood transfusions in these patients.

EPOGEN® sales were $2.5 billion for each of the years ended December 31, 2007, 2006 and 2005.

Neulasta® (pegfilgrastim)

Neulasta® is our registered trademark for a pegylated protein that selectively stimulates production of certain white blood cells known as neutrophils and is based on the Filgrastim molecule (see *NEUPOGEN® (Filgrastim)*). Neutrophils defend against infection. Treatments for various diseases and diseases themselves can

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result in extremely low numbers of neutrophils, a condition called neutropenia. Myelosuppressive chemotherapy, one treatment option for individuals with certain types of cancers, targets cell types that grow rapidly, such as tumor cells. Normal cells that also divide rapidly, such as those in the bone marrow that become neutrophils, are also vulnerable to the effects of cytotoxic chemotherapy, resulting in neutropenia with an increased risk of severe infection. Very often, neutropenia is the dose limiting side effect of chemotherapy and can thus be responsible for a reduction in the amount of chemotherapy that can be administered safely. Such reductions in chemotherapy dose can compromise the effectiveness of chemotherapy on the cancer it is being used to treat, with the result of a higher treatment failure rate. As mentioned above, the pegfilgrastim molecule is based on the Filgrastim molecule. A polyethylene glycol molecule or (PEG) is added to enlarge the Filgrastim molecule, thereby extending its half-life and causing it to be removed more slowly from the body. Because pegfilgrastim is eliminated through binding to its receptor on neutrophils and their precursors, pegfilgrastim remains in the circulation until neutrophil recovery has occurred. This neutrophil-mediated clearance allows for administration as a single dose per chemotherapy cycle, compared with NEUPOGEN®, which requires more frequent dosing. Neulasta® is prescribed more frequently in the curative setting, in which myelosuppressive chemotherapy is administered with the intent to cure cancer, rather than in the palliative setting, in which myelosuppressive chemotherapy is administered to treat other complications of cancer by managing tumor growth.

We were granted an exclusive license to manufacture and market pegfilgrastim in the United States, Europe, Canada, Australia and New Zealand under a licensing agreement with KA (see *Joint Ventures and Business Relationships Kirin Holdings Company, Limited*).

We market Neulasta® primarily in the United States, Europe and Canada. Pegfilgrastim is marketed under the brand name Neupopeg in Italy. Neulasta® was initially launched in the United States and Europe in 2002 and is indicated for reducing the incidence of infection associated with chemotherapy-induced neutropenia in cancer patients with non-myeloid malignancies. Subsequently, the FDA approved an update to the Neulasta® prescribing information to include data from a landmark phase 3 study demonstrating that Neulasta® helps protect patients with breast cancer undergoing moderately myelosuppressive chemotherapy from infection, as manifested by febrile neutropenia. Administration of Neulasta® in all cycles of chemotherapy is now approved for patients receiving myelosuppressive chemotherapy associated with at least a 17% risk of febrile neutropenia.

Worldwide Neulasta® sales for the years ended December 31, 2007, 2006 and 2005 were $3.0 billion, $2.7 billion and $2.3 billion, respectively.

NEUPOGEN® (Filgrastim)

NEUPOGEN® is our registered trademark for our recombinant-methionyl human granulocyte colony-stimulating factor (G-CSF), a protein that selectively stimulates production of certain white blood cells known as neutrophils (see *Neulasta® (pegfilgrastim)* for additional information on neutrophils). Similar to Neulasta® , NEUPOGEN® is prescribed more frequently in the curative setting, in which myelosuppressive chemotherapy is administered with the intent to cure cancer, rather than in the palliative setting, in which myelosuppressive chemotherapy is administered to treat other complications of cancer by managing tumor growth.

We were granted an exclusive license to manufacture and market G-CSF in the United States, Europe, Canada, Australia and New Zealand under a licensing agreement with KA (see *Joint Ventures and Business Relationships Kirin Holdings Company, Limited*).

We market NEUPOGEN® primarily in the United States, Europe and Canada. Filgrastim is marketed under the brand name GRANULOKINE® in Italy. NEUPOGEN® was initially launched in the United States and Europe in 1991. NEUPOGEN® is indicated for reducing the incidence of infection as manifested by febrile neutropenia for patients with non-myeloid malignancies undergoing myelosuppressive chemotherapy; reducing the duration of neutropenia and neutropenia-related consequences for patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation; reducing the incidence and duration of neutropenia-related consequences in symptomatic patients with congenital neutropenia, cyclic neutropenia or idiopathic neutropenia (collectively, severe chronic neutropenia); mobilizing peripheral blood progenitor cells (PBPC) in cancer patients who have undergone myeloablative chemotherapy for stem cell

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transplantation; and reducing the recovery time of neutrophils and the duration of fever following induction or consolidation chemotherapy treatment in adult patients with acute myeloid leukemia (AML).

Worldwide NEUPOGEN® sales for the years ended December 31, 2007, 2006 and 2005 were $1.3 billion, $1.2 billion and $1.2 billion, respectively.

Enbrel® (etanercept)

ENBREL is our registered trademark for our TNF receptor fusion protein that inhibits the binding of TNF to TNF receptors, which can result in a significant reduction in inflammatory activity. TNF is one of the chemical messengers that help regulate the inflammatory process. When the body produces too much TNF, it overwhelms the immune system s ability to control inflammation of the joints or of psoriasis-affected skin areas. ENBREL is similar to a protein that the body produces naturally, and like this protein, it binds and deactivates certain TNF molecules before they can trigger inflammation.

We acquired the rights to ENBREL in July 2002 as part of our acquisition of Immunex Corporation (Immunex).

We market ENBREL under a co-promotion agreement with Wyeth in the United States and Canada (see *Joint Ventures and Business Relationships Wyeth*). The rights to market ENBREL outside of the United States and Canada are reserved to Wyeth. ENBREL was initially launched in November 1998 by Immunex for the treatment of rheumatoid arthritis. In addition, ENBREL is now indicated for the treatment of adult patients with the following conditions: moderately to severely active rheumatoid arthritis, chronic moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy; active psoriatic arthritis and active ankylosing spondylitis. ENBREL is also approved for the treatment of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more disease-modifying medicines.

We are in discussions with the FDA with respect to the class of TNF inhibitor agents around several safety issues which may result in additional patient safety information in the form of a boxed warning that will apply to the ENBREL label as has been the case with other TNF inhibitor agents.

ENBREL sales for the years ended December 31, 2007, 2006 and 2005 were $3.2 billion, $2.9 billion and $2.6 billion, respectively.

Other

Other marketed products are principally comprised of Sensipar® (cinacalcet HCl) and Vectibix (panitumumab).

Sensipar® (cinacalcet HCl)

Sensipar® (Mimpara® in Europe) is our registered trademark for our first small molecule medicine used in treating CKD patients on dialysis who produce too much parathyroid hormone, a condition known as secondary hyperparathyroidism. In 2004, Sensipar®/Mimpara® was approved in the United States, Canada and Europe for the treatment of secondary hyperparathyroidism in CKD patients on dialysis and for the treatment of hypercalcemia in patients with parathyroid carcinoma. We market Sensipar®/Mimpara® primarily in the United States and Europe.

Sensipar® sales for the years ended December 31, 2007, 2006 and 2005 were $463 million, $321 million and $157 million, respectively.

Vectibix (panitumumab)

Vectibix is our trademark for our first entirely human monoclonal antibody for the treatment of patients with EGFr expressing mCRC after disease progression on, or following fluoropyrimidine-, oxaliplatin- and irinotecan- containing chemotherapy regimens. EGFr is a protein that plays an important role in cancer cell sig-

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naling and is over-expressed in many human cancers. Vectibix is an entirely human IgG2 monoclonal antibody that binds with high affinity to EGF receptors and interferes with signals that might otherwise stimulate growth and survival of the cancer cell. The goal of developing entirely human monoclonal antibodies is to offer effective targeted therapies with lessened risk of immune response against these agents. Vectibix received FDA approval in late September 2006 and became commercially available in the United States in October 2006.

On October 24, 2007, we announced changes to the U.S. prescribing information for Vectibix based on the results of the PACCE trial. On December 5, 2007, the European Commission granted a conditional marketing authorization for Vectibix as a monotherapy for the treatment of patients with EGFr expressing mCRC with non-mutated (wild-type) KRAS genes after failure of standard chemotherapy regimens. (See *Key Developments* for further discussion.)

We acquired full ownership of Vectibix as part of our acquisition of Abgenix, Inc. (Abgenix) in April 2006.

Vectibix sales for the year ended December 31, 2007 and 2006 were $170 million and $39 million, respectively.

Postmarketing and Safety Activities

We must conduct extensive clinical trials designed to establish the safety and efficacy of our product candidates in order to file for regulatory approval to market a product. After we have obtained approval to market our products, we monitor adverse events from the use of our products and report these events to regulatory agencies, along with information from postmarketing surveillance or studies. We may utilize other research approaches to learn or confirm information about our marketed products, including observational studies and patient registries, and may engage in risk minimization activities such as physician education initiatives and patient and patient advocacy group initiatives. We may also conduct or be required by regulatory agencies to conduct further clinical trials to provide additional information on our marketed products safety and efficacy. These additional trials may include, among other things, studying different doses or schedules of administration that were used in previous studies, use in other patient populations or other stages of the disease or use over a longer period of time. Additional trials of this nature are sometimes required by regulatory agencies as a condition of their approval to market our products; such trials are sometimes referred to as PMCs. Regulatory agencies may also request or require that we conduct specific studies in order to identify or assess possible safety risks of our marketed products that are observed or suggested by available scientific data.

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Certain ESA Postmarketing Commitments

Following the ODAC meeting in May 2004, we proposed a pharmacovigilance program comprised of five ongoing studies for Aranesp®, which sought to explore the use of ESAs in settings different from those outlined in the FDA approved label. These studies were subsequently designated by the FDA as PMCs. One of the five studies, the 20010145 (145) study, was an Amgen sponsored study, with the other four studies being investigator-sponsored studies. The following table summarizes the five studies:

Sponsor	Study	Tumor Type	Target Hb (g/dL)	Study Results
Amgen	20010145	Small cell lung	13	At median follow-up of 2 1/2 years, ESA and placebo group had similar PFS and overall survival; PFS based on blinded central review similar between ESA and placebo
DAHANCA	DAHANCA-10	Head and neck	14-15.5	5-year locoregional control poorer in ESA group; No significant difference in overall survival
AGO	PREPARE	Neoadjuvant breast	12.5-13	No significant difference in pathologic complete remission between groups; Decreased 3-year relapse-free and overall survival
GELA[1]	LNH-03-6B	NHL[2]	13-15 initially, amended to 13-14	At 1 year, ESA and control groups had similar overall survival and event-free survival[3]
WSG[4]	ARA-03	Adjuvant breast	13-14	Interim results published[5]

(1) Groupe d Etudes des Lymphomes de l Adulte (GELA)
(2) Non-Hodgkin s Lymphoma (NHL)
(3) The final study report is expected in 2010. Late in 2007, an independent Data Safety Monitoring Committee recommended continuation of the study unchanged.
(4) West German Study Group (WSG)
(5) Interim results presented by study investigator at the 2007 American Society of Clinical Oncologists conference indicated a higher incidence of thromboembolic events in the ESA group. The final study report is expected in 2011.

In addition, J&JPRD and/or its investigators have conducted numerous studies proposed at the 2004 ODAC meeting including: the EPO-GBR-7 and RTOG-9903 studies in HNC, the EPO-GER-22 and EPO-CAN-20 studies in NSCLC, the EPO-CAN-17 and EPO-GER-7 studies in breast cancer and the EPO-GER-8/AGO-NOGGO study in cervical cancer. All of the above studies are closed to enrollment and summary results were submitted to the FDA. Final study reports for many of these studies are expected in 2008. In addition