GENENTECH INC
Form 10-K
February 17, 2006

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

FORM 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2005
or

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

For the transition period from _____ to _____

Commission file number: 1-9813

GENENTECH, INC.
(Exact name of registrant as specified in its charter)

A Delaware Corporation	**94-2347624**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
1 DNA Way, South San Francisco, California	**94080**
(Address of principal executive offices)	(Zip Code)

(650) 225-1000
(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, $0.02 par value	New York Stock Exchange

Securities registered pursuant to Section 12(g) of the Act:
None
(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 þ No o

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 o No þ

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No o

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. þ

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of Act). Yes þ No o

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

The aggregate market value of Common Stock held by non-affiliates as of June 30, 2005 was $33,746,869,526.(A) All executive officers and directors of the registrant and Roche Holdings, Inc. have been deemed, solely for the purpose of the foregoing calculation, to be “affiliates” of the registrant.

Number of shares of Common Stock outstanding as of February 13, 2006: 1,053,871,674

Documents incorporated by reference:

Definitive Proxy Statement with respect to the 2006 Annual Meeting of Stockholders to be filed by Genentech, Inc. with the Securities and Exchange Commission (hereinafter referred to as "Proxy Statement")	Part III

(A) Excludes 587,256,075 shares of Common Stock held by directors and executive officers of Genentech and Roche Holdings, Inc.

GENENTECH, INC.

2005 Form 10-K Annual Report

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In this report, "Genentech," "we," "us" and "our" refer to Genentech, Inc. "Common Stock" refers to Genentech's Comm Stock, par value $0.02 per share, "Special Common Stock" refers to Genentech's callable putable Common Stock, par value $0.02 per share, all of which was redeemed by Roche Holdings, Inc. (or "Roche") on June 30, 1999.

We own or have rights to various copyrights, trademarks and trade names used in our business including the following: Activase® (alteplase, recombinant) tissue-plasminogen activator; Avastin® (bevacizumab) anti-VEGF antibody; Cathflo® Activase® (alteplase for catheter clearance); Herceptin® (trastuzumab) anti-HER2 antibody; Lucentis™ (ranibizumab, rhuFab V2) anti-VEGF antibody fragment; Nutropin® (somatropin (rDNA origin) for injection) growth hormone; Nutropin AQ® and Nutropin AQ Pen® (somatropin (rDNA origin) for injection) liquid formulation growth hormone; Nutropin Depot® (somatropin (rDNA origin) for injectable suspension) encapsulated

sustained-release growth hormone; Omnitarg™ (pertuzumab) HER dimerization inhibitor; Protropin® (somatrem for injection) growth hormone; Pulmozyme® (dornase alfa, recombinant) inhalation solution; Raptiva® (efalizumab) anti-CD11a antibody; and TNKase™ (tenecteplase) single-bolus thrombolytic agent. Rituxan® (rituximab) anti-CD20 antibody is a registered trademark of Biogen Idec Inc.; Tarceva® (erlotinib) is a trademark of OSI Pharmaceuticals, Inc.; and Xolair® (omalizumab) anti-IgE antibody is a trademark of Novartis AG. This report also includes other trademarks, service marks and trade names of other companies.

PART I

Item 1. BUSINESS

Overview

Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes biotherapeutics for significant unmet medical needs. A number of the currently approved biotechnology products originated from or are based on Genentech science. Genentech manufactures and commercializes multiple biotechnology products, and receives royalties from companies that are licensed to market products based on our technology. See "Marketed Products" and "Licensed Products" below. Genentech was organized in 1976 as a California corporation and was reincorporated in Delaware in 1987.

Marketed Products

We commercialize in the United States (or "U.S.") the biotechnology products listed below.

Rituxan (rituximab) is an anti-CD20 antibody, which we commercialize with Biogen Idec Inc. (or "Biogen Idec"). It is approved for the treatment of patients with relapsed or refractory, low-grade or follicular, CD20-positive, B-cell non-Hodgkin's lymphoma, including retreatment and bulky disease, and on February 10, 2006, it was approved for use in the first-line treatment of patients with diffuse large B-cell, CD20-positive, non-Hodgkin's lymphoma, in combination with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) or other anthracycline-based chemotherapy regimens.

Avastin (bevacizumab) is an anti-VEGF humanized antibody approved for use in combination with intravenous 5-fluorouracil (or "5-FU")-based chemotherapy as a treatment for patients with first-line (or previously untreated) metastatic cancer of the colon or rectum.

Herceptin (trastuzumab) is a humanized anti-HER2 antibody approved for the treatment of certain patients with metastatic breast cancer. Herceptin is approved for use as a first-line therapy in combination with paclitaxel and as a single agent in second- and third-line therapy for patients with metastatic breast cancer who have tumors that overexpress the human epidermal growth factor receptor 2 (or "HER2") protein.

Tarceva (erlotinib), which we commercialize with OSI Pharmaceuticals, Inc. (or "OSI"), is a small molecule inhibitor of the tyrosine kinase activity of the HER1/epidermal growth factor receptor (or "EGFR") signaling pathway. Tarceva is approved for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (or "NSCLC") after failure of at least one prior chemotherapy regimen and in combination with gemcitabine chemotherapy for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

Xolair (omalizumab) is a humanized anti-IgE antibody, which we commercialize with Novartis AG (or "Novartis"), approved for the treatment of moderate-to-severe persistent allergic asthma in adults and adolescents.

Raptiva (efalizumab) is a humanized anti-CD11a antibody approved for the treatment of chronic moderate-to-severe plaque psoriasis in adults age 18 or older who are candidates for systemic therapy or phototherapy.

Nutropin (somatropin [rDNA origin] for injection) and *Nutropin AQ* are growth hormone products approved for the treatment of growth hormone deficiency in children and adults, growth failure associated with chronic renal insufficiency prior to kidney transplantation, short stature associated with Turner syndrome and long-term treatment of idiopathic short stature (or "ISS").

Activase (alteplase, recombinant) is a tissue plasminogen activator (or "t-PA") approved for the treatment of acute myocardial infarction (heart attack), acute ischemic stroke (blood clots in the brain) within three hours of the onset of symptoms and acute massive pulmonary embolism (blood clots in the lungs).

TNKase (tenecteplase) is a modified form of t-PA approved for the treatment of acute myocardial infarction (heart attack).

Cathflo Activase (alteplase, recombinant) is a t-PA approved in adult and pediatric patients for the restoration of function to central venous access devices that have become occluded due to a blood clot.

Pulmozyme (dornase alfa, recombinant) is an inhalation solution of deoxyribonuclease (rhDNase) I approved for the treatment of cystic fibrosis.

See "Total Product Sales" under Results of Operations in Part II, Item 7 of this Form 10-K for a discussion of the sales of each of our products in the last three years.

Licensed Products

Royalty Revenue

We receive royalty revenue under license agreements with companies that sell and/or manufacture products based on technology developed by us or intellectual property to which we have rights. These licensed products are sometimes sold under different trademarks or trade names. Significant licensed products, including all related party licenses, representing approximately 92% of our royalty revenues in 2005, are presented in the following table:

Product	Trade Name	Licensee	Licensed Territory
D2E7/adalimumab	Humira®	Abbott Laboratories	Worldwide
Antihemophilic factor, recombinant	Kogenate®/Helixate®	Bayer Corporation	Worldwide
Alteplase, recombinant	Actilyse®	Boehringer Ingelheim	A number of countries outside of U.S., Canada and Japan
Tenecteplase	Metalyse®	Boehringer Ingelheim	A number of countries outside of U.S., Canada and Japan
Infliximab	Remicade®	Celltech Pharmaceuticals plc (which transferred rights to Centocor, Inc. / Johnson & Johnson)	Worldwide
Rituximab	Rituxan/MabThera®	F. Hoffmann-La Roche	Worldwide excluding U.S. and Japan
Trastuzumab	Herceptin	F. Hoffmann-La Roche	Worldwide excluding U.S.
Dornase alfa, recombinant	Pulmozyme	F. Hoffmann-La Roche	Worldwide excluding U.S.

Alteplase and Tenecteplase	Activase and TNKase	F. Hoffmann-La Roche	Canada
Bevacizumab	Avastin	F. Hoffmann-La Roche	Worldwide excluding U.S.
Somatropin	Nutropin	F. Hoffmann-La Roche	Canada
Cetuximab	ERBITUX®	ImClone Systems, Inc.	Worldwide
Etanercept	ENBREL®	Immunex Corporation (whose rights were acquired by Amgen Inc.)	Worldwide

Other Revenues

We have granted a license to Zenyaku Kogyo Co., Ltd. (or "Zenyaku"), a Japanese pharmaceutical company, for the manufacture, use and sale of rituximab in Japan. Zenyaku co-promotes rituximab in Japan with Chugai Pharmaceutical Co., Ltd., a Japanese subsidiary of F. Hoffmann-La Roche, under the trademark Rituxan. The revenue earned from our sales of rituximab to Zenyaku is included in net product sales.

Products in Development

Our product development efforts, including those of our collaborators, cover a wide range of medical conditions, including cancer and immune diseases. Below is a summary of products, current stages of development, and the estimate of completion of the current phase of development.

Product	**Description**	**Estimate of Completion of Phase***
Awaiting Regulatory Approval		
Avastin	A supplemental Biologics License Application (or "sBLA") was submitted in December 2005 to the U.S. Food and Drug Administration (or "FDA") for Avastin in combination with 5-FU-based chemotherapy for patients with relapsed, metastatic colorectal cancer. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006
Herceptin	An sBLA was submitted on February 15, 2006 to the FDA for the use of Herceptin to treat early-stage, HER2-positive breast cancer. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006
Lucentis	A Biologics License Application (or "BLA") was submitted in December 2005 to the FDA for the use of Lucentis (ranibizumab) to treat neovascular wet form age-related macular degeneration. This product is being developed in collaboration with Novartis Ophthalmics.	2006
Rituxan Immunology	An sBLA was submitted in August 2005 to the FDA for Rituxan to treat patients with active rheumatoid arthritis (or "RA") who inadequately respond to an anti-tumor necrosis factor therapy. This product is being developed in collaboration with F. Hoffmann-La Roche and Biogen Idec.	2006

Preparing for Filing

Avastin	We are preparing for sBLA submissions to the FDA for the use of Avastin in combination with chemotherapy for the treatment of first-line metastatic breast cancer and first-line metastatic non-squamous NSCLC. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006
Herceptin	We are preparing for an sBLA submission to the FDA for the use of Herceptin in the first-line metastatic setting in combination with Taxotere® for HER2 positive patients. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006
Rituxan Hematology/Oncology	We are preparing an sBLA submission to the FDA for use of Rituxan for indolent NHL induction therapy in combination with chemotherapy or following induction chemotherapy. This product is being developed in collaboration with F. Hoffmann-La Roche and Biogen Idec.	2006

Phase III

Avastin	Avastin is being evaluated in Phase III clinical trials in adjuvant colorectal cancer, first-line metastatic renal cell carcinoma, hormone refractory prostate cancer, first-line metastatic breast cancer in combination with several chemotherapy regimens, first-line ovarian cancer, and first-line metastatic and locally advanced pancreatic cancer. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006-2011
Rituxan Hematology/Oncology	Rituxan is being evaluated in Phase III clinical trials for relapsed chronic lymphocytic leukemia (or "CLL"). This product is being developed in collaboration with F. Hoffmann-La Roche and Biogen Idec.	2010
Rituxan Immunology	Rituxan is being evaluated in the following indications: primary progressive multiple sclerosis, ANCA-associated vasculitis, lupus nephritis, and systemic lupus erythematosus. This product is being developed in collaboration with Biogen Idec for these potential indications. In addition, Rituxan is being evaluated in a Phase III clinical trial for disease-modifying anti-rheumatic drug refractory moderate-to-severe RA in collaboration with F. Hoffmann-La Roche and Biogen Idec.	2006-2009
Tarceva +/- Avastin	Avastin and Tarceva are being evaluated as combination therapy in second-line NSCLC and as maintenance therapy following first-line treatment for NSCLC. Tarceva is being developed in collaboration with F. Hoffmann-La Roche and OSI.	2008
Xolair	Xolair is being evaluated in pediatric asthma. Xolair is being developed in collaboration with Novartis and Tanox, Inc. (or "Tanox").	2008

Preparing for Phase III

Avastin	We are preparing for Phase III clinical trials in second-line metastatic breast cancer, adjuvant breast cancer and adjuvant NSCLC. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006-2007

Tarceva	We are preparing for a Phase III trial in adjuvant NSCLC. This product is being developed in collaboration with F. Hoffmann-La Roche and OSI.	2006
Phase II		
2nd Generation anti-CD20	A Phase I/II clinical trial in patients with RA completed enrollment in 2005. This product is being developed in collaboration with F. Hoffmann-La Roche and Biogen Idec.	2006
Omnitarg	A Phase II clinical trial in combination with chemotherapy for the treatment of platinum-resistant ovarian cancer was initiated in 2005. This product is being developed in collaboration with F. Hoffmann-La Roche.	2007
Rituxan Immunology	A Phase II trial in relapsing remitting multiple sclerosis completed enrollment in early 2006. This product is being developed in collaboration with Biogen Idec.	2007

Avastin +/- Tarceva	A Phase II clinical trial in second-line NSCLC has completed enrollment. Tarceva is being developed in collaboration with F. Hoffmann-La Roche and OSI.	2006
Xolair	Patient enrollment has been discontinued in the Phase II peanut allergy study due to severe hypersensitivity reactions in the oral food challenge portion of the trial prior to patients receiving Xolair. This decision was based on a recommendation from an independent Data Monitoring Committee in conjunction with Novartis and Tanox who are our collaborators in the development of Xolair. We are working with the physicians and the FDA on determining a path forward for Xolair in this indication.	2006
Preparing for Phase II		
Avastin	We are preparing to initiate a Phase II clinical trial for relapsed glioblastoma multiforme. This product is being developed in collaboration with F. Hoffmann-La Roche.	2006
Topical VEGF	We are preparing to initiate a Phase II trial for treatment of diabetic foot ulcers.	2007
Phase I	Apo2L/TRAIL for cancer therapy, BR3-Fc for RA and Topical Hedgehog Antagonist for Basal Cell Carcinoma are projects in Phase I.	2006

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* Note: For those projects preparing for a Phase, the estimated date of completion refers to the date the project is expected to enter the Phase for which it is preparing.

Related Party Arrangements

See “Relationship with Roche” and “Related Party Transactions” sections below in Part II, Item 7 of this Form 10-K for information on our collaboration arrangements with Roche, F. Hoffmann-La Roche and Novartis.

Distribution and Commercialization

We have a U.S.-based pharmaceutical marketing, sales and distribution organization. Our sales efforts are focused on specialist physicians in private practice or at hospitals and major medical centers in the U.S. In general, our products are sold largely to wholesalers, specialty distributors or directly to hospital pharmacies. We utilize common pharmaceutical company marketing techniques, including sales representatives calling on individual physicians and distributors, advertisements, professional symposia, direct mail, public relations and other methods.

The Genentech Access to Care Foundation offers our products at no charge to patients in the U.S. that are uninsured. We have established the Genentech Endowment for Cystic Fibrosis to assist cystic fibrosis patients in the U.S. with

obtaining Pulmozyme and the Genentech Access to Care Foundation for all other Genentech products. We also provide customer service programs relating to our products. We maintain a comprehensive physician-related product wastage replacement program for Rituxan, Avastin, Herceptin, Activase and TNKase that, subject to specific conditions, provides physicians the right to return these products to us for replacement. We also maintain expired product programs for all our products that, subject to certain specific conditions, provide customers the right to return products to us for replacement or credit at a price based on a 6 month rolling average. To further support patient access to therapies for various diseases, in the fourth quarter of 2005, we donated approximately $21.2 million to various independent, third party, public charities that offer financial assistance, such as co-pay assistance, to eligible patients. We maintain the right to renew, modify or discontinue any of the patient programs described above.

As discussed in Note 11, “Segment, Significant Customer and Geographic Information,” in the Notes to Consolidated Financial Statements of Part II, Item 8 of this Form 10-K, we had three major customers who each

provided over 10% of our total operating revenues in each of the last three years. Also discussed in the note are material net foreign revenues by country in 2005, 2004, and 2003.

Manufacturing and Raw Materials

Manufacturing biotherapeutics is difficult and complex, and requires facilities specifically designed and validated for this purpose. It can take longer than five years to design, construct, validate, and license a new biotechnology manufacturing facility. We currently produce all of our products at our manufacturing facilities located in South San Francisco, California; Vacaville, California; Porriño, Spain; or, increasingly, through various contract-manufacturing arrangements.

In order to maintain adequate supply to keep up with growing demand for our products, we must successfully implement a number of manufacturing capacity enhancement projects on schedule, utilize nearly 100 percent of our production capacity in the next several years and maintain a state of regulatory compliance at all production sites. If we or any or our contract manufacturers for any reason fail to obtain licensure for our capacity enhancement projects on schedule, fail to operate at or near full capacity utilization, fail to maintain a state of regulatory compliance, or if actual demand significantly exceeds our internal forecasts, we may be unable to maintain an adequate supply of our products to meet all demand. Key capacity enhancement projects, which we must successfully implement, include the following: (i) licensure of Wyeth Pharmaceuticals contract manufacturing facility at Andover, Massachusetts to produce Herceptin bulk drug substance by the end of 2006; (ii) licensure of additional capacity at our Porriño, Spain facility in 2006 to produce Avastin bulk drug substance; (iii) licensure of yield improvement processes for Rituxan by the end of 2006 and for Avastin by early 2007; (iv) licensure of our recently acquired Oceanside, California manufacturing facility during the first half of 2007; and (v) construction, qualification and licensure of our new plant in Vacaville, California by the end of 2009.

Raw materials and supplies required for the production of our principal products are available, in some instances from one supplier and in other instances, from multiple suppliers. In those cases where raw materials are only available through one supplier, such supplier may be either a sole source (the only recognized supply source available to us) or a single source (the only approved supply source for us among other sources). We have adopted policies to attempt, to the extent feasible, to minimize raw material supply risks to the Company, including maintenance of greater levels of raw materials inventory and coordination with our collaborators to implement raw materials sourcing strategies.

For risks associated with manufacturing and raw materials, see “Difficulties or delays in product manufacturing or in obtaining materials from our suppliers could harm our business and/or negatively affect our financial performance” under “Risk Factors.”

Proprietary Technology — Patents and Trade Secrets

We seek patents on inventions originating from our ongoing research and development (or “R&D”) activities. Patents, issued or applied for, cover inventions ranging from basic recombinant DNA techniques to processes relating to specific products and to the products themselves. Our issued patents extend for varying periods according to the date of patent application filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends upon the type of patent, the scope of its coverage and the availability of legal remedies in the country. We have either been issued patents or have patent applications pending that relate to a number of current and potential products including products licensed to others. We consider that in the aggregate our patent applications, patents and licenses under patents owned by third-parties are of material importance to our operations. Important legal issues remain to be resolved as to the extent and scope of available patent protection for biotechnology products and processes in the U.S. and other important markets outside of the U.S. We expect that litigation will likely be necessary to determine the validity and scope of certain of our proprietary rights. We are currently involved in a number of legal proceedings

relating to the scope of protection and validity of our patents and those of others. These proceedings may result in a significant commitment of our resources in the future and, depending on their outcome, may adversely affect the validity and scope of certain of our patent or other proprietary rights. We cannot assure you that the patents we obtain or the unpatented proprietary technology we hold will afford us significant commercial protection.

We have obtained licenses from various parties that we deem to be necessary or desirable for the manufacture, use or sale of our products. These licenses (both exclusive and non-exclusive) generally require us to pay royalties to the parties on product sales. In conjunction with these licenses, disputes sometimes arise regarding whether royalties are owed on certain product sales or the amount of royalties that are owed. The resolution of such disputes may cause us to incur significant additional royalty expenses or other expenses.

Our trademarks, Activase, Avastin, Cathflo, Herceptin, Lucentis, Nutropin, Nutropin AQ, Nutropin AQ Pen, Omnitarg, Pulmozyme, Raptiva, Rituxan (licensed from Biogen Idec), TNKase, Xolair (licensed from Novartis) and Tarceva (licensed from OSI), in the aggregate are considered to be of material importance. All are covered by registrations or pending applications for registration in the U.S. Patent and Trademark Office and in other countries. Trademark protection continues in some countries for as long as the mark is used and, in other countries, for as long as it is registered. Registrations generally are for fixed, but renewable, terms.

Our royalty income for patent licenses, know-how and other related rights amounted to $935.1 million in 2005, $641.1 million in 2004, and $500.9 million in 2003. Royalty expenses were $462.4 million in 2005, $355.0 million in 2004, and $244.6 million in 2003.

Competition

We face competition from pharmaceutical companies, pharmaceutical divisions of chemical companies, and biotechnology companies.

The introduction of new competitive products or follow-on biologics or new information about existing products may result in lost market share for us, reduced utilization of our products, and/or lower prices, even for products protected by patents.

Rituxan: Rituxan's current competitors include BEXXAR® (GlaxoSmithKline) and ZEVALIN® (Biogen Idec), both of which are radioimmunotherapies and indicated for treatment of patients with relapsed or refractory low-grade, follicular, or transformed B-cell NHL. Other competitors include CAMPATH® (Berlex, Inc.), which is indicated for B-cell chronic lymphocytic leukemia (an unapproved use of Rituxan), and VELCADE® (Millennium Pharmaceuticals, Inc.) which is indicated for multiple myeloma (an unapproved use of Rituxan).

Avastin: Avastin competes with ImClone/Bristol-Myers Squibb's ERBITUX®, which is an EGFR-inhibitor approved for the treatment of irinotecan refractory or intolerant metastatic colorectal cancer patients. While ERBITUX® and Avastin are approved for use in different settings (Avastin in front-line and ERBITUX® in relapsed patients), physicians use both products across all lines of therapy. In December 2005, the FDA approved Nexavar® (sorafenib) from Bayer Corporation/Onyx Pharmaceuticals, Inc. for the treatment of patients with advanced renal cell carcinoma (or "RCC"), or kidney cancer (an unapproved use for Avastin). In January 2006, Pfizer, Inc. received FDA approval for Sutent® (sunitinib malate) for use in advanced RCC and Gleevec-refractory / intolerant gastrointestinal stromal tumor (both unapproved uses of Avastin). Avastin could face competition from products in development that currently do not have regulatory approval, including Amgen Inc.'s panitumumab. Amgen has announced that it expects panitumumab may be approved for refractory metastatic colorectal cancer in late 2006.

Lucentis: We are aware that some retinal specialists are currently using Avastin to treat the wet form of age-related macular degeneration, an unapproved use, and that there may be continued Avastin use in this setting even after Lucentis has been approved for commercial use.

Herceptin: Herceptin could face competition in the future from experimental drugs and products in development that do not currently have regulatory approval for any use outside of clinical trials, including lapatinib, which is being developed by GlaxoSmithKline.

Tarceva: Tarceva competes with the chemotherapeutic products Taxotere® and Alimta®, both of which are indicated for the treatment of relapsed NSCLC. Although not FDA approved for use in pancreatic cancer, Xeloda®

and 5-FU represent competitors in this market. Tarceva could also face competition in the future from products in development that currently do not have regulatory approval for use outside of clinical trials, including Zactima™.

Xolair: In mid-October 2005, Critical Therapeutics, Inc. (or "Critical Therapeutics") launched Zyflo®, a leukotriene antagonist, for the prevention and chronic treatment of asthma in patients 12 years of age and older. While not a direct competitor to Xolair, we understand that Critical Therapeutics' marketing efforts are directed at the use of Zyflo® prior to Xolair. Xolair also faces competition from other asthma therapies, including inhaled corticosteroids, long-acting beta agonists, combination products such as fixed dose inhaled corticosteroids/long-acting beta agonists and leukotriene inhibitors, as well as oral corticosteroids.

Raptiva: Raptiva competes with established therapies for moderate-to-severe psoriasis including oral systemics such as methotrexate and cyclosporin, as well as ultraviolet light therapies. In addition, Raptiva competes with FDA-approved biologic agents Amevive® and ENBREL®, which are marketed by Biogen Idec and Amgen, respectively. Remicade® and Humira®, marketed by Centocor, Inc. (or "Centocor") and Abbott Laboratories (or "Abbott"), respectively, are used off-label in the psoriasis market. In October 2005, Centocor filed with the FDA for approval of Remicade® for the treatment of psoriasis.

Nutropin: In the growth hormone market, we face competition from other companies currently selling growth hormone products and delivery devices. Nutropin's current competitors include Genotropin® (Pfizer), Norditropin® (Novo Nordisk), Humatrope® (Eli Lilly and Company), Tev-Tropin® (Teva Pharmaceutical Industries Ltd.), and Saizen® (Serono, Inc.). As a result of multiple competitors, we have experienced and may continue to experience a loss of market share and a demand for increasing discounts to managed care. Some competitors have additional indications, including Prader Willi Syndrome and SGA (small for gestational age) for which Nutropin is not approved. Nutropin has five approved indications in the U.S., more than any other growth hormone.

Thrombolytics: We face competition in our acute myocardial infarction market with sales of TNKase and Activase affected by the adoption by physicians of mechanical reperfusion strategies. We expect that the use of mechanical reperfusion in lieu of thrombolytic therapy for the treatment of acute myocardial infarction will continue to grow. TNKase and Activase for acute myocardial infarction also face competition from aggressive price discounting on Retavase (reteplase), marketed by ESP Pharma, Inc. (a wholly owned subsidiary of PDL BioPharma, Inc.). Activase may face competition in the catheter clearance market from Nuvelo's Alfimeprase, which is in ongoing phase III clinical trials.

Pulmozyme: Pulmozyme faces competition from an emerging, inexpensive approach to clearing the lungs of cystic fibrosis patients. Specifically, the use of hypertonic saline could limit or reduce penetration into specific segments of the cystic fibrosis population. Research continues on new approaches to disease modification of cystic fibrosis which could reduce the number of patients in need of therapy.

In addition to the commercial and late stage development products listed above, there are numerous products in earlier stages of development at other biotechnology and pharmaceutical companies that, if successful in clinical trials, may compete with our products.

For risks associated with competition, see "We face competition" under "Risk Factors."

Government Regulation

Regulation by governmental authorities in the U.S. and other countries is a significant factor in the manufacture and marketing of our products and in ongoing research and product development activities. All of our products require regulatory approval by governmental agencies prior to commercialization. Our products are subject to rigorous preclinical and clinical testing and other premarket approval requirements by the FDA and regulatory authorities in

other countries. Various statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of such products. The lengthy process of seeking these approvals, and the subsequent compliance with applicable statutes and regulations, require the expenditure of substantial resources.

The activities required before a pharmaceutical product may be marketed in the U.S. begin with preclinical testing. Preclinical tests include laboratory evaluation of product chemistry and required animal studies to assess the

potential safety and efficacy of the product and its formulations. The results of these studies must be submitted to the FDA as part of an Investigational New Drug Application, which must be reviewed by the FDA before proposed clinical testing in humans can begin. Typically, clinical testing involves a three-phase process. In Phase I, clinical trials are conducted with a small number of subjects to determine the early safety profile and the pattern of drug distribution and metabolism. In Phase II, clinical trials are conducted with groups of patients afflicted with a specified disease in order to provide enough data to evaluate the preliminary efficacy, optimal dosages and expanded evidence of safety. In Phase III, large scale, multicenter clinical trials are conducted with patients afflicted with a target disease in order to provide enough data to statistically evaluate the efficacy and safety of the product, as required by the FDA. The results of the preclinical and clinical testing of a chemical pharmaceutical product are then submitted to the FDA in the form of a New Drug Application (or "NDA"), or for a biological pharmaceutical product in the form of a BLA, for approval to commence commercial sales. In responding to an NDA or a BLA, the FDA may grant marketing approval, request additional information or deny the application if it determines that the application does not provide an adequate basis for approval. See also "The successful development of biotherapeutics is highly uncertain and requires significant expenditures" under "Risk Factors."

Among the conditions for an NDA or a BLA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform on an ongoing basis with current Good Manufacturing Practices (or "GMP"). Before approval of a BLA, the FDA will usually perform a preapproval inspection of the facility to determine its compliance with GMP and other rules and regulations. Manufacturers must continue to expend time, money and effort in the area of production and quality control to ensure full compliance with GMP. After the establishment is licensed for the manufacture of any product, manufacturers are subject to periodic inspections by the FDA.

The requirements that we and our collaborators must satisfy to obtain regulatory approval by governmental agencies in other countries prior to commercialization of our products in such countries can be as rigorous, costly and uncertain.

We are also subject to various laws and regulations relating to safe working conditions, clinical, laboratory and manufacturing practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research.

The levels of revenues and profitability of biopharmaceutical companies may be affected by the continuing efforts of government and third-party payers to contain or reduce the costs of health care through various means. For example, in certain foreign markets, pricing or profitability of therapeutic and other pharmaceutical products is subject to governmental control. In the U.S. there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control.

In addition, in the U.S. and elsewhere, sales of therapeutic and other pharmaceutical products are dependent in part on the availability of reimbursement to the physician or consumer from third-party payers, such as the government or private insurance plans. Government and private third-party payers are increasingly challenging the prices charged for medical products and services, through class action litigation and otherwise. For example, the Medicare Prescription Drug Improvement and Modernization Act, enacted in December 2003 (or "Medicare Act"), decreased the Medicare reimbursement rate for many drugs, including our oncology products, possibly offset to some extent by increased physician payment rates for drug administration services related to certain of our oncology products. It is unclear how these changes in reimbursement rates for products administered by oncologists in the office setting will affect physician prescribing practices and ultimately the sales of our products. See also "Decreases in third party reimbursement rates may affect our product sales, results of operations and financial condition" under "Risk Factors."

We are also subject to various federal and state laws pertaining to health care fraud and abuse, including anti-kickback laws and false claims laws. For risks associated with health care fraud and abuse, see "If there is an adverse outcome

in our pending litigation or other legal actions our business may be harmed" under "Risk Factors."

Research and Development

A significant portion of our operating expenses is related to R&D. Generally, R&D expenses consist of independent R&D costs and costs associated with collaborative R&D and in-licensing arrangements. R&D expenses were $1,261.8 million in 2005, $947.5 million in 2004, and $722.0 million in 2003. We intend to maintain our strong commitment to R&D. Biotechnology products generally take 10 to 15 years to research, develop and bring to market in the U.S. As discussed above, clinical development typically involves three phases of study: Phase I, II, and III. The most significant costs associated with clinical development are the Phase III trials as they tend to be the longest and largest studies conducted during the drug development process. Product completion dates and completion costs vary significantly by product and are difficult to predict.

Human Resources

As of December 31, 2005, we had over 9,500 employees.

Environment

We have made, and will continue to make, expenditures for environmental compliance and protection. Expenditures for compliance with environmental laws have not had, and are not expected to have, a material effect on our capital expenditures, results of operations, or competitive position.

Available Information

The following information can be found on our website at http://www.gene.com or can be obtained free of charge by contacting our Investor Relations Department at (650) 225-1599 or by sending an e-mail message to investor.relations@gene.com:

- our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with the Securities and Exchange Commission;

- our policies related to corporate governance, including Genentech's Principles of Corporate Governance, Good Operating Principles (Genentech's code of ethics applying to Genentech's directors, officers and employees) as well as Genentech's Code of Ethics applying to our CEO, CFO and senior financial officials; and

- the charter of the Audit Committee of our Board of Directors.

Item 1A. RISK FACTORS

This Form 10-K contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements made by Genentech, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our product sales, royalties, contract revenues, expenses, net income and earnings per share.

The successful development of biotherapeutics is highly uncertain and requires significant expenditures

Successful development of biotherapeutics is highly uncertain. Products that appear promising in research or early phases of development may be delayed or fail to reach later stages of development or the market for several reasons

including:

- Preclinical tests may show the product to be toxic or lack efficacy in animal models.
- Clinical trial results may show the product to be less effective than desired or to have harmful or problematic side effects.

- Failure to receive the necessary regulatory approvals or a delay in receiving such approvals. Among other things, such delays may be caused by slow enrollment in clinical studies, extended length of time to achieve study endpoints, additional time requirements for data analysis or Biologic Licensing Application (or "BLA") preparation, discussions with the U.S. Food and Drug Administration (or "FDA"), an FDA request for additional preclinical or clinical data, or unexpected safety, efficacy or manufacturing issues.

- Difficulties formulating the product, scaling the manufacturing process or in getting approval for manufacturing.

- Manufacturing costs, pricing or reimbursement issues, or other factors that make the product uneconomical.

- The proprietary rights of others and their competing products and technologies that may prevent the product from being developed or commercialized.

Success in preclinical and early clinical trials does not ensure that large-scale clinical trials will be successful. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly and may be difficult to predict. If our large-scale clinical trials are not successful, we will not recover our substantial investments in the product.

Factors affecting our research and development (or "R&D") productivity and the amount of our R&D expenses include, but are not limited to:

- The number of and the outcome of clinical trials currently being conducted by us and/or our collaborators. For example, our R&D expenses may increase based on the number of late-stage clinical trials being conducted by us and/or our collaborators.

- The number of products entering into development from late-stage research. For example, there is no guarantee that internal research efforts will succeed in generating sufficient data for us to make a positive development decision or that an external candidate will be available on terms acceptable to us. In the past, some promising candidates did not yield sufficiently positive preclinical results to meet our stringent development criteria.

- Decisions by F. Hoffmann-La Roche (or "Hoffmann-La Roche") whether to exercise its options to develop and sell our future products in non-U.S. markets and the timing and amount of any related development cost reimbursements.

- In-licensing activities, including the timing and amount of related development funding or milestone payments. For example, we may enter into agreements requiring us to pay a significant upfront fee for the purchase of in-process R&D, which we may record as an R&D expense.

- Participation in a number of collaborative research arrangements. On many of these collaborations, our share of expenses recorded in our financial statements is subject to volatility based on our collaborators' spending activities as well as the mix and timing of activities between the parties.

- Charges incurred in connection with expanding our product manufacturing capabilities, as described in "Difficulties or delays in product manufacturing or in obtaining materials from our suppliers could harm our business and/or negatively affect our financial performance" below.

- Future levels of revenue.

We may be unable to obtain or maintain regulatory approvals for our products

We are subject to stringent regulation with respect to product safety and efficacy by various international, federal, state and local authorities. Of particular significance are the FDA's requirements covering R&D, testing, manufacturing, quality control, labeling and promotion of drugs for human use. A biotherapeutic cannot be marketed in the United States (or "U.S.") until it has been approved by the FDA, and then can only be marketed for the indications approved by the FDA. As a result of these requirements, the length of time, the level of expenditures and the laboratory and clinical information required for approval of a New Drug Application or a BLA, are substantial and can require a number of years. In addition, even if our products receive regulatory approval, they remain subject to ongoing FDA regulation, including, for example, changes to the product label, new or revised regulatory requirements for manufacturing practices, written advisements to physicians or a product recall.

We may not obtain necessary regulatory approvals on a timely basis, if at all, for any of the products we are developing or manufacturing or maintain necessary regulatory approvals for our existing products, and all of the following could have a material adverse effect on our business:

- Significant delays in obtaining or failing to obtain required approvals as described in "The successful development of biotherapeutics is highly uncertain and requires significant expenditures" above.

- Loss of, or changes to, previously obtained approvals, including those resulting from post-approval safety or efficacy issues.

- Failure to comply with existing or future regulatory requirements.

- Changes to manufacturing processes, manufacturing process standards or Good Manufacturing Practices following approval or changing interpretations of these factors.

In addition, the current regulatory framework could change or additional regulations could arise at any stage during our product development or marketing, which may affect our ability to obtain or maintain approval of our products or require us to make significant expenditures to obtain or maintain such approvals.

Difficulties or delays in product manufacturing or in obtaining materials from our suppliers could harm our business and/or negatively affect our financial performance

Manufacturing biotherapeutics is difficult and complex, and requires facilities specifically designed and validated for this purpose. It can take longer than five years to design, construct, validate, and license a new biotechnology manufacturing facility. We currently produce all of our products at our manufacturing facilities located in South San Francisco, California; Vacaville, California; Porriño, Spain; or increasingly through various contract-manufacturing arrangements. Problems with any of our or our contractors' manufacturing processes could result in failure to produce adequate product supplies or product defects which could require us to delay shipment of products, recall products previously shipped or be unable to supply products at all. In addition, we may need to record period charges associated with manufacturing or inventory failures or other production-related costs that are not absorbed into inventory or incur costs to secure additional sources of capacity. Furthermore, there are inherent uncertainties associated with forecasting future demand, especially for newly introduced products of ours or of those for whom we produce products, and as a consequence we may have inadequate capacity to meet our own actual demands and/or the actual demands of those for whom we produce product.

In order to maintain adequate supply to keep up with growing demand for our products, we must successfully implement a number of manufacturing capacity enhancement projects on schedule, utilize nearly 100 percent of our production capacity in the next several years and maintain a state of regulatory compliance at all production sites. If

we or any of our contract manufacturers for any reason fail to obtain licensure for our capacity enhancement projects on schedule, fail to operate at or near full capacity utilization, fail to maintain a state of regulatory compliance, or if actual demand significantly exceeds our internal forecasts, we may be unable to maintain an adequate supply of our products to meet all demand. Key capacity enhancement projects, which we must successfully implement, include the following: (i) licensure of Wyeth Pharmaceuticals contract manufacturing facility at Andover, Massachusetts to produce Herceptin bulk drug substance by the end of 2006; (ii) licensure of additional capacity at our Porriño, Spain

facility in 2006 to produce Avastin bulk drug substance; (iii) licensure of yield improvement processes for Rituxan by the end of 2006 and for Avastin by early 2007; (iv) licensure of our recently acquired Oceanside, California manufacturing facility during the first half of 2007; and (v) construction, qualification and licensure of our new plant in Vacaville, California by the end of 2009.

If we experience a significant malfunction in our filling facility, we could experience a shortfall or stock out of one or more products, which, if it were to continue for a significant period of time, could result in a material adverse effect on our product sales and our business.

Furthermore, certain of our raw materials and supplies required for the production of our principal products or products we make for others are available only through sole source suppliers (the only recognized supplier available to us) or single source suppliers (the only approved supplier for us among other sources), and such raw materials cannot be obtained from other sources without significant delay or at all. If such sole source or single source suppliers were to limit or terminate production or otherwise fail to supply these materials for any reason, such failures could also have a material adverse impact on our products sales and our business.

Any prolonged interruption in the operations of our or our contractors' manufacturing facilities could result in cancellations of shipments, loss of product in the process of being manufactured, or a shortfall or stock-out of available product inventory, any of which could have a material adverse impact on our business. A number of factors could cause prolonged interruptions, including:

- the inability of a supplier to provide raw materials used for manufacture of our products;
- equipment obsolescence, malfunctions or failures;
- product contamination problems;
- damage to a facility, including our warehouses and distribution facilities, due to natural disasters, including, but not limited to, earthquakes as our South San Francisco, Oceanside and Vacaville facilities are located in areas where earthquakes could occur;
- changes in FDA regulatory requirements or standards that require modifications to our manufacturing processes;
- action by the FDA or by us that results in the halting or slowdown of production of one or more of our products or products we make for others due to regulatory issues;
- a contract manufacturer going out of business or failing to produce product as contractually required;
- other similar factors.

Because our manufacturing processes and those of our contractors are highly complex and are subject to a lengthy FDA approval process, alternative qualified production capacity may not be available on a timely basis or at all. Difficulties or delays in our or our contractors' manufacturing and supply of existing or new products could increase our costs, cause us to lose revenue or market share, damage our reputation and could result in a material adverse effect on our product sales, financial condition and results of operations.

We face competition

We face competition from pharmaceutical companies, pharmaceutical divisions of chemical companies, and biotechnology companies.

The introduction of new competitive products or follow-on biologics or new information about existing products may result in lost market share for us, reduced utilization of our products, and/or lower prices, even for products protected by patents.

Rituxan: Rituxan's current competitors include BEXXAR® (GlaxoSmithKline) and ZEVALIN® (Biogen Idec), both of which are radioimmunotherapies and indicated for treatment of patients with relapsed or refractory low-grade, follicular, or transformed B-cell NHL. Other competitors include CAMPATH® (Berlex, Inc.), which is indicated for B-cell chronic lymphocytic leukemia (an unapproved use of Rituxan), and VELCADE® (Millennium Pharmaceuticals, Inc.) which is indicated for multiple myeloma (an unapproved use of Rituxan).

Avastin: Avastin competes with ImClone/Bristol-Myers Squibb's ERBITUX®, which is an EGFR-inhibitor approved for the treatment of irinotecan refractory or intolerant metastatic colorectal cancer patients. While ERBITUX® and Avastin are approved for use in different settings (Avastin in front-line and ERBITUX® in relapsed patients), physicians use both products across all lines of therapy. In December 2005, the FDA approved Nexavar® (sorafenib) from Bayer Corporation/Onyx Pharmaceuticals, Inc. for the treatment of patients with advanced renal cell carcinoma (or "RCC"), or kidney cancer (an unapproved use for Avastin). In January 2006, Pfizer, Inc. received FDA approval for Sutent® (sunitinib malate) for use in advanced RCC and Gleevec-refractory / intolerant gastrointestinal stromal tumor (both unapproved uses of Avastin). Avastin could face competition from products in development that currently do not have regulatory approval, including Amgen Inc.'s panitumumab. Amgen has announced that it expects panitumumab may be approved for refractory metastatic colorectal cancer in late 2006.

Lucentis: We are aware that some retinal specialists are currently using Avastin to treat the wet form of age-related macular degeneration, an unapproved use, and that there may be continued Avastin use in this setting even after Lucentis has been approved for commercial use.

Herceptin: Herceptin could face competition in the future from experimental drugs and products in development that do not currently have regulatory approval for any use outside of clinical trials, including lapatinib, which is being developed by GlaxoSmithKline.

Tarceva: Tarceva competes with the chemotherapeutic products Taxotere® and Alimta®, both of which are indicated for the treatment of relapsed NSCLC. Although not FDA approved for use in pancreatic cancer, Xeloda® and 5-FU represent competitors in this market. Tarceva could also face competition in the future from products in development that currently do not have regulatory approval for use outside of clinical trials, including Zactima™.

Xolair: In mid-October 2005, Critical Therapeutics, Inc. (or "Critical Therapeutics") launched Zyflo®, a leukotriene antagonist, for the prevention and chronic treatment of asthma in patients 12 years of age and older. While not a direct competitor to Xolair, we understand that Critical Therapeutics' marketing efforts are directed at the use of Zyflo® prior to Xolair. Xolair also faces competition from other asthma therapies, including inhaled corticosteroids, long-acting beta agonists, combination products such as fixed dose inhaled corticosteroids/long-acting beta agonists and leukotriene inhibitors, as well as oral corticosteroids.

Raptiva: Raptiva competes with established therapies for moderate-to-severe psoriasis including oral systemics such as methotrexate and cyclosporin, as well as ultraviolet light therapies. In addition, Raptiva competes with FDA-approved biologic agents Amevive® and ENBREL®, which are marketed by Biogen Idec and Amgen, respectively. Remicade® and Humira®, marketed by Centocor, Inc. (or "Centocor") and Abbott Laboratories (or "Abbott"), respectively, are used off-label in the psoriasis market. In October 2005, Centocor filed with the FDA for approval of Remicade® for the treatment of psoriasis.

Nutropin: In the growth hormone market, we face competition from other companies currently selling growth hormone products and delivery devices. Nutropin's current competitors include Genotropin® (Pfizer), Norditropin® (Novo Nordisk), Humatrope® (Eli Lilly and Company), Tev-Tropin® (Teva Pharmaceutical Industries Ltd.), and Saizen® (Serono, Inc.). As a result of multiple competitors, we have experienced and may continue to experience a loss of market share and a demand for increasing discounts to managed care. Some competitors have additional indications, including Prader Willi Syndrome and SGA (small for gestational age) for which Nutropin is not approved.

Nutropin has five approved indications in the U.S., more than any other growth hormone.

Thrombolytics: We face competition in our acute myocardial infarction market with sales of TNKase and Activase affected by the adoption by physicians of mechanical reperfusion strategies. We expect that the use of mechanical

reperfusion in lieu of thrombolytic therapy for the treatment of acute myocardial infarction will continue to grow. TNKase and Activase for acute myocardial infarction also face competition from aggressive price discounting on Retavase (reteplase), marketed by ESP Pharma, Inc. (a wholly owned subsidiary of PDL BioPharma, Inc.). Activase may face competition in the catheter clearance market from Nuvelo's Alfimeprase, which is in ongoing phase III clinical trials.

Pulmozyme: Pulmozyme faces competition from an emerging, inexpensive approach to clearing the lungs of cystic fibrosis patients. Specifically, the use of hypertonic saline could limit or reduce penetration into specific segments of the cystic fibrosis population. Research continues on new approaches to disease modification of cystic fibrosis which could reduce the number of patients in need of therapy.

In addition to the commercial and late stage development products listed above, there are numerous products in earlier stages of development at other biotechnology and pharmaceutical companies that, if successful in clinical trials, may compete with our products.

Decreases in third party reimbursement rates may affect our product sales, results of operations and financial condition

Sales of our products will depend significantly on the extent to which reimbursement for the cost of our products and related treatments will be available from government health administration authorities, private health insurers and other organizations to physicians. Third party payers and governmental health administration authorities are increasingly attempting to limit and/or regulate the price of medical products and services, especially branded prescription drugs. For example, the Medicare Prescription Drug Improvement and Modernization Act, enacted in December 2003 (or "Medicare Act"), provides for, among other things, a reduction in the Medicare reimbursement rates to physicians for many drugs, including many of our products. The Medicare Act as well as other changes in government legislation or regulation or in private third-party payers' policies toward reimbursement for our products may reduce reimbursement of our products' costs to physicians. Decreases in third-party reimbursement for our products could reduce physician usage of the product and may have a material adverse effect on our product sales, results of operations and financial condition.

Protecting our proprietary rights is difficult and costly

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. Accordingly, we cannot predict with certainty the breadth of claims allowed in these companies' patents. Patent disputes are frequent and can preclude the commercialization of products. We have in the past been, are currently, and may in the future be, involved in material litigation and other legal proceedings relating to our proprietary rights, such as the Cabilly reexaminations discussed in Note 7, "Leases, Commitments and Contingencies," in the Notes to Consolidated Financial Statements of Part II, Item 8 of this Form 10-K. Such litigation and other legal proceedings are costly in their own right and could subject us to significant liabilities to third-parties. An adverse decision could force us to either obtain third-party licenses at a material cost or cease using the technology or commercializing the product in dispute. An adverse decision with respect to one or more of our patents or other intellectual property rights could cause us to incur a material loss of royalties and other revenue from licensing arrangements that we have with third-parties, and could significantly interfere with our ability to negotiate future licensing arrangements.

The presence of patents or other proprietary rights belonging to other parties may lead to our termination of the R&D of a particular product, a loss of our entire investment in the product and subject us to infringement claims.

If there is an adverse outcome in our pending litigation or other legal actions our business may be harmed

Litigation to which we are currently or have been subjected relates to, among other things, our patent and other intellectual property rights, licensing arrangements with other persons, product liability and financing activities. We cannot predict with certainty the eventual outcome of pending litigation, which may include an injunction against the manufacture or sale of a product or potential product or a judgment with significant monetary award, including the possibility of punitive damages, or a judgment that certain of our patent or other intellectual property rights are

invalid or unenforceable. Furthermore, we may have to incur substantial expense in defending these lawsuits and these lawsuits could divert management's attention from ongoing business concerns.

Our activities relating to the sale and marketing of our products are subject to regulation under the U.S. Federal Food, Drug and Cosmetic Act and other federal statutes. Violations of these laws may be punishable by criminal and/or civil sanctions, including fines and civil monetary penalties, as well as the possibility of exclusion from federal health care programs (including Medicare and Medicaid). In 1999 we agreed to pay $50 million to settle a federal investigation relating to our past clinical, sales and marketing activities associated with human growth hormone. We are currently being investigated by the Department of Justice with respect to our promotional practices of Rituxan, and may in the future be investigated for our promotional practices relating to any of our products. If the government were to bring charges against or convict us of violating these laws, or if we were subject to third party litigation relating to the same promotional practices, there could be a material adverse effect on our business, including our financial condition and results of operations.

We are subject to various U.S. federal and state laws pertaining to healthcare fraud and abuse, including anti-kickback and false claims laws. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. 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 our practices might be challenged under anti-kickback or similar laws. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment to third-party payers (including Medicare and Medicaid) 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 the possibility of exclusion from federal health care programs (including Medicare and Medicaid). If a court were to find us liable for violating these laws, or if the government were to allege against or convict us of violating these laws, there could be a material adverse effect on our business, including on our stock price.

We may be unable to manufacture certain of our products if there is BSE contamination of our bovine source raw material

Most biotechnology companies, including Genentech, have historically used bovine source raw materials to support cell growth in cell production processes. Bovine source raw materials from within or outside the U.S. are increasingly subject to greater public and regulatory scrutiny because of the perceived risk of contamination with bovine spongiform encephalopathy (or "BSE"). Should BSE contamination occur during the manufacture of any of our products that require the use of bovine source raw materials, it would negatively impact our ability to manufacture those products for an indefinite period of time (or at least until an alternative process is approved), negatively affect our reputation and could result in a material adverse effect on our product sales, financial condition and results of operations.

We may be unable to retain skilled personnel and maintain key relationships

The success of our business depends, in large part, on our continued ability to (i) attract and retain highly qualified management, scientific, manufacturing and sales and marketing personnel, (ii) successfully integrate large numbers of new employees into our corporate culture, and (iii) develop and maintain important relationships with leading research and medical institutions and key distributors. Competition for these types of personnel and relationships is intense.

Among other benefits, we use stock options to attract and retain personnel. Our affiliation agreement with Roche provides that, among other things, we will establish a stock repurchase program designed to maintain Roche's percentage ownership in our Common Stock if we issue or sell any shares. In addition, changes in stock option

accounting rules will require us to recognize all stock-based compensation costs as expenses. These or other factors could reduce the number of shares management and our board of directors choose to grant under our stock option plans. We cannot be sure that we will be able to attract or retain skilled personnel or maintain key relationships or that the costs of retaining such personnel or maintaining such relationships will not materially increase.

Other factors could affect our product sales

Other factors that could affect our product sales include, but are not limited to:

- The timing of FDA approval, if any, of competitive products.
- Our pricing decisions, including a decision to increase or decrease the price of a product, and the pricing decisions of our competitors.
- Government and third-party payer reimbursement and coverage decisions that affect the utilization of our products and competing products.
- Negative safety or efficacy data from new clinical studies conducted either in the U.S. or internationally by any party could cause the sales of our products to decrease or a product to be recalled.
- Negative safety or efficacy data from post-approval marketing experience could cause sales of our products to decrease or a product to be recalled.
- The degree of patent protection afforded our products by patents granted to us and by the outcome of litigation involving our patents.
- The outcome of litigation involving patents of other companies concerning our products or processes related to production and formulation of those products or uses of those products.
- The increasing use and development of alternate therapies.
- The rate of market penetration by competing products.
- The termination of, or change in, an existing arrangement with any major wholesalers who supply our products.

Any of these factors could have a material adverse effect on our sales and results of operations.

Our results of operations are affected by our royalty and contract revenues

Royalty and contract revenues in future periods could vary significantly. Major factors affecting these revenues include, but are not limited to:

- Hoffmann-La Roche's decisions whether to exercise its options and option extensions to develop and sell our future products in non-U.S. markets and the timing and amount of any related development cost reimbursements.
- Variations in Hoffmann-La Roche's sales and other licensees' sales of licensed products.
- The expiration or termination of existing arrangements with other companies and Hoffmann-La Roche, which may include development and marketing arrangements for our products in the U.S., Europe and other countries outside the U.S.
- The timing of non-U.S. approvals, if any, for products licensed to Hoffmann-La Roche and to other licensees.
- Fluctuations in foreign currency exchange rates.

· The initiation of new contractual arrangements with other companies.

- Whether and when contract milestones are achieved.
- The failure of or refusal of a licensee to pay royalties.
- The expiration or invalidation of our patents or licensed intellectual property. For example, patent litigations, interferences, oppositions, and other proceedings involving our patents often include claims by third-parties that such patents are invalid or unenforceable. If a court, patent office, or other authority were to determine that a patent under which we receive royalties and/or other revenues is invalid or unenforceable, that determination could cause us to suffer a loss of such royalties and/or revenues, and could cause us to incur other monetary damages.
- Decreases in licensees' sales of product due to competition, manufacturing difficulties or other factors that affect the sales of product.

Our affiliation agreement with Roche Holdings, Inc. could adversely affect our cash position

Our affiliation agreement with Roche provides that we establish a stock repurchase program designed to maintain Roche's percentage ownership interest in our Common Stock based on an established Minimum Percentage. For more information on our stock repurchase program, see discussion below in "Liquidity and Capital Resources — Cash Provided by or Used in Financing Activities." See Note 8, "Relationship with Roche and Related Party Transactions," in the Notes to Consolidated Financial Statements in Part II, Item 8 of this Form 10-K for information regarding the Minimum Percentage.

While the dollar amounts associated with future stock repurchase programs cannot currently be determined, future stock repurchases could have a material adverse impact on our liquidity, credit rating and ability to access additional capital in the financial markets, and may have the effect of limiting our ability to use our capital stock as consideration for acquisitions.

Our affiliation agreement with Roche could limit our ability to make acquisitions and could have a material negative impact on our liquidity

The affiliation agreement between us and Roche contains provisions that:

- Require the approval of the directors designated by Roche to make any acquisition or any sale or disposal of all or a portion of our business representing 10% or more of our assets, net income or revenues.
- Enable Roche to maintain its percentage ownership interest in our Common Stock.
- Require us to establish a stock repurchase program designed to maintain Roche's percentage ownership interest in our Common Stock based on an established Minimum Percentage. For information regarding Minimum Percentage, see Note 8, "Relationship with Roche and Related Party Transactions," in the Notes to Consolidated Financial Statements in Part II, Item 8 of this Form 10-K for a discussion of our relationship with Roche and Roche's ability to maintain its percentage ownership interest in our stock. For more information on our stock repurchase program, see discussion below in "Liquidity and Capital Resources — Cash Provided by or Used in Financing Activities."

These provisions may have the effect of limiting our ability to make acquisitions and while the dollar amounts associated with our future stock repurchases cannot currently be estimated, stock repurchases could have a material adverse impact on our liquidity, credit rating and ability to access additional capital in the financial markets.

Future sales of our Common Stock by Roche could cause the price of our Common Stock to decline

As of December 31, 2005, Roche owned 587,189,380 shares of our Common Stock, or 55.7% of our outstanding shares. All of our shares owned by Roche are eligible for sale in the public market subject to compliance with the applicable securities laws. We have agreed that, upon Roche's request, we will file one or more registration statements under the Securities Act in order to permit Roche to offer and sell shares of our Common Stock. Sales of

a substantial number of shares of our Common Stock by Roche in the public market could adversely affect the market price of our Common Stock.

Roche Holdings, Inc., our controlling stockholder, may have interests that are adverse to other stockholders

Roche, as our majority stockholder, controls the outcome of most actions requiring the approval of our stockholders. Our bylaws provide, among other things, that the composition of our board of directors shall consist of at least three directors designated by Roche, three independent directors nominated by the nominating committee and one Genentech executive officer nominated by the nominating committee. Currently, three of our directors, Mr. William Burns, Dr. Erich Hunziker and Dr. Jonathan K.C. Knowles, also serve as officers and employees of Roche Holding Ltd and its affiliates. As long as Roche owns in excess of 50% of our Common Stock, Roche directors will comprise two of the three members of the nominating committee. However, at any time until Roche owns less than 5% of our stock, Roche will have the right to obtain proportional representation on our board. We cannot assure you that Roche will not seek to influence our business operations in a manner that is contrary to our goals or strategies.

Our stockholders may be unable to prevent transactions that are favorable to Roche but adverse to us

Our certificate of incorporation includes provisions relating to the following matters:

- Competition by Roche affiliates with us.
- Offering of corporate opportunities.
- Transactions with interested parties.
- Intercompany agreements.
- Provisions limiting the liability of specified employees.

Our certificate of incorporation provides that any person purchasing or acquiring an interest in shares of our capital stock shall be deemed to have consented to the provisions in the certificate of incorporation relating to competition with Roche, conflicts of interest with Roche, the offer of corporate opportunities to Roche and intercompany agreements with Roche. This deemed consent might restrict the ability to challenge transactions carried out in compliance with these provisions.

Potential conflicts of interest could limit our ability to act on opportunities that are favorable to us but adverse to Roche

Persons who are directors and/or officers of Genentech and who are also directors and/or officers of Roche may decline to take action in a manner that might be favorable to us but adverse to Roche. Three of our directors currently serve as officers and employees of Roche Holding Ltd and its affiliates.

We may incur material product liability costs

The testing and marketing of medical products entail an inherent risk of product liability. Liability exposures for biotherapeutics could be extremely large and pose a material risk. Our business may be materially and adversely affected by a successful product liability claim or claims in excess of any insurance coverage that we may have.

Insurance coverage is increasingly more difficult and costly to obtain or maintain

While we currently have a certain amount of insurance to minimize our direct exposure to certain business risks, premiums are generally increasing and coverage is narrowing in scope. As a result, we may be required to assume more risk in the future or make significant expenditures to maintain our current levels of insurance. If we are subject to third-party claims or suffer a loss or damages in excess of our insurance coverage, we will incur the cost of the portion of the retained risk. Furthermore, any claims made on our insurance policies may affect our ability to obtain or maintain insurance coverage at reasonable costs.

We are subject to environmental and other risks

We use certain hazardous materials in connection with our research and manufacturing activities. In the event such hazardous materials are stored, handled or released into the environment in violation of law or any permit, we could be subject to loss of our permits, government fines or penalties and/or other adverse governmental or private actions. The levy of a substantial fine or penalty, the payment of significant environmental remediation costs or the loss of a permit or other authorization to operate or engage in our ordinary course of business could materially adversely affect our business.

We also have acquired, and may continue to acquire in the future, land and buildings as we expand our operations. Some of these properties are "brownfields" for which redevelopment or use is complicated by the presence or potential presence of a hazardous substance, pollutant or contaminant. Certain events could occur which may require us to pay significant clean-up or other costs in order to maintain our operations on those properties. Such events include, but are not limited to, changes in environmental laws, discovery of new contamination, or unintended exacerbation of existing contamination. The occurrence of any such event could materially affect our ability to continue our business operations on those properties.

Fluctuations in our operating results could affect the price of our Common Stock

Our operating results may vary from period to period for several reasons including:

- The overall competitive environment for our products as described in "We face competition" above.
- The amount and timing of sales to customers in the U.S. For example, sales of a product may increase or decrease due to pricing changes, fluctuations in distributor buying patterns or sales initiatives that we may undertake from time to time.
- The amount and timing of our sales to Hoffmann-La Roche and our other collaborators of products for sale outside of the U.S. and the amount and timing of sales to their respective customers, which directly impacts both our product sales and royalty revenues.
- The timing and volume of bulk shipments to licensees.
- The availability and extent of government and private third-party reimbursements for the cost of therapy.
- The extent of product discounts extended to customers.
- The effectiveness and safety of our various products as determined both in clinical testing and by the accumulation of additional information on each product after the FDA approves it for sale.
- The rate of adoption by physicians and use of our products for approved indications and additional indications. Among other things, the rate of adoption by physicians and use of our products may be affected by results of clinical studies reporting on the benefits or risks of a product.
- The potential introduction of new products and additional indications for existing products.
- The ability to successfully manufacture sufficient quantities of any particular marketed product.
- Pricing decisions we may adopt.

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Our integration of new information systems could disrupt our internal operations, which could harm our revenues and increase our expenses

Portions of our information technology infrastructure may experience interruptions, delays or cessations of service or produce errors. As part of our Enterprise Resource Planning efforts, we are implementing new information systems, but we may not be successful in implementing all of the new systems, and transitioning data and other aspects of the process could be expensive, time consuming, disruptive and resource intensive. Any disruptions that may occur in the implementation of new systems or any future systems could adversely affect our ability to report in an accurate and timely manner the results of our consolidated operations, our financial position and cash flows. Disruptions to these systems also could adversely affect our ability to fulfill orders and interrupt other operational processes. Delayed sales, lower margins or lost customers resulting from these disruptions could adversely affect our financial results.

Our stock price, like that of many biotechnology companies, is volatile

The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be highly volatile in the future. In addition, the market price of our Common Stock has been and may continue to be volatile.

In addition, the following factors may have a significant impact on the market price of our Common Stock.

- Announcements of technological innovations or new commercial products by us or our competitors.
- Publicity regarding actual or potential medical results relating to products under development or being commercialized by us or our competitors.
- Developments or outcome of litigation, including litigation regarding proprietary and patent rights.
- Regulatory developments or delays concerning our products in the U.S. and foreign countries.
- Issues concerning the safety of our products or of biotechnology products generally.
- Economic and other external factors or a disaster or crisis.
- Period to period fluctuations in our financial results.

Our effective income tax rate may vary significantly

Various internal and external factors may have favorable or unfavorable effects on our future effective income tax rate. These factors include but are not limited to changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, future levels of R&D spending, and changes in overall levels of income before taxes.

To pay our indebtedness will require a significant amount of cash and may adversely affect our operations and financial results

As of December 31, 2005, we had approximately $2.1 billion of long-term debt. Our ability to make payments on and to refinance our indebtedness, including our long-term debt obligations, and to fund planned capital expenditures, R&D, as well as stock repurchases and expansion efforts will depend on our ability to generate cash in the future. This, to a certain extent, is subject to general economic, financial, competitive, legislative, regulatory and other factors that are and will remain beyond our control. Additionally, our indebtedness may increase our vulnerability to general

adverse economic and industry conditions, require us to dedicate a substantial portion of our cash flow from operations to payments on our indebtedness, which would reduce the availability of our cash flow to fund working capital, capital expenditures, R&D, expansion efforts and other general corporate purposes, and limit our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate.

Accounting pronouncements may affect our future financial position and results of operations

There may be new accounting pronouncements or regulatory rulings, which may have an affect on our future financial position and results of operations. In December 2004, the FASB issued a revision of Statement of Financial Accounting Standards (or "FAS") No. 123, "Accounting for Stock-Based Compensation." The revision is referred to as "FAS 123R — Share-Based Payment", which supersedes APB Opinion No. 25, "Accounting for Stock Issued to Employees," and will require companies to recognize compensation expense, using a fair-value based method, for costs related to share-based payments including stock options and stock issued under our employee stock plans. We have adopted FAS 123R using the modified prospective basis on January 1, 2006. Our adoption of FAS 123R is expected to result in compensation expense that will reduce diluted net income per share by approximately $0.15 to $0.17 per share for 2006. However, our estimate of future stock-based compensation expense is affected by our stock price, the number of stock-based awards our board of directors may grant in 2006, as well as a number of complex and subjective valuation assumptions and the related tax impact. These valuation assumptions include, but are not limited to, the volatility of our stock price and employee stock option exercise behaviors.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

Our headquarters facilities are located in a research and industrial area in South San Francisco, California where we currently occupy 43 owned and 5 leased buildings which house our research and development, marketing and administrative activities, as well as bulk manufacturing facilities, a fill and finish facility and a warehouse. We have made and will continue to make improvements to these properties to accommodate our growth. We also have a commitment to lease an additional eight buildings which will begin occupancy in 2006. In addition, we own other property in South San Francisco for future expansion.

We own a manufacturing facility in Vacaville, California, which is licensed to produce commercial quantities of select products. We are currently expanding our Vacaville site by constructing an additional manufacturing facility adjacent to the existing facility as well as office buildings to support the added manufacturing capacity. We expect construction, qualification and licensure of our new Vacaville plant by the end of 2009.

In June 2005, we acquired a biologics manufacturing facility in Oceanside, California. We expect manufacturing of Avastin bulk drug substance at the plant to commence in 2006 with U.S. Food and Drug Administration licensure anticipated in the first half of 2007.

We also lease additional office facilities as regional sales and marketing offices in several locations throughout the United States.

In Porriño, Spain, we own a warehouse and a cell culture manufacturing facility currently licensed for the manufacture of Avastin.

In general, our existing facilities owned or leased are in good condition and adequate for all present and near term uses and we believe our capital resources are sufficient to purchase, lease or construct any additional facilities required to meet our long-term growth needs.

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Item 3. LEGAL PROCEEDINGS

We are a party to various legal proceedings, including patent infringement litigation and licensing and contract disputes, and other matters.

On October 4, 2004, we received a subpoena from the U.S. Department of Justice, requesting documents related to the promotion of Rituxan, a prescription treatment approved for the treatment of relapsed or refractory, low-grade or follicular, CD20 positive, B-cell non-Hodgkin's lymphoma. We are cooperating with the associated investigation, which we have been advised is both civil and criminal in nature. The government has informed us that it expects to call Genentech employees to appear before a grand jury in connection with this investigation. The outcome of this matter cannot be determined at this time.

On July 29, 2005, a former Genentech employee whose employment ended in April 2005, filed a qui tam complaint under seal in the United States District Court for the District of Maine against Genentech and Biogen Idec Inc., alleging violations of the False Claims Act and retaliatory discharge of employment. On December 20, 2005, the United States District Court filed notice of its election to decline intervention in the lawsuit. The complaint was subsequently unsealed and we were served on January 5, 2006. The outcome of this matter cannot be determined at this time.

We and the City of Hope National Medical Center (or "COH") are parties to a 1976 agreement relating to work conducted by two COH employees, Arthur Riggs and Keiichi Itakura, and patents that resulted from that work, which are referred to as the "Riggs/Itakura Patents." Since that time, we have entered into license agreements with various companies to make, use and sell the products covered by the Riggs/Itakura Patents. On August 13, 1999, the COH filed a complaint against us in the Superior Court in Los Angeles County, California, alleging that we owe royalties to the COH in connection with these license agreements, as well as product license agreements that involve the grant of licenses under the Riggs/Itakura Patents. On June 10, 2002, a jury voted to award the COH approximately $300 million in compensatory damages. On June 24, 2002, a jury voted to award the COH an additional $200 million in punitive damages. Such amounts were accrued as an expense in the second quarter of 2002 and were included in the accompanying consolidated balance sheets in "litigation-related and other long-term liabilities" at December 31, 2005 and December 31, 2004. We filed a notice of appeal of the verdict and damages awards with the California Court of Appeal. On October 21, 2004, the California Court of Appeal affirmed the verdict and damages awards in all respects. On November 22, 2004, the California Court of Appeal modified its opinion without changing the verdict and denied Genentech's request for rehearing. On November 24, 2004, we filed a petition seeking review by the California Supreme Court. On February 2, 2005, the California Supreme Court granted that petition. The amount of cash paid, if any, or the timing of such payment in connection with the COH matter will depend on the outcome of the California Supreme Court's review of the matter; however, it may take longer than one year to further resolve the matter.

We recorded accrued interest and bond costs related to the COH trial judgment of $54.0 million in 2005 and $53.8 million in 2004. In conjunction with the COH judgment, we posted a surety bond and were required to pledge cash and investments of $682.0 million at December 31, 2004 to secure the bond. During the third quarter of 2005, COH requested that we increase the surety bond value by $50.0 million to secure the accruing interest, and we correspondingly increased the amount pledged to secure the bond by $53.0 million to $735.0 million at December 31, 2005. These amounts are reflected in "restricted cash and investments" in the accompanying consolidated balance sheets. We expect that we will continue to incur interest charges on the judgment and service fees on the surety bond each quarter through the process of appealing the COH trial results.

On April 11, 2003, MedImmune, Inc. (or "MedImmune") filed a lawsuit against Genentech, COH, and Celltech R & D Ltd. in the U.S. District Court for the Central District of California (Los Angeles). The lawsuit relates to U.S. Patent No. 6,331,415 (or "the '415 patent" or "Cabilly patent") that we co-own with COH and under which MedImmune and other companies have been licensed and are paying royalties to us. The lawsuit includes claims for violation of antitrust,

patent, and unfair competition laws. MedImmune is seeking to have the ‘415 patent declared invalid and/or unenforceable, a determination that MedImmune does not owe royalties under the ‘415 patent on sales of its Synagis® antibody product, an injunction to prevent us from enforcing the ‘415 patent, an award of actual and exemplary damages, and other relief. On January 14, 2004 (amending a December 23, 2003 Order), the U.S. District

Court granted summary judgment in our favor on all of MedImmune's antitrust and unfair competition claims. MedImmune sought to amend its complaint to reallege certain claims for antitrust and unfair competition. On February 19, 2004, the Court denied this motion in its entirety and final judgment was entered in favor of Genentech and Celltech and against MedImmune on March 15, 2004 on all antitrust and unfair competition claims. MedImmune filed a notice of appeal of this judgment with the U.S. Court of Appeals for the Federal Circuit. Concurrently, in the District Court litigation, we filed a motion to dismiss all remaining claims in the case. On April 23, 2004, the District Court granted our motion and dismissed all remaining claims. Final judgment was entered in our favor on May 3, 2004, thus concluding proceedings in the District Court. On October 18, 2005, the U.S. Court of Appeals for the Federal Circuit affirmed the judgment of the District Court in all respects. MedImmune filed a petition for a writ of certiorari with the United States Supreme Court on November 22, 2005 and we filed our response on December 27, 2005. No decision on the petition has been issued.

On May 13, 2005, a request was filed by a third party for reexamination of the '415 or Cabilly patent. The request sought reexamination on the basis of non-statutory double patenting over U.S. Patent No. 4,816,567. On July 7, 2005, the U.S. Patent Office ordered reexamination of the '415 patent. On September 13, 2005, the Patent Office issued an initial "non-final" Office action rejecting the claims of the '415 patent. This action is a routine and expected next step in the reexamination procedure. We filed our response to the Office action on November 25, 2005. The Patent Office has not yet acted on this response. The reexamination process is ongoing. The '415 patent, which expires in 2018, relates to methods we and others use to make certain antibodies or antibody fragments, as well as cells and DNA used in these methods. We have licensed the '415 patent to other companies and derive significant royalties from those licenses. The claims of the '415 patent remain valid and enforceable throughout the reexamination process.

On December 23, 2005, a second request for reexamination of the '415 patent was filed by another third party. On January 23, 2006, the Patent Office granted the reexamination request. Because the second request for reexamination and the above-described reexamination proceeding are ongoing, the final outcome of these matters cannot be determined at this time.

Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

Not applicable.

Executive Officers of the Company

The executive officers of the Company and their respective ages (ages as of December 31, 2005) and positions with the Company are as follows:

Name	Age	Position
Arthur D. Levinson, Ph.D.*	55	Chairman and Chief Executive Officer
Susan D. Desmond-Hellmann, M.D., M.P.H.*	48	President, Product Development
Ian T. Clark*	45	Executive Vice President, Commercial Operations
David A. Ebersman*	36	Executive Vice President and Chief Financial Officer
Stephen G. Juelsgaard, D.V.M., J.D.*	57	Executive Vice President, General Counsel, Secretary and Chief Compliance Officer
Richard H. Scheller, Ph.D.*	52	Executive Vice President, Research
Patrick Y. Yang, Ph.D.*	57	Executive Vice President, Product Operations
Robert L. Garnick, Ph.D.	56	Senior Vice President, Regulatory, Quality and Compliance
John M. Whiting	50	Vice President, Controller and Chief Accounting Officer

* Members of the Executive Committee of the Company.

The Board of Directors appoints all executive officers annually. There is no family relationship between or among any of the executive officers or directors.

Business Experience

Arthur D. Levinson, Ph.D. was appointed Chairman of the Board of Directors of Genentech, Inc. in September 1999 and was elected its Chief Executive Officer and a director of the Company in July 1995. Since joining the Company in 1980, Dr. Levinson has been a Senior Scientist, Staff Scientist and the Director of the Company's Cell Genetics Department. Dr. Levinson was appointed Vice President of Research Technology in April 1989, Vice President of Research in May 1990, Senior Vice President of Research in December 1992, Senior Vice President of Research and Development in March 1993 and President in July 1995. Dr. Levinson also serves as a member of the Board of Directors of Apple Computer, Inc. and Google, Inc.

Susan D. Desmond-Hellmann, M.D., M.P.H. was appointed President, Product Development of Genentech in March 2004. She previously served as Executive Vice President, Development and Product Operations from September 1999 to March 2004, Chief Medical Officer from December 1996 to March 2004, and as Senior Vice President,

Development from December 1997 to September 1999, among other positions, since joining Genentech in March 1995 as a Clinical Scientist. Prior to joining Genentech, she held the position of Associate Director at Bristol-Myers Squibb.

Ian T. Clark was appointed Executive Vice President, Commercial Operations of Genentech in December 2005. He previously served as Senior Vice President, Commercial Operations of Genentech from August 2005 to December 2005 and joined Genentech as Senior Vice President and General Manager, BioOncology and served in that role from January 2003 through August 2005. Prior to joining Genentech, he served as president for Novartis Canada from 2001 to 2003. Before assuming his post in Canada, he served as chief operating officer for Novartis United Kingdom from 1999 to 2001.

David A. Ebersman was appointed Executive Vice President of Genentech in December 2005 and Chief Financial Officer in March 2005. Previously, he served as Senior Vice President, Finance from January 2005 through March 2005 and Senior Vice President, Product Operations from May 2001 through January 2005. He joined Genentech in February 1994 as a Business Development Analyst and subsequently served as Manager, Business Development from February 1995 to February 1996, Director, Business Development from February 1996 to March 1998, Senior Director, Product Development from March 1998 to February 1999 and Vice President, Product Development from February 1999 to May 2001. Prior to joining Genentech, he held the position of Research Analyst at Oppenheimer & Company, Inc.

Stephen G. Juelsgaard, D.V.M., J.D. was appointed Chief Compliance Officer of Genentech in June 2005, Executive Vice President in September 2002, Vice President and General Counsel in July 1994 and Secretary in April 1997. He joined Genentech in July 1985 as Corporate Counsel and subsequently served as Senior Corporate Counsel from 1988 to 1990, Chief Corporate Counsel from 1990 to 1993, Vice President, Corporate Law from 1993 to 1994, Assistant Secretary from 1994 to 1997 and Senior Vice President from April 1998 to September 2002.

Richard H. Scheller, Ph.D. was appointed Executive Vice President, Research of Genentech in September 2003. Previously, he served as Senior Vice President, Research from March 2001 to September 2003. Prior to joining Genentech, he served as Professor of Molecular and Cellular Physiology and of Biological Sciences at Stanford University Medical Center from September 1982 to February 2001 and as an investigator at the Howard Hughes Medical Institute from September 1990 to February 2001. He received his first academic appointment to Stanford University in 1982. He was appointed to the esteemed position of professor of Molecular and Cellular Physiology in 1993 and as an investigator in the Howard Hughes Medical Institute in 1994.

Patrick Y. Yang, Ph.D. was appointed Executive Vice President, Product Operations of Genentech in December 2005. Previously, he served as Senior Vice President, Product Operations from January 2005 through December 2005 and Vice President, South San Francisco Manufacturing and Engineering from December 2003 to January 2005. Prior to joining Genentech, he worked for General Electric from 1980 to 1992 in manufacturing and technology and for Merck & Co. Inc. from 1992 to 2003 in manufacturing. At Merck, he held several executive positions including Vice President, Supply Chain Management from 2001 to 2003 and Vice President, Asia/Pacific Manufacturing Operations from 1997 to 2000.

Robert L. Garnick, Ph.D. was appointed Senior Vice President, Regulatory, Quality and Compliance of Genentech in February 2001. Previously, he served as Vice President, Regulatory Affairs from February 1998 to February 2001, Vice President, Quality from April 1994 to February 1998, Senior Director, Quality Control from 1990 to 1994 and Director, Quality Control from 1988 to 1990. He joined Genentech in August 1984 from Armour Pharmaceutical, where he held various positions.

John M. Whiting was appointed Vice President of Genentech in January 2001 and Controller and Chief Accounting Officer in October 1997. He previously served in a variety of financial positions at Genentech from 1989 to 1997. Prior to joining Genentech, he served as Senior Audit Manager at Arthur Young.

PART II

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

See "Liquidity and Capital Resources — Cash Provided by or Used in Financing Activities" in "Management's Discussion and Analysis of Financial Condition and Results of Operations" of Part II, Item 7 of this Form 10-K, Note 1, "Description of Business — Redemption of Our Special Common Stock," Note 8, "Relationship with Roche and Related Party Transactions," and Note 9, "Capital Stock," in the Notes to Consolidated Financial Statements of Part II, Item 8 of this Form 10-K.

Stock Trading Symbol: DNA

Stock Exchange Listing

Our Common Stock trades on the New York Stock Exchange under the symbol "DNA." No dividends have been paid on the Common Stock. We currently intend to retain all future income for use in the operation of our business and for future stock repurchases and, therefore, do not anticipate paying any cash dividends in the near future.

Common Stockholders

As of December 31, 2005, there were approximately 2,350 stockholders of record of our Common Stock, one of which is Cede & Co., a nominee for Depository Trust Company (or "DTC"). All of the shares of Common Stock held by brokerage firms, banks and other financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC, and are therefore considered to be held of record by Cede & Co. as one stockholder.

Stock Prices

	Common Stock			
	2005		2004	
	High	Low	High	Low
4th Quarter	$ 100.20	$ 79.87	$ 55.98	$ 41.00
3rd Quarter	94.99	79.71	56.61	43.00
2nd Quarter	84.10	54.68	68.25	50.11
1st Quarter	59.00	43.90	56.98	44.74

All information in this report relating to the number of shares, price per share and per share amounts of Common Stock give effect to the May 2004 two-for-one stock split of our Common Stock.

Stock Repurchases

See "Liquidity and Capital Resources — Cash Provided by or Used in Financing Activities" in "Management's Discussion and Analysis of Financial Condition and Results of Operations" of Part II, Item 7 of this Form 10-K for information on our stock repurchases.

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Item 6. SELECTED FINANCIAL DATA

The following selected consolidated financial information has been derived from the audited consolidated financial statements. The information below is not necessarily indicative of results of future operations, and should be read in conjunction with Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" of this Form 10-K and the consolidated financial statements and related notes thereto included in Item 8 of this Form 10-K in order to fully understand factors that may affect the comparability of the information presented below.

SELECTED CONSOLIDATED FINANCIAL DATA

(in millions, except per share amounts)

	2005	2004	2003	2002	2001
Total operating revenues	$ 6,633.4	$ 4,621.2	$ 3,300.2	$ 2,583.7	$ 2,044.1
Product sales	5,488.1	3,748.9	2,621.4	2,163.6	1,742.9
Royalties	935.1	641.1	500.9	365.6	264.5
Contract revenue	210.2	231.2	177.9	54.5	36.7
Income before cumulative effect of accounting changes	$ 1,279.0	$ 784.8	$ 610.1	$ 63.8	$ 155.9
Cumulative effect of accounting changes, net of tax	-	-	(47.6)[6]	-	(5.6)[9]
Net income[1]	$ 1,279.0 [2]	$ 784.8 [5]	$ 562.5 [6]	$ 63.8 [8]	$ 150.3 [9]
Basic earnings per share	$ 1.21	$ 0.74	$ 0.54	$ 0.06	$ 0.14
Diluted earnings per share	1.18	0.73	0.53	0.06	0.14
Total assets	$ 12,146.9	$ 9,403.4 [4]	$ 8,759.5 [4]	$ 6,775.5	$ 7,161.5
Long-term debt	2,083.0 [3]	412.3 [4]	412.3 [4]	- [7]	- [7]
Stockholders' equity	7,469.6	6,782.2	6,520.3	5,338.9	5,919.8

We have paid no dividends.

All per share amounts reflect the two-for-one stock split that was effected in 2004.

Certain prior year amounts have been reclassified to conform with the current year presentation.

(1) Net income includes pre-tax recurring charges of $122.7 million in 2005, $145.5 million in 2004, $154.3 million in 2003, $155.7 million in 2002, and $321.8 million in 2001 related to the June 30, 1999 redemption of our Special Common Stock (or "the Redemption").

(2) Net income in 2005 includes accrued interest and bond costs related to the City of Hope (or "COH") trial judgment and net amounts paid related to other litigation settlements.

(3) Includes approximately $2 billion related to our debt issuance in July 2005, and reflects the repayment of the consolidated debt related to the manufacturing facility located in Vacaville, California.

(4) Upon adoption of FIN 46, we consolidated the entity from which we lease our manufacturing facility located in Vacaville, California. Accordingly, we included in property, plant and equipment assets with net book values of $325.9 million at

December 31, 2004 and $348.4 million at December 31, 2003. We also consolidated the entity's debt of $412.3 million and noncontrolling interest of $12.7 million, which amounts are included in long-term debt and litigation-related and other long-term liabilities, respectively, at December 31, 2004 and 2003. During the third quarter of 2005, we paid $425.0 million to extinguish the debt and noncontrolling interest related to the synthetic lease obligation.

(5) Net income in 2004 includes accrued interest and bond costs related to the COH trial judgment, net of a released accrual on a separate litigation matter.

(6) Net income in 2003 includes litigation settlements with Amgen Inc. and Bayer Inc., net of accrued interest and bond costs related to the COH judgment. Net income in 2003 also reflects our adoption of the Financial Accounting Standards Board Interpretation No. 46 (or “FIN 46”), “Consolidation of Variable Interest Entities,” on July 1, 2003, which resulted in a $47.6 million charge, net of $31.8 million in taxes, (or $0.05 per share) as a cumulative effect of an accounting change in 2003.

(7) The $149.7 million of convertible subordinated debentures was reclassified to current liabilities in 2001 to reflect the March 27, 2002 maturity. We redeemed the debentures in cash at maturity.

(8) Net income in 2002 includes $543.9 million of pre-tax litigation-related special charges, which are comprised of the COH litigation judgment in 2002, and accrued interest and bond costs, and certain other litigation-related matters. Net income in 2002 also reflects our adoption of Statement of Financial Accounting Standards (or “FAS”) 141 and 142 on January 1, 2002. As a result of our adoption, reported net income increased by approximately $157.6 million (or $0.15 per share) due to the cessation of goodwill amortization and the amortization of our trained and assembled workforce intangible asset.

(9) Net income in 2001 reflects a $5.6 million charge (net of $3.8 million in taxes) as a cumulative effect of a change in accounting principle and changes in estimated fair value of certain derivatives ($10.0 million gain) as a result of our adoption of FAS 133 on January 1, 2001.

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

Overview

The Company

Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes biotherapeutics for significant unmet medical needs. We commercialize multiple biotechnology products, and also receive royalties from companies that are licensed to market products based on our technology.

Major Developments in 2005

Our total operating revenues in 2005 were $6.63 billion, an increase of 44% from $4.62 billion in 2004. Our net income in 2005 was $1.28 billion, an increase of 63% from $784.8 million in 2004.

In 2005 we announced positive data from eight Phase III clinical trials and we, in certain instances with our collaborators OSI or Biogen Idec, submitted several filings to the U.S. Food and Drug Administration (or "FDA") including: (i) Avastin for use in combination with 5-fluorouracil (or "5-FU")-based chemotherapy for patients with relapsed, metastatic colorectal cancer; (ii) Rituxan to treat front-line intermediate grade or aggressive non-Hodgkin's lymphoma (or "NHL"), which was approved by the FDA on February 10, 2006; (iii) Rituxan to treat patients with active rheumatoid arthritis (or "RA") who inadequately respond to anti-tumor necrosis factor therapy; (iv) Tarceva for use in combination with gemcitabine chemotherapy for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, which was approved by the FDA in November 2005; and (v) Lucentis (ranibizumab) to treat neovascular wet form age-related macular degeneration (or "AMD").

We are aware that some retinal specialists are currently using Avastin to treat wet AMD, an unapproved use. We have no clinical data on either the safety or efficacy of Avastin in this use, nor do we have any plans for a clinical development program evaluating Avastin in AMD. Further, we are concerned about the potential sterility issues associated with aliquoting vials of Avastin into smaller portions for use as an intravitreal injection. However, there may be continued Avastin use in this setting even after Lucentis has been approved for commercial use, which may decrease the market potential for Lucentis. We remain focused on making Lucentis available to patients by seeking FDA approval as soon as possible.

In June 2005, we acquired Biogen Idec's Oceanside, California biologics manufacturing facility (or "Oceanside plant") for $408.1 million in cash plus $9.3 million in closing costs. The 60-acre, 500,000 square-foot Oceanside plant has 90,000 liters of bioreactor capacity. We expect manufacturing of Avastin bulk drug substance at the plant to commence in 2006 with FDA licensure anticipated in the first half of 2007.

On July 18, 2005, we completed a private placement of the following debt instruments: $500.0 million principal amount of 4.40% Senior Notes due 2010, $1.0 billion principal amount of 4.75% Senior Notes due 2015 and $500.0 million principal amount of 5.25% Senior Notes due 2035. We received approximately $1.99 billion in net proceeds from this offering, after deducting selling and offering expenses.

Our Strategy

2005 was the final year of our 5x5 business plan. We exceeded our most important goal of average annual non-GAAP EPS growth. We exceeded our goal of five significant products/indications in late stage development and have exceeded our goal of five new products or indications approved through 2005. We did not meet our goal of $500 million in new revenue from alliances and/or acquisitions. We did not meet our non-GAAP net income as a

percentage of total operating revenues goal, due primarily to the success of Rituxan, net of the associated profit split with Biogen Idec. Information on our 5x5 plan can be found on our website at http://www.gene.com.

Economic and Industry-wide Factors

Our goals and objectives are challenged by economic and industry-wide factors that affect our business. Some of the most important factors are discussed below:

- Successful development of biotherapeutics is highly difficult and uncertain. Our long-term business growth depends upon our ability to commercialize important new therapeutics to treat unmet medical needs such as cancer. Since the underlying biology of these diseases is not completely understood, it is very challenging to discover and develop safe and effective treatments, and the majority of potential new therapeutics fail to generate the safety and efficacy data required to obtain regulatory approval. In addition, there is tremendous competition in the diseases of interest to us. Our business requires significant investments in research and development (or "R&D") over many years, often for products that fail during the R&D process. In addition, after our products receive FDA approval, they remain subject to ongoing FDA regulation, including changes to the product label, new or revised regulatory requirements for manufacturing practices, written advisement to physicians, or product recalls. We believe that our continued focus on excellent science, compelling biological mechanisms, and designing high quality clinical trials to address significant medical needs positions us well to deliver sustainable growth.

- Intellectual property protection of our products is crucial to our business. Loss of effective intellectual property protection on one or more products could result in lost sales to competing products and negatively affect our sales, royalty revenues and operating results. We are often involved in disputes over contracts and intellectual property and we work to resolve these disputes in confidential negotiations or litigation. We expect legal challenges in this area to continue. We plan to continue to build upon and defend our intellectual property position.

    - Manufacturing biotherapeutics is difficult and complex, and requires facilities specifically designed and validated to run biotechnology production processes. The manufacture of a biotherapeutic requires developing and maintaining a process to reliably manufacture and formulate the product at an appropriate scale, obtaining regulatory approval to manufacture the product, and is subject to changes in regulatory requirements or standards that may require modifications to the involved manufacturing process or FDA action (see above in "Difficulties or delays in product manufacturing or in obtaining materials from our suppliers could harm our business and/or negatively affect our financial performance" of "Risk Factors" in Part I, Item 1A of this Form 10-K).

- The Medicare Prescription Drug Improvement and Modernization Act (or "Medicare Act") was enacted into law in December 2003. On November 3, 2004, the 2005 Physician Fee Schedule and Hospital Outpatient Prospective Payment System Final Rules were announced and were in-line with our expectations. As Centers for Medicare and Medicaid Services (or "CMS") is our single largest payer, the new rules represented an important area of focus in 2005. To date, we have not seen any detectable effects of the new rules on our product sales. We continue to anticipate minimal effects on our revenues in 2006. On November 2, 2005, CMS released its Final Rule with comment on the Medicare Part B Competitive Acquisition Program (or "CAP"). The CAP option, which the CMS expects to begin in July 2006, required under the Medicare Act, will be available to physicians providing services under Part B of Medicare. Under the CAP, physicians could choose to either obtain drugs directly from qualified CAP vendors, or continue to purchase drugs directly and be reimbursed by CMS at the Average Selling Price + 6% rate. Although CMS is still finalizing details of the program, we anticipate that the impact of the program on our sales will be minimal.

- With respect to follow-on biologics, we believe that current technology cannot prove a follow-on biotechnology product to be safe and effective outside the New Drug Application and Biologics License Application (or "BLA") process. We filed a Citizen Petition with the FDA in April 2004 requesting that the agency re-assess its approach to approvals of follow-on biologics and put processes in place to protect trade secrets and confidential information from use by others. The FDA initiated a public process to discuss the complex scientific issues surrounding

follow-on biologics and we participated in the FDA Stakeholder meeting in September 2004. Following this meeting, the FDA and Drug Information Association held a scientific workshop in February 2005, which we hope will be followed by a similar public discussion of the

critical legal issues involved with establishing an approval pathway for follow-on biologics.

- Our ability to attract and retain highly qualified and talented people in all areas of the company, and our ability to maintain our unique culture, will be critical to our success over the long-term. During 2005, we experienced a 25% growth in the number of employees to over 9,500 employees company-wide as of December 31, 2005. This significant growth in employees is challenging to manage and we are working diligently across the company to make sure that we successfully hire, train and integrate new employees into the Genentech culture and environment.

Critical Accounting Policies and the Use of Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States (or "GAAP"). The preparation of these consolidated financial statements requires management to make estimates, assumptions and judgments that affect the reported amounts in our consolidated financial statements and accompanying notes. These estimates form the basis for making judgments about the carrying values of assets and liabilities. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, and we have established internal controls related to the preparation of these estimates. Actual results and the timing of the results could differ materially from these estimates.

We believe the following policies to be critical to understanding our financial condition, results of operations, and our expectations for 2006 because these policies require management to make significant estimates, assumptions and judgments about matters that are inherently uncertain.

Legal Contingencies

We are currently, or have been, involved in certain legal proceedings as discussed in Note 7, "Leases, Commitments and Contingencies," in the Notes to Consolidated Financial Statements of Part II, Item 8 of this Form 10-K. We assess the likelihood of any adverse judgments or outcomes to these legal matters as well as potential ranges of probable losses. Included in "litigation-related and other long-term liabilities" in the accompanying consolidated balance sheet at December 31, 2005 is $676.1 million, which represents our estimate of the costs for the current resolution of these matters. The nature of these matters is highly uncertain and subject to change; as a result, the amount of our liability for certain of these matters could exceed or be less than the amount of our current estimates, depending on the final outcome of these matters. An outcome of such matters different than previously estimated could have a material effect on our financial position or our results of operations in any one quarter.

Product Sales Allowances

Revenues from product sales, which are principally generated in the United States (or "U.S."), are recorded net of allowances for rebates, wholesaler chargebacks, prompt pay sales discounts, product returns, wholesaler incentives, and bad debts, all of which are established at the time of sale. In order to prepare our consolidated financial statements, we are required to make estimates regarding the amounts earned or to be claimed on the related product sales.

Rebate reserves and accruals represent our estimated obligations to wholesalers and third parties (clinics, hospitals and pharmacies), respectively. These rebates and accruals result from performance-based offers that are primarily based on attaining contractually specified sales volumes and growth. As a result, the calculation of the accrual for these rebates requires an estimate of the customer's buying patterns and the resulting applicable contractual rebate rate(s) to be earned over a contractual period. If our estimate of a customer's buying patterns is incorrect, we may need to adjust our estimates in future periods. In 2005, the majority of these rebates related to our non-oncology products.

To date, we have not recorded any adjustments to our estimates of product sales allowances that were material to our consolidated financial statements. However, it is possible that we may need to adjust our estimates in future periods. As of December 31, 2005, our consolidated balance sheet reflected product sales allowance reserves and accruals

totaling approximately $126.4 million and for the year ended December 31, 2005, our net product sales were approximately $5,488.1 million.

Royalties

Under some of our agreements with licensees that include receipt of royalty revenue, we do not have sufficient historical information to estimate royalty revenues or receivables in the period that these royalties are earned. For these contracts, we record royalty revenue upon cash receipt. However, for the majority of our agreements with licensees, we estimate royalty revenue and royalty receivables in the periods these royalties are earned, in advance of collection. Our estimate of royalty revenue and receivables in those instances is based upon communication with some licensees, historical information and forecasted sales trends. Differences between actual revenues and estimated royalty revenue are adjusted for in the period which they become known, typically the following quarter. Historically, such adjustments have not been material to our consolidated financial condition or results of operations. As of December 31, 2005, our royalties accounts receivable was approximately $296.7 million and for the year ended December 31, 2005, our royalty revenues were approximately $935.1 million.

Income Taxes

Income tax expense is based on income before taxes and is computed using the liability method. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Significant estimates are required in determining our provision for income taxes. Some of these estimates are based on interpretations of existing tax laws or regulations. Various internal and external factors may have favorable or unfavorable effects on our future effective income tax rate. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, future levels of R&D spending, and changes in overall levels of income before taxes. During 2005, we recorded various adjustments to our tax provision based on changes in one or more of the factors noted above.

Inventories

Inventories consist of currently marketed products, products manufactured under contract, product candidates awaiting regulatory approval and currently marketed products manufactured at facilities awaiting regulatory approval, which are capitalized based on management's judgment of probable near term commercialization. The valuation of inventory requires us to estimate the value of inventory that may become obsolete prior to use or that may fail to be released. The determination of obsolete inventory requires us to estimate the future demands for our products, and in the case of pre-approval inventories, an estimate of the regulatory approval date for the product. We may be required to expense previously capitalized inventory costs upon a change in our judgment, due to, among other potential factors, a denial or delay of approval by the necessary regulatory bodies or new information that suggests that the inventory will not be releasable. In the event that a pre-approval product candidate receives regulatory approval, subsequent sales of previously reserved inventory may result in increased gross margins.

Valuation of Stock Options

In order to estimate the value of stock options, we use the Black-Scholes model, which requires the use of certain subjective assumptions. The most significant assumptions are our estimates of the expected volatility and the expected term of the award. Due to the redemption of our Special Common Stock in June 1999 (or "Redemption") by Roche Holdings, Inc. (or "Roche"), there is limited historical information available to support our estimate of certain assumptions required to value stock options. The value of a stock option is derived from its potential for appreciation. The more volatile the stock, the more valuable the option becomes because of the greater possibility of significant changes in stock price. Because there is an active market for options on our Common Stock, we believe that it is

appropriate to place greater weight on implied volatilities than on historical realized volatilities when developing an estimate of expected volatility. We believe that implied volatilities of options with appropriate terms are better indicators of market participants' expectations about future volatility. The expected option term also has a significant effect on the value of the option. The longer the term, the more time the option holder has to allow the stock price to increase without a cash investment and thus, the more valuable the option. Further, lengthier option

terms provide more opportunity to exploit market highs. However, empirical data shows that employees, for a variety of reasons, typically do not wait until the end of the contractual term of a nontransferable option to exercise. Accordingly, companies are required to estimate the expected term of the option for input to an option-pricing model. When establishing an estimate of the expected term, we consider the vesting period for the award, our historical experience of employee stock option exercises, the expected volatility, and a comparison to relevant peer group data. As required under the accounting rules, we review our valuation assumptions at each grant date and, as a result, we are likely to change our valuation assumptions used to value stock based awards granted in future periods.

Results of Operations
(In millions)

				Annual Percent Change	
	2005	**2004**	**2003**	**2005/2004**	**2004/2003**
Product sales	$ 5,488.1	$ 3,748.9	$ 2,621.4	46%	43%
Royalties	935.1	641.1	500.9	46	28
Contract revenue	210.2	231.2	177.9	(9)	30
Total operating revenues	6,633.4	4,621.2	3,300.2	44	40
Cost of sales	1,011.1	672.5	480.1	50	40
Research and development	1,261.8	947.5	722.0	33	31
Marketing, general and administrative	1,435.0	1,088.2	794.8	32	37
Collaboration profit sharing	823.1	593.6	457.5	39	30
Recurring charges related to redemption	122.7	145.5	154.3	(16)	(6)
Special items: litigation-related	57.8	37.1	(113.1)	56	*
Total costs and expenses	4,711.5	3,484.4	2,495.6	35	40
Operating income	1,921.9	1,136.8	804.6	69	41
Other income (expense):					
Interest and other income (expense), net	140.9	90.0	95.7	57	(6)
Interest expense	(49.9)	(7.4)	(2.9)	574	155
Total other income, net	91.0	82.6	92.8	10	(11)
Income before taxes and cumulative effect of accounting change	2,012.9	1,219.4	897.4	65	36
Income tax provision	733.9	434.6	287.3	69	51
Income before cumulative effect of accounting change	1,279.0	784.8	610.1	63	29
Cumulative effect of accounting change, net of tax	-	-	(47.6)	-	*
Net income	$ 1,279.0	$ 784.8	$ 562.5	63	40
Earnings per share:					
Basic:					
Earnings before cumulative effect of accounting change	$ 1.21	$ 0.74	$ 0.59	64	25
Cumulative effect of accounting change, net of tax	-	-	(0.05)	-	*
Net earnings per share	$ 1.21	$ 0.74	$ 0.54	64	37
Diluted:					
Earnings before cumulative effect of accounting change	$ 1.18	$ 0.73	$ 0.58	62	26
Cumulative effect of accounting change, net of tax	-	-	(0.05)	-	*
Net earnings per share	$ 1.18	$ 0.73	$ 0.53	62%	38%
Pretax operating margin	29%	25%	24%		
COS as a % of product sales	18	18	18		
R&D as a % of operating revenues	19	21	22		
MG&A as a % of operating revenues	22	24	24		
NI as a % of operating revenues	19	17	17		

Percentages in this table and throughout our discussion and analysis of financial condition and results of operations may reflect rounding adjustments.

* Calculation not meaningful.

Total Operating Revenues

Total operating revenues increased 44% to $6,633.4 million in 2005 and increased 40% to $4,621.2 million in 2004. These increases were primarily due to higher product sales and royalty revenue, and are further discussed below.

Total Product Sales
(In millions)

Product Sales	2005	2004	2003	Annual Percent Change 2005/2004	2004/2003
Net U.S. Product Sales					
Rituxan	$ 1,831.4	$ 1,574.0	$ 1,360.2	16%	16%
Avastin	1,132.9	544.6	-	108	-
Herceptin	747.2	479.0	406.0	56	18
Tarceva	274.9	13.3	-	*	-
Xolair	320.6	187.6	25.1	71	647
Raptiva	79.2	52.4	1.4	51	*
Nutropin products	370.5	348.8	319.5	6	9
Thrombolytics	218.5	194.4	181.7	12	7
Pulmozyme	186.5	157.1	143.7	19	9
Total U.S. product sales	5,161.7	3,551.2	2,437.6	45	46
Net product sales to collaborators	326.4	197.7	183.8	65	8
Total product sales	$ 5,488.1	$ 3,748.9	$ 2,621.4	46	43

* Calculation not meaningful.

Total net product sales increased 46% to $5,488.1 million in 2005 and increased 43% to $3,748.9 million in 2004. Net U.S. sales increased 45% to $5,161.7 million in 2005 and increased 46% to $3,551.2 million in 2004. These increases in U.S. sales were due to higher sales across all products, in particular higher sales of our oncology products. U.S. oncology sales accounted for 77% of U.S. product sales in 2005 compared to 74% in 2004 and 72% in 2003. Increased U.S. sales volume accounted for 88%, or $1,411.2 million, of the increase in U.S. net product sales in 2005, and 92%, or $1,020.2 million in 2004. The increased U.S. sales volume in 2004 also included new product shipments. Changes in net U.S. sales prices across the portfolio accounted for most of the remainder of the increases in U.S. net product sales in 2005 and 2004.

Rituxan

Net U.S. sales of Rituxan increased 16% to $1,831.4 million in 2005 and 16% to $1,574.0 million in 2004. Net U.S. sales in 2005 included $9.6 million for a reorder to replace a shipment that was destroyed while in transit to a wholesaler in the first quarter of 2005. U.S. sales growth in the past two years resulted from increased physician adoption for treatment of indolent NHL with a maintenance regimen (or “Rituxan maintenance”), treatment of aggressive NHL, and chronic lymphocytic leukemia (or “CLL”) (all unapproved uses of Rituxan during those respective periods). Rituxan’s overall adoption rate in combined markets of NHL and CLL, including areas of unapproved uses, was 82% at the end of 2005 compared to 75% at the end of 2004. Also contributing to the increase in 2005 sales compared to 2004 were price increases that were effective on July 6, 2005 and October 5, 2005. The 2004 sales increase also resulted from increased physician adoption for the treatment of relapsed aggressive NHL and, to a lesser extent, a price increase in 2003.

In September 2005, we obtained FDA licensure of Lonza Biologic’s Portsmouth, New Hampshire manufacturing plant for the production of Rituxan bulk drug substance.

The U.S. Pharmacopeia Drug Information® (or “USP DI”) compendium was updated in October 2005, and now includes Rituxan for front-line CLL as an accepted indication. We expect that most payers who have not updated their coverage will do so shortly.

On October 25, 2005, we and Biogen Idec announced that the FDA granted Priority Review for Rituxan's supplemental Biologics License Application (or "sBLA") submitted for the front-line treatment of intermediate-grade or aggressive NHL, and on February 10, 2006, the FDA approved the use of Rituxan in this indication.

On October 31, 2005, we and Biogen Idec announced that the FDA accepted, and granted priority review for, the sBLA submitted for Rituxan for treatment of patients with active RA who inadequately respond to anti-tumor necrosis factor therapy.

Avastin

Net U.S. sales of Avastin increased 108% to $1,132.9 million in 2005. Net U.S. sales in 2004 were $544.6 million after launch in February 2004. The increase in sales was primarily a result of increased use of Avastin in colorectal cancer (or "CRC") in first-line metastatic CRC (our approved indication) and unapproved CRC uses. In the treatment of colorectal cancer in both the first-line metastatic and relapsed/refractory (unapproved uses) settings, Avastin is being combined with a wide range of 5-FU-based chemotherapies. While there has been rapid uptake in the first-line setting, opportunities remain to further increase duration of therapy on Avastin and to continue efforts to appropriately identify eligible patients. We also anticipate growth from use in potential new (but currently unapproved) uses, including relapsed metastatic colorectal cancer, metastatic non-small cell lung and breast cancers. In 2005, use of Avastin in unapproved indications contributed to increased sales relative to 2004.

In August and September 2005, the USP DI issued certain decisions on the use of Avastin in lung, renal cell carcinoma (or "RCC") and relapsed colorectal cancer. On September 6, 2005, the USP DI accepted the Avastin NSCLC data. A review that is deemed acceptable by the USP DI supports Medicare reimbursement by statute and facilitates reimbursement with the private payers. In contrast, the USP DI has deemed the data on Avastin use in RCC and relapsed colorectal cancer as not sufficient to establish acceptance at this time. We plan to re-submit the request in relapsed colorectal cancer. We are still waiting for the decision on the first-line metastatic breast cancer submission for Avastin.

On December 19, 2005, we announced that an sBLA was submitted to the FDA for Avastin in combination with 5-FU-based chemotherapy for patients with relapsed, metastatic colorectal cancer.

On February 12, 2006, we announced that enrollment into an international Phase III study evaluating FOLFOX, FOLFOX plus Avastin, and XELOX plus Avastin in early-stage colon cancer was temporarily suspended to enable the Data Safety Monitoring Board (or "DSMB") to conduct a review of 60-day safety data. The DSMB's recommendations are based on certain adverse events observed at a higher rate in the XELOX plus Avastin arm of the study compared to the other two arms of the study (FOLFOX and FOLFOX plus Avastin).

Herceptin

Net U.S. sales of Herceptin increased 56% to $747.2 million in 2005 and 18% to $479.0 million in 2004. The 2005 growth resulted from an increased use of Herceptin in the adjuvant breast cancer setting, which is not an approved indication, increased treatment of first-line HER2 positive metastatic breast cancer, and increased cumulative treatment duration relative to 2004. Also contributing to the growth in sales in 2005, although to a lesser extent, was a price increase that was effective on February 24, 2005. The growth in 2004 resulted from multiple factors, including physicians' extension of the average treatment duration and increased first-line penetration, and a growing adoption by physicians of a number of combinations of Herceptin with different agents. In addition to the above factors, we implemented price increases in 2004 and 2003, which contributed to a lesser extent to the 2004 growth.

The USP DI compendium was updated in October 2005, and now includes Herceptin in the adjuvant breast cancer setting. We expect that most payers who have not updated their coverage will do so shortly.

On February 15, 2006, we announced that an sBLA was submitted to the FDA for Herceptin for treatment of patients with early-stage, HER2-positive breast cancer.