BIOGEN IDEC INC.
Form 10-K
February 14, 2008

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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, 2007

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: 0-19311
Biogen Idec Inc.
(Exact name of registrant as specified in its charter)

Delaware	**33-0112644**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
14 Cambridge Center, Cambridge, Massachusetts	**02142**
(Address of principal executive offices)	*(Zip code)*

(Registrant s telephone number, including area code)
(617) 679-2000
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.0005 par value **Series X Junior Participating Preferred Stock Purchase Rights**	**The Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Act:
None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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 the Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

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

Large accelerated filer þ	Accelerated filer o	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes o No þ

The aggregate market value of the Registrant s Common Stock held by non-affiliates of the Registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the Registrant s most recently completed second fiscal quarter was $18,378,524,103.

As of February 8, 2008, the Registrant had 297,750,601 shares of Common Stock, $0.0005 par value, issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for our 2008 Annual Meeting of Stockholders are incorporated by reference into Part III of this Report.

BIOGEN IDEC INC.

ANNUAL REPORT ON FORM 10-K

For the Year Ended December 31, 2007

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PART I

Item 1. *Business*

Overview

Biogen Idec creates new standards of care in therapeutic areas with high unmet medical needs. Biogen Idec is a global leader in the development, manufacturing, and commercialization of innovative therapies. Patients in more than 90 countries benefit from Biogen Idec s significant products that address diseases such as multiple sclerosis, lymphoma and rheumatoid arthritis. We currently have four products:

AVONEX® (interferon beta-1a)

AVONEX is approved worldwide for the treatment of relapsing forms of multiple sclerosis, or MS, and is the most prescribed therapeutic product in MS worldwide. Globally over 135,000 patients use AVONEX.

RITUXAN® (rituximab)

RITUXAN is approved worldwide for the treatment of relapsed or refractory low-grade or follicular, CD20-positive, B-cell non-Hodgkin s lymphomas, or B-cell NHLs. The U.S. Food and Drug Administration, or FDA, has also approved RITUXAN for (1) the treatment of patients with previously untreated diffuse, large B-cell NHL in combination with anthracycline-based chemotherapy regimens, (2) treatment of patients with previously-untreated follicular NHL in combination with CVP (cyclophosphamide, vincristine and prednisone) chemotherapy, and (3) the treatment of patients with non-progressing (including stable disease) low grade B-cell NHL following first-line treatment with CVP chemotherapy. We believe that RITUXAN is the second highest-selling oncology therapeutic in the United States and has had more than 1,000,000 patient exposures worldwide across all indications. In addition, RITUXAN, in combination with methotrexate, is also approved for reducing signs and symptoms and to slow the progression of structural damage in adult patients with moderately-to-severely active rheumatoid arthritis, or RA, who have had an inadequate response to one or more tumor necrosis factor, or TNF, antagonist therapies. We are working with Genentech and Roche on the development of RITUXAN in additional oncology, neurology and immunology indications.

RITUXAN is the trade name for the compound rituximab in the U.S., Canada and Japan. MabThera is the trade name for rituximab in the European Union, or EU. In this Annual Report, we refer to rituximab, RITUXAN, and MabThera collectively as RITUXAN, except where we have otherwise indicated.

TYSABRI® (natalizumab)

TYSABRI is approved for the treatment of relapsing forms of MS in the U.S. and other countries, and in the U.S. for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn s disease, or CD, with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-alpha. Under the terms of a collaboration agreement with Elan Corporation plc, or Elan, we are solely responsible for the manufacture of TYSABRI, and we collaborate with Elan on the product s marketing, commercial distribution and on-going development activities. The collaboration agreement with Elan is designed to effect an equal sharing of profits and losses generated by the activities of the collaboration between Elan and us.

FUMADERM® (dimethylfumarate and monoethylfumarate salts)

FUMADERM was acquired with the purchase of Fumapharm AG, or Fumapharm, in June 2006. In December 2006, we acquired the right to distribute FUMADERM in Germany from Fumedica effective May 1, 2007. FUMADERM acts as an immunomodulator and has been approved in Germany for the treatment of severe psoriasis since 1994.

Other Revenue and Programs

In 2007, we recorded product revenues from sales of *ZEVALIN® (ibritumomab tiuxetan)* prior to our sale of U.S. rights to this product line in December 2007.

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We also receive royalty revenues on sales by our licensees of a number of products covered under patents that we control. In addition, we have a pipeline of research and development products in our core therapeutic areas and in other areas of interest.

We devote significant resources to research and development programs and external business and corporate development efforts. We intend to focus our research and development efforts on finding novel therapeutics in areas of high unmet medical need, both within our current focus areas of oncology, neurology, immunology and cardiology as well as in new therapeutic areas. Our current late stage efforts include our work with Genentech and Roche on the development of RITUXAN in additional oncology indications, RA, MS and lupus and the co-development of additional anti-CD20 antibody products including the humanized anti-CD20 antibody (ocrelizumab), which is in Phase 3 studies in rheumatoid arthritis and systemic lupus erythematosus; BG-12 for relapsing forms of MS in Phase 3; galiximab for NHL in Phase 3; and lumiliximab for chronic lymphocytic leukemia, or CLL, in Phase 2/3; and lixivaptan for acute hyponatremia, currently initiating Phase 3 clinical studies.

Available Information

We are a Delaware corporation with principal executive offices located at 14 Cambridge Center, Cambridge, Massachusetts 02142. Our telephone number is (617) 679-2000 and our website address is www.biogenidec.com. We make available free of charge through the Investor Relations section of our website our Annual Reports 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 or furnished to the Securities and Exchange Commission, or the SEC. We include our website address in this Annual Report on Form 10-K only as an inactive textual reference and do not intend it to be an active link to our website. You may read and copy materials we file with the SEC at the SEC s Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. You may get information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at www.sec.gov.

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Our Products and Late-Stage Product Candidates

Our products are targeted to address a variety of key medical needs in the areas of oncology, neurology, immunology and cardiology. Our marketed products and late stage product candidates are as follows:

Product	Product Indications	Status	Development and/or Marketing Collaborators
AVONEX	Relapsing forms of MS	Approved numerous countries worldwide	None
RITUXAN	Certain B-cell NHLs	Approved numerous countries worldwide	*All RITUXAN Indications:* U.S. Genentech Japan Roche and Zenyaku Outside U.S. and Japan Roche
	Rheumatoid arthritis	Approved U.S. for anti-TNF-inadequate responders	See above
		Phase 3 DMARD inadequate responders	See above
	Relapsed CLL	Phase 3	See above
	Lupus	Phase 2/3	Genentech
	MS	Phase 2/3	See above, except for PPMS indication which is only Genentech
TYSABRI	Relapsing forms of MS	Approved U.S., EU Switzerland, Canada, Australia, New Zealand and Israel	Elan
	Crohn s disease	Approved U.S.	See above
FUMADERM	Severe psoriasis	Approved Germany	Almirall
BG-12	MS	Phase 3	None
Anti-CD80 MAb/ galiximab	Relapsed or refractory NHL	Phase 3	None

Anti-CD23 MAb/ lumiliximab	Relapsed or refractory chronic lymphocytic leukemia	Phase 2/3	None
Humanized Anti-CD20 MAb/Ocrelizumab	Rheumatoid Arthritis	Phase 3	U.S. Genentech Japan Roche and Zenyaku Outside U.S. and Japan Roche
	Systemic Lupus Erythematosus	Phase 3	See above
Lixivaptan	Acute Hyponatremia	Phase 3 planned	Cardiokine Biopharma LLC

Approved Indications and Ongoing Development

AVONEX

We currently market and sell AVONEX worldwide for the treatment of relapsing forms of MS. In 2007, sales of AVONEX generated worldwide revenues of $1,867.8 million as compared to worldwide revenues of $1,706.7 million in 2006.

MS is a progressive neurological disease in which the body loses the ability to transmit messages along nerve cells, leading to a loss of muscle control, paralysis and, in some cases, death. Patients with active relapsing MS experience an uneven pattern of disease progression characterized by periods of stability that are interrupted by flare-ups of the disease after which the patient returns to a new baseline of functioning. AVONEX is a recombinant form of a protein produced in the body by fibroblast cells in response to viral infection. AVONEX has been shown in clinical trials in relapsing forms of MS both to slow the accumulation of disability and to reduce the frequency of flare-ups. AVONEX is approved to treat relapsing forms of MS, including patients with a first clinical episode and MRI features consistent with MS. We began selling AVONEX in the U.S. in 1996, and in the EU in 1997. AVONEX is on the market in over 70 countries. Based on data from an independent third party research organization, information from our distributors and internal analysis, we believe that AVONEX is the most prescribed therapeutic product for the treatment of MS worldwide. Globally over 135,000 patients use AVONEX.

We continue to work to expand the data available about AVONEX and MS treatments. In October 2007, we presented at the Congress of the European Committee for Treatment and Research of Multiple Sclerosis, or ECTRIMS, in Prague, Czech Republic, on the final results from a worldwide comparative study (QUASIMS) of the efficacy and tolerability of interferon-beta products for the treatment of relapsing multiple sclerosis. This retrospective, observational study presented at ECTRIMS involved 7,542 MS patients. This geographically diverse

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group from a range of clinical practice settings is the largest cohort of patients with relapsing remitting MS, or RRMS, that has been studied to evaluate and compare patient outcomes with interferon beta. The effects of all currently available interferon beta treatments were similar over 2 years in patients with RRMS. Even in patients with higher baseline annualized relapse rates or expanded disability status scale scores, there was no clear benefit of one interferon over another. This is in contrast to two earlier studies suggesting there were differences in efficacy between certain interferon beta formulations and dosing regimens (the Independent Comparison of Interferon (INCOMIN) and Evidence of Interferon Dose-Response and European North American Comparative Efficacy (EVIDENCE) trials). Of the treatments studied, however, AVONEX requires the least frequent administration.

We have also extended the Controlled High Risk AVONEX Multiple Sclerosis Prevention Study In Ongoing Neurological Surveillance, or CHAMPIONS. CHAMPIONS was originally designed to determine whether the effect of early treatment with AVONEX in delaying relapses and reducing the accumulation of MS brain lesions could be sustained for up to five years. The study results showed that AVONEX altered the long-term course of MS in patients who began treatment immediately after their initial MS attack compared to initiation of treatment more than two years after onset of symptoms. The five-year study extension is intended to determine if the effects of early treatment with AVONEX can be sustained for up to ten years. We also continue to support Phase 4 investigator-run studies evaluating AVONEX in combination with other therapies.

RITUXAN

RITUXAN is approved worldwide for the treatment of relapsed or refractory low-grade or follicular, CD20-positive, B-cell NHLs, which comprise approximately half of the B-cell NHLs diagnosed in the U.S. In the U.S., RITUXAN is approved for NHL with the following label indications:

- The treatment of patients with relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent;

- The treatment of patients with previously untreated diffuse large B-cell, CD20-positive, NHL, or DLBCL, in combination with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) or other anthracycline-based chemotherapy regimens;

- The treatment of patients with previously untreated follicular, CD20-positive, B-cell NHL in combination with CVP (cyclophosphamide, vincristine and prednisone) chemotherapy; and

- The treatment of patients with non-progressing (including stable disease), low grade CD20-positive, B-cell NHL, as a single agent, after first line CVP chemotherapy.

In addition, RITUXAN, in combination with methotrexate, is also approved for reducing signs and symptoms and to slow the progression of structural damage in adult patients with moderately-to-severely active rheumatoid arthritis, or RA, who have had an inadequate response to one or more TNF antagonist therapies.

Our interest in RITUXAN is recognized as revenue from unconsolidated joint business, and is made up of three components:

- We copromote RITUXAN in the U.S. in collaboration with Genentech. All U.S. sales of RITUXAN are recognized by Genentech, and we record our share of the pretax copromotion profits on a quarterly basis. In 2007, RITUXAN generated U.S. net sales of $2.3 billion, of which we recorded $616.8 million as our share of copromotion profits, as compared to U.S. net sales of $2.1 billion in 2006, of which we recorded $555.8 million as our share of copromotion profits;

Roche sells RITUXAN outside the U.S., except in Japan where it co-markets RITUXAN in collaboration with Zenyaku Kogyo Co. Ltd., or Zenyaku. We received royalties through Genentech on sales of RITUXAN outside of the U.S. of $250.8 million in 2007 as compared to $194.0 million in 2006; and

Finally, we receive reimbursement from Genentech for our selling and development expenses.

In the U.S., we share responsibility with Genentech for continued development. Such continued development includes conducting supportive research and post-approval clinical studies and seeking potential approval for additional indications. Genentech provides the support functions for the commercialization of RITUXAN in the U.S. and has worldwide manufacturing responsibilities. See Sales, Marketing and Distribution RITUXAN and Manufacturing and Raw Materials. We also have the right to collaborate with Genentech on the development of

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other humanized anti-CD20 antibodies targeting B-cell disorders for a broad range of indications, and to copromote with Genentech any new products resulting from such development in the U.S. The most advanced such humanized anti-CD20 antibody under development, ocrelizumab, is in Phase 3 trials in rheumatoid arthritis and systemic lupus erythematosus. We are currently in arbitration with Genentech as to whether Genentech has the right to develop collaboration products, including the second-generation humanized anti-CD20 molecule, without our approval. See Item 3 Legal Proceedings for a description of that arbitration. Our agreement with Genentech provides that the successful development and commercialization of new anti-CD20 product candidates in our collaboration (which also includes RITUXAN) will decrease our participation in the operating profits from the collaboration (including as to RITUXAN). See Consolidated Financial Statements Note 16, Unconsolidated Joint Business Arrangement.

RITUXAN in Oncology

We believe that RITUXAN is the second-highest-selling oncology therapeutic in the United States and has had more than 1,000,000 patient exposures worldwide across all indications. RITUXAN is generally administered as outpatient therapy by personnel trained in administering chemotherapies or biologics. RITUXAN is unique in the treatment of B-cell NHLs due to its specificity for the antigen CD20, which is expressed only on the surface of normal B-cells and malignant B-cells. Stem cells (including B-cell progenitors or precursor B-cells) in bone marrow lack the CD20 antigen. This allows healthy B-cells to regenerate after treatment with RITUXAN and to return to normal levels within several months. RITUXAN s mechanism of action, in part, utilizes the body s own immune system as compared to conventional lymphoma therapies.

In an effort to identify additional applications for RITUXAN, we, in conjunction with Genentech and Roche, continue to support RITUXAN post-marketing studies. We, along with Genentech and Roche, are conducting a multi-center global Phase 3 registrational study known as REACH in patients with relapsed chronic lymphocytic leukemia, or CLL, comparing the use of fludarabine, cyclophosphamide and RITUXAN together, known as FCR, versus fludarabine and cyclophosphamide alone. Enrollment for this study was completed in the third quarter of 2007. We, along with Genentech and Roche, are also conducting a trial known as PRIMA that is evaluating the added efficacy of RITUXAN maintenance therapy after previously untreated follicular non-Hodgkin s lymphoma patients are given a combination of chemotherapy and RITUXAN. To date, the added benefit of RITUXAN has only been evaluated in relapsed patients. PRIMA completed enrollment in 2007. Additional clinical studies are ongoing in other B-cell malignancies such as lymphoproliferative disorders associated with solid organ transplant therapies, relapsed aggressive non-Hodgkin s lymphoma and mantle cell non-Hodgkin s lymphoma.

RITUXAN in RA

RITUXAN, in combination with methotrexate, is approved for reducing signs and symptoms and to slow the progression of structural damage in adult patients with moderately-to-severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies. We, along with Genentech and Roche, initiated a Phase 3 clinical study of RITUXAN in RA patients who are inadequate responders to disease-modifying anti-rheumatic drugs, or DMARDs, in 2006. In January 2008 we announced that the study, known as SERENE, met its primary endpoint of a significantly greater proportion of RITUXAN-treated patients achieving an American College of Rheumatology (ACR) 20 response (the proportion of patients who achieve at least 20% improvement) at week 24, compared to placebo. In this study patients who received either 500 mg or 1000 mg of RITUXAN as a single treatment course of two infusions in combination with a stable dose of methotrexate displayed a statistically significant improvement in symptoms compared to patients who received placebo in combination with methotrexate. Although the study was not designed to compare the RITUXAN doses, the efficacy of the two doses appeared to be similiar. Further analyses of the data are ongoing and will be submitted for presentation at an upcoming medical meeting. In 2007 we received positive results from the Phase 3 study known as SUNRISE, investigating the controlled re-treatment of patients who are inadequate responders to TNF therapies. Patients who were not in remission at

24 weeks following administration of a course of RITUXAN were randomized to receive either a second course of RITUXAN or placebo. The primary endpoint, the proportion of retreated patients with an ACR 20 response at Week 48 relative to baseline, was achieved with significantly more patients achieving an ACR 20 with RITUXAN retreatment compared to placebo. Genentech and Biogen Idec will continue to analyze the study results and we anticipate presenting the results at an upcoming meeting in 2008.

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RITUXAN in Other Immunology Indications

Based primarily on results from the studies of RITUXAN in RA, as well as other small investigator-sponsored studies in various autoimmune-mediated diseases, we, along with Genentech, are conducting a Phase 3 clinical study of RITUXAN in primary progressive MS, or PPMS, and a registrational program in systemic lupus erythematosus, or SLE, comprised of a Phase 3 study in lupus nephritis and a Phase 2/3 study in a general SLE population. We anticipate reporting results from the PPMS and SLE studies in the first half of 2008. Enrollment in the Lupus Nephritis study is still ongoing. In August 2006, we and Genentech announced that a Phase 2 study of RITUXAN in relapsing-remitting MS met its primary endpoint. Results were presented at the American Academy of Neurology annual meeting in May 2007. The study of 104 patients showed a statistically significant reduction in the total number of gadolinium enhancing T1 lesions observed on serial MRI scans of the brain at weeks 12, 16, 20 and 24 in the RITUXAN-treated group compared to placebo. At week 24, the total cumulative mean number of gadolinium lesions per patient was reduced by 91%, to 0.5 in the RITUXAN-treated group from 5.5 in the placebo group (p0.001). In addition, the proportion of patients with relapses over 24 weeks in the RITUXAN-treated arm was 14.5% compared to 34.3% in the placebo arm (58% relative reduction) (p=0.02). The result of statistical testing is often defined in terms of a p-value, with a level of 0.05 or less considered to be a statistically significant difference, which means the result is unlikely due to chance.

In December 2006, we and Genentech issued a dear healthcare provider letter informing healthcare providers that two cases of progressive multifocal leukoencephalopathy, or PML, a rare and frequently fatal demyelinating disease of the central nervous system, resulting in death were reported in patients receiving RITUXAN for treatment of SLE, an indication where RITUXAN is not approved for treatment. The prescribing information for RITUXAN has been updated to reflect these reports.

TYSABRI

TYSABRI is approved for the treatment of relapsing forms of MS. On June 5, 2006, we and Elan announced the FDA s approval of the supplemental Biologics License Application, or sBLA, for the reintroduction of TYSABRI as a monotherapy treatment for relapsing forms of MS to slow the progression of disability and reduce the frequency of clinical relapses. On June 29, 2006, we and Elan announced that the European Medicines Agency, or EMEA, had approved TYSABRI as a similar treatment. TYSABRI is also approved for MS in Switzerland, Canada, Australia, New Zealand and Israel.

TYSABRI was initially approved by the FDA in November 2004 to treat relapsing forms of MS to reduce the frequency of clinical relapses. In February 2005, in consultation with the FDA, we and Elan voluntarily suspended the marketing and commercial distribution of TYSABRI based on reports of cases of PML in patients treated with TYSABRI in clinical studies. In consideration of these events, TYSABRI is marketed under risk management or minimization plans as agreed with local regulatory authorities. In the U.S., TYSABRI was reintroduced with a risk minimization action plan, or RiskMAP, known as the TYSABRI Outreach: Unified Commitment to Health, or TOUCH, Prescribing Program, a rigorous system intended to educate physicians and patients about the risks involved and assure appropriate use of the product.

As of late December 2007, more than 21,000 patients were on commercial and clinical TYSABRI therapy worldwide. As of mid-December 2007, up to 30,900 patients had been treated with TYSABRI cumulatively in the combined clinical trial and post-marketing settings. There have been no new cases of PML since relaunch in the U.S. and launch internationally in July 2006.

On January 14, 2008, we and Elan announced the FDA s approval of the sBLA for use of TYSABRI for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn s disease, or

CD, with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-alpha. TYSABRI will be available for the treatment of CD upon the completion of key implementation activities related to the approved risk management plan. We anticipate TYSABRI will be available to Crohn s patients by the end of the first quarter of 2008.

The FDA granted approval based on its review of overall safety data and the results of three randomized, double-blind, placebo-controlled, multi-center trials of TYSABRI assessing the safety and efficacy as both an induction and maintenance therapy ENCORE (Efficacy of Natalizumab in Crohn s Disease Response and Remission), ENACT-1 (Efficacy of Natalizumab as Active Crohn s Therapy) and ENACT-2 (Evaluation of

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Natalizumab As Continuous Therapy). The approval contains labeling and a risk management plan, both of which are similar to those approved for the MS indication. One of the confirmed cases of PML was in a patient who was in a clinical study of TYSABRI in Crohn s disease.

In September 2004, Elan submitted a Marketing Authorisation Application, or MAA, to the EMEA for approval of TYSABRI as a treatment for Crohn s disease. A committee of the EMEA adopted a negative recommendation in November 2007. The European Commission affirmed the committee s decision in the first quarter of 2008, which means that Crohn s disease will not be included in our label for TYSABRI in the EU.

TYSABRI binds to adhesion molecules on the immune cell surface known as alpha-4 integrin. Adhesion molecules on the surface of the immune cells play an important role in the migration of the immune cells in the inflammatory process. Research suggests that by binding to alpha-4 integrin, TYSABRI prevents immune cells from migrating from the bloodstream into tissue where they can cause inflammation and potentially damage nerve fibers and their insulation.

Under the terms of the collaboration, we are solely responsible for the manufacture of TYSABRI, and we collaborate with Elan on the product s marketing, commercial distribution and ongoing development activities. The collaboration agreement with Elan is designed to effect an equal sharing of profits and losses generated by the activities of the collaboration between Elan and us. Under our agreement with Elan, however, in the event that sales of TYSABRI exceed specified thresholds, Elan is required to make milestone payments to us in order to continue sharing equally in the collaboration s results.

In the U.S., we sell TYSABRI to Elan who sells the product to third party distributors. Elan and we co-market the product. The sales price to Elan in the U.S. is set at the beginning of each quarterly period to effect an approximate equal sharing of the gross margin between Elan and us. In addition, both parties share equally in the operating costs, which include research and development, selling, general and administrative expenses and other similar costs. Sales of TYSABRI to Elan are reported as revenues and are recognized upon Elan s shipment of the product to third party distributors, at which time all revenue recognition criteria have been met. As of December 31, 2007 and 2006, we had deferred revenue of $9.0 and $5.0 million, respectively, for shipments to Elan that remained in Elan s ending inventory. Elan s reimbursement of TYSABRI operating costs is reflected as a reduction of the respective costs within our consolidated statement of income.

For sales outside of the U.S., we are responsible for distributing TYSABRI to customers and are primarily responsible for all operating activities. We and Elan share equally in the operating results of TYSABRI outside the U.S. Sales of TYSABRI are reported as revenue and are recognized at the time of product delivery to our customer, at which time all revenue recognition criteria have been met. Payments to or from Elan for their share of the collaboration operating losses relating to sales outside the U.S. are reflected in the collaboration profit (loss) sharing line in our consolidated statement of income. For 2007 and 2006, we provided and received net payments of $14.1 million and ($9.7) million, respectively, related to reimbursements made in connection with this arrangement.

In July 2006, we began to ship TYSABRI in both the United States and Europe. In 2007, we recorded sales of TYSABRI in the U.S. and Europe of $104.4 million and $125.5 million, respectively. In 2006, we recorded sales of TYSABRI in the U.S. and Europe relating to current activity of $11.9 million and $10.0 million, respectively. Prior to the suspension of TYSABRI in 2005, we shipped product to Elan in the U.S. and recognized revenue in accordance with the policy described above. As a result of the suspension of TYSABRI, we deferred $14.0 million in revenue from Elan as of March 31, 2005 related to TYSABRI product that remained in Elan s ending inventory. This amount was paid by Elan during 2005 and was subsequently recognized as revenue during 2006, when the uncertainty about the ultimate disposition of the product was eliminated.

PHASE 3 Studies of TYSABRI in MS

Prior to the suspension of dosing in clinical studies of TYSABRI we, along with Elan, completed the AFFIRM study and the SENTINEL study. The AFFIRM study was designed to evaluate the ability of natalizumab to slow the progression of disability in MS and reduce the rate of clinical relapses. The SENTINEL study was designed to evaluate the effect of the combination of natalizumab and AVONEX compared to treatment with AVONEX alone in slowing progression of disability and reducing the rate of clinical relapses. Both studies were two-year studies which had protocols that included a one-year analysis of the data.

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The AFFIRM study

The one-year data from the AFFIRM study showed that TYSABRI reduced the rate of clinical relapses by 66% relative to placebo, the primary endpoint at one year. AFFIRM also met all one-year secondary endpoints, including MRI measures. In the TYSABRI treated group, 60% of patients developed no new or newly enlarging T2 hyperintense lesions compared to 22% of placebo treated patients. On the one-year MRI scan, 96% of TYSABRI treated patients had no gadolinium-enhancing lesions compared to 68% of placebo treated patients. The proportion of patients who remained relapse free was 76% in the TYSABRI treated group compared to 53% in the placebo treated group. In February 2005, we and Elan announced that the AFFIRM study also achieved the two-year primary endpoint of slowing the progression of disability in patients with relapsing forms of MS. In the TYSABRI treated group, there was a 42% reduction in the risk of disability progression relative to placebo, and a 67% reduction in the rate of clinical relapses over two years relative to placebo which was sustained and consistent with the one-year results. Other efficacy data, including MRI measures, were similar to the one-year results.

In May 2007 at the annual meeting of the American Academy of Neurology in Boston, we presented extension study data that showed that TYSABRI has a sustained treatment effect on clinical relapses and the risk of disability progression in MS patients treated for up to three years. Patients who participated in the Phase 3 TYSABRI program (including the AFFIRM trial) were eligible to enroll in an open-label extension study that evaluated the therapy s long-term effects. In the intent-to-treat analysis, the annualized relapse rate for patients treated with TYSABRI over the three-year period was 0.23, translating into an average of one relapse every 4.3 years. The relapse rate also continued to remain low over the three-year treatment period with TYSABRI: 0.27 during the first year; 0.20 during the second year; and 0.15 during the third year (based on 531 patients who entered the extension study, which includes approximately 250 patients with nearly three years of continuous therapy). In addition, TYSABRI also decreased the cumulative probability of disability progression sustained for six months compared to placebo. The estimated proportion of patients who had 24-week sustained disability progression at two years was 11% in patients treated with TYSABRI compared to 23% in patients treated with placebo, a 54% relative reduction. This effect was maintained in patients treated with TYSABRI for up to three years with 13% showing 24-week sustained disability progression.

In October 2007 at the 23rd Congress of ECTRIMS in Prague, Czech Republic, we presented a poster on a post hoc analysis of the Phase 3 AFFIRM study. The study data suggest the proportion of disease-free patients over two years was significantly higher in the TYSABRI-treated group compared with the placebo group, as determined based upon both clinical and MRI criteria. Using clinical and MRI disease-free criteria combined, the most stringent definition of disease free, 36.7% of TYSABRI-treated patients had no relapses, disability progression or MRI activity compared with 7.2% of placebo patients (p0.0001). In the clinical analysis, 64.3% of TYSABRI-treated patients vs. 38.9% placebo-treated patients (p0.0001) were disease free or without relapses and disability progression. Using MRI measures, 57.7% of TYSABRI-treated patients vs. 14.2% placebo-treated patients (p0.0001) were disease free, or without gadolinium-enhancing lesions and new or enlarging T2-hyperintense lesions.

The SENTINEL study

The one-year data from the SENTINEL combination study also showed that the study achieved its one-year primary endpoint. The addition of TYSABRI to AVONEX resulted in a 54% reduction in the rate of clinical relapses over the effect of AVONEX alone. SENTINEL also met all secondary endpoints, including MRI measures. In the group treated with TYSABRI plus AVONEX, 67% of the patients developed no new or newly enlarging T2 hyperintense lesions compared to 40% in the AVONEX plus placebo group. On the one-year MRI scan, 96% of TYSABRI plus AVONEX-treated patients had no gadolinium-enhancing lesions compared to 76% of AVONEX plus placebo treated patients. The proportion of patients who remained relapse free was 67% in the TYSABRI plus AVONEX-treated group compared to 46% in the AVONEX plus placebo-treated group. In the TYSABRI-treated group, 60% of patients developed no new or newly enlarging T2 hyperintense lesions compared to 22% of placebo treated patients. On the

one-year MRI scan, 96% of TYSABRI treated patients had no gadolinium-enhancing lesions compared to 68% of placebo treated patients. In July 2005, we and Elan announced that the SENTINEL study also achieved the two-year primary endpoint of slowing the progression of disability in patients with relapsing forms of MS. The addition of TYSABRI to AVONEX resulted in a 24% reduction in the risk of disability progression compared to the effect of AVONEX alone, and a 56% reduction in the rate of clinical relapses over two

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years compared to that provided by AVONEX alone. Other efficacy data, including MRI measures, were similar to the one-year results.

Phase 3 Studies of TYSABRI in Crohn s Disease

We, along with Elan, have completed three Phase 3 studies of TYSABRI in Crohn s disease, a chronic and progressive inflammatory disease of the gastrointestinal tract, which commonly affects both men and women. The three completed Phase 3 studies are known as ENACT-2 (Evaluation of Natalizumab as Continuous Therapy-2), ENACT-1 (Evaluation of Natalizumab as Continuous Therapy-1), and ENCORE (Efficacy of Natalizumab for Crohn s Disease Response and Remission).

ENACT-1/ENACT-2

In ENACT-2, 339 patients who were responders in ENACT-1, the Phase 3 induction study, were re-randomized to one of two treatment groups, TYSABRI or placebo, both administered monthly for a total of 12 months. In ENACT-1, the primary endpoint of response, as defined by a 70-point decrease in the Crohn s Disease Activity Index, or CDAI, at week 10, was not met. In ENACT-2, the primary endpoint, which was met, was maintenance of response through six additional months of therapy. A loss of response was defined as a greater than 70 point increase in CDAI score and a total CDAI score above 220 or any rescue intervention. Through month six, there was a significant treatment difference of greater than 30% in favor of patients taking TYSABRI compared to those taking placebo. Twelve-month data from ENACT-2 showed a sustained and clinically significant response throughout 12 months of extended TYSABRI infusion therapy, confirming findings in patients who had previously shown a sustained response throughout six months. Maintenance of response was defined by a CDAI score of less than 220, and less than 70-point increase from baseline, in the absence of rescue intervention throughout the study. Response was maintained by 54% of patients treated with natalizumab compared to 20% of those treated with placebo (p0.001). In addition, 39% of patients on TYSABRI maintained clinical remission during the study period, versus 15% of those on placebo (p0.001). By the end of month six, 58% of patients treated with TYSABRI who had previously been treated with corticosteroids were able to withdraw from steroid therapy compared to 28% of placebo-treated patients.

The ENCORE study

In June 2005, we and Elan announced that ENCORE, the second Phase 3 induction trial of TYSABRI for the treatment of moderately to severely active Crohn s disease in patients with evidence of active inflammation, met the primary endpoint of clinical response as defined by a 70-point decrease in baseline CDAI score at both weeks 8 and 12. The study also met all of its secondary endpoints, including clinical remission at both weeks 8 and 12. Clinical remission was defined as achieving a CDAI score of equal to or less than 150 at weeks 8 and 12. At the time of the TYSABRI suspension, all ENCORE study patients had completed dosing based on the study protocol and collection of data and analysis followed.

TYSABRI in Oncology

We plan to initiate a Phase 1/2 study of TYSABRI in multiple myeloma in 2008.

FUMADERM

FUMADERM (dimethylfumarate and monoethylfumarate salts) was acquired with the purchase of Fumapharm in June 2006. In December 2006, we acquired the right to distribute FUMADERM in Germany from Fumedica effective May 1, 2007. FUMADERM acts as an immunomodulator and is approved in Germany for the treatment of severe psoriasis. In 2007 and 2006, sales of FUMADERM in Germany totaled $21.5 million and $9.5 million, respectively,

which we recorded from the date of acquisition of Fumapharm. The product has been in commercial use in Germany for approximately eleven years and is the most prescribed oral systemic treatment for severe psoriasis in Germany.

Late-Stage Product Candidates

BG-12

BG-12, an oral fumarate derivative, is an immunomodulatory with a novel mechanism of action with a combination of neuroprotective and anti-inflammatory properties. We acquired BG-12 with the purchase of

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Fumapharm in June 2006. We completed a Phase 2b clinical study of BG-12 in patients with relapsing-remitting MS in October 2005. In January 2006, we announced that this study had achieved its primary efficacy endpoint. Based on the results of the Phase 2 study, we announced that we initiated a Phase 3 program of BG-12 in relapsing remitting MS in January 2007. Fumapharm has also completed a small Phase 3 study in Germany of BG-12 in psoriasis.

Galiximab/(ANTI-CD80 Antibody)

The CD80 antigen is expressed on the surface of follicular and other lymphoma cells, and is also known as B7.1. In the fourth quarter of 2005, we completed a Phase 2a study designed to evaluate the anti-tumor activity of an anti-CD80 antibody, galiximab, that we developed using our Primatized® antibody technology in patients with relapsed non-Hodgkin s lymphoma simultaneously receiving rituximab. In this study, the combination of the two antibodies was well tolerated, with observation of clinical responses in patients treated with higher doses. Based on the results of the Phase 2a study, we announced that we initiated a Phase 3 study of the antibody in relapsed non-Hodgkin s lymphoma in combination with RITUXAN in January 2007. We anticipate initial data from a Cancer and Leukemia Group B trial using RITUXAN and galiximab combination therapy in previously untreated subjects with follicular non-Hodgkin s lymphoma in 2008.

Lumiliximab/(ANTI-CD23 Antibody)

The CD23 antigen is expressed on the surface of mature B-cells and other immune system cells, and is also known as Fc epsilon RII. We have completed a Phase 2a study designed to evaluate the anti-tumor activity of an anti-CD23 antibody that we developed using our Primatized® antibody technology when administered in combination with FCR, a standard chemotherapy, in patients with relapsed chronic lymphocytic leukemia, or CLL. In this study, the combination of lumiliximab with FCR was well tolerated, with observation of a high proportion of clinical complete responses in patients. Based on the results of the Phase 2a study, we announced that we initiated a Phase 2/3 study evaluating lumiximab plus FCR versus FCR alone in relapsed or refractory CLL in January 2007, which could lead to approval of the antibody if the study meets its endpoints.

Ocrelizumab/(Humanized ANTI-CD20 Antibody)

The second generation anti-CD20 (ocrelizumab) is a humanized monoclonal antibody directed against the CD20 surface antigen on human B-cells, the same antigen that RITUXAN targets. Anti-CD20 antibodies work by binding to a particular protein (the CD20 antigen) on the surface of normal and malignant B-cells. From there, they recruit the body s natural defenses to attack and kill the marked B-cells. Genentech, with which we collaborate on this product candidate, initiated three Phase 3 studies of ocrelizumab in rheumatoid arthritis in 2007, each targeting a separate patient group: those currently not on methotrexate, methotrexate inadequate responders and TNF inadequate responders. Genentech also initiated a Phase 3 study of ocrelizumab in SLE in the fourth quarter of 2007. We are currently in arbitration with Genentech as to whether Genentech has the right to develop collaboration products, including the second-generation humanized anti-CD20 molecule, without our approval. See Item 3 Legal Proceedings for a description of that arbitration.

Lixivaptan

Lixivaptan is an oral compound for the potential treatment of hyponatremia. Cardiokine Biopharma LLC, with which we entered a collaboration in 2007, is planning a Phase 3 study of lixivaptan in congestive heart failure patients. Lixivaptan is a highly potent, non-peptide, selective V2 vasopressin receptor antagonist. It antagonizes the action of vasopressin (also known as antidiuretic hormone, ADH) on the V2 receptors in the kidney-collecting duct, causing water to be excreted from the kidney, without affecting sodium or other electrolytes. Based on this mechanism of action, lixivaptan shows promise in the treatment of disease states associated with water retention and electrolyte

imbalance, including hyponatremia, which is the most common electrolyte disorder in clinical practice. Hyponatremia is recognized as an independent contributor to negative patient outcomes in many chronic diseases, most notably congestive heart failure, as well as cirrhosis and syndrome of inappropriate anti-diuretic hormone.

Pursuant to our 2007 collaboration, we made a $50 million upfront payment to Cardiokine Biopharma LLC and will make up to $170 million in additional milestone payments for successful development and global commercialization of lixivaptan, as well as royalties on commercial sales. We will be responsible for the global commercialization of lixivaptan, and Cardiokine Biopharma LLC has an option for limited copromotion in the United States.

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Products We No Longer Sell

ZEVALIN

In December 2007, we sold the U.S. marketing, sales, manufacturing and development rights for ZEVALIN to Cell Therapeutics, Inc., or CTI, for an upfront purchase price of $10.0 million and up to an additional $20.0 million in milestone payments. In addition, we also will receive royalty payments on future sales of ZEVALIN. As part of the overall arrangement, we have entered into a contract with CTI to supply ZEVALIN product through 2014 and a related services and security agreement under which CTI has agreed to reimburse us for costs incurred in an ongoing randomized clinical trial for ZEVALIN with respect to aggressive non-Hodgkin s lymphoma. The $10.0 million upfront payment will be recognized in our consolidated statement of income over the term of the supply agreement. The royalty payments and proceeds from the supply contract are not expected to be significant.

The ZEVALIN therapeutic regimen is a radioimmunotherapy and part of a regimen that is approved for the treatment of patients with relapsed or refractory low-grade, or follicular, B-cell NHL, including patients with RITUXAN relapsed or refractory NHL. The current label also includes transformed B-cell NHL although we have asked the FDA to remove that indication as we found the post-marketing commitment studies necessary for that indication to not be feasible. ZEVALIN is approved in the EU for the treatment of adult patients with CD20-positive follicular B-cell NHL who are refractory to or have relapsed following RITUXAN therapy.

In 2007, sales of ZEVALIN in the U.S. generated revenues of $13.9 million, until we sold all U.S. rights in the product in December 2007 to CTI, as compared to revenues of $16.4 million in 2006. We will continue to sell ZEVALIN to Bayer Schering Pharma AG for distribution in the EU, and receive royalty revenues from Schering AG on sales of ZEVALIN in the EU. Rest of world product sales for ZEVALIN in 2007 and 2006 were $3.0 and $1.4 million, respectively.

AMEVIVE

We sold all rights in AMEVIVE to Astellas Pharma US, Inc., or Astellas, in the second quarter of 2006. AMEVIVE is approved in the U.S. and other countries for the treatment of adult patients with moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy. Under the terms of the agreement with Astellas, we will continue to manufacture AMEVIVE and supply product to Astellas for a period of up to 11 years. Under the terms of the supply agreement, we charge Astellas fixed amounts based on