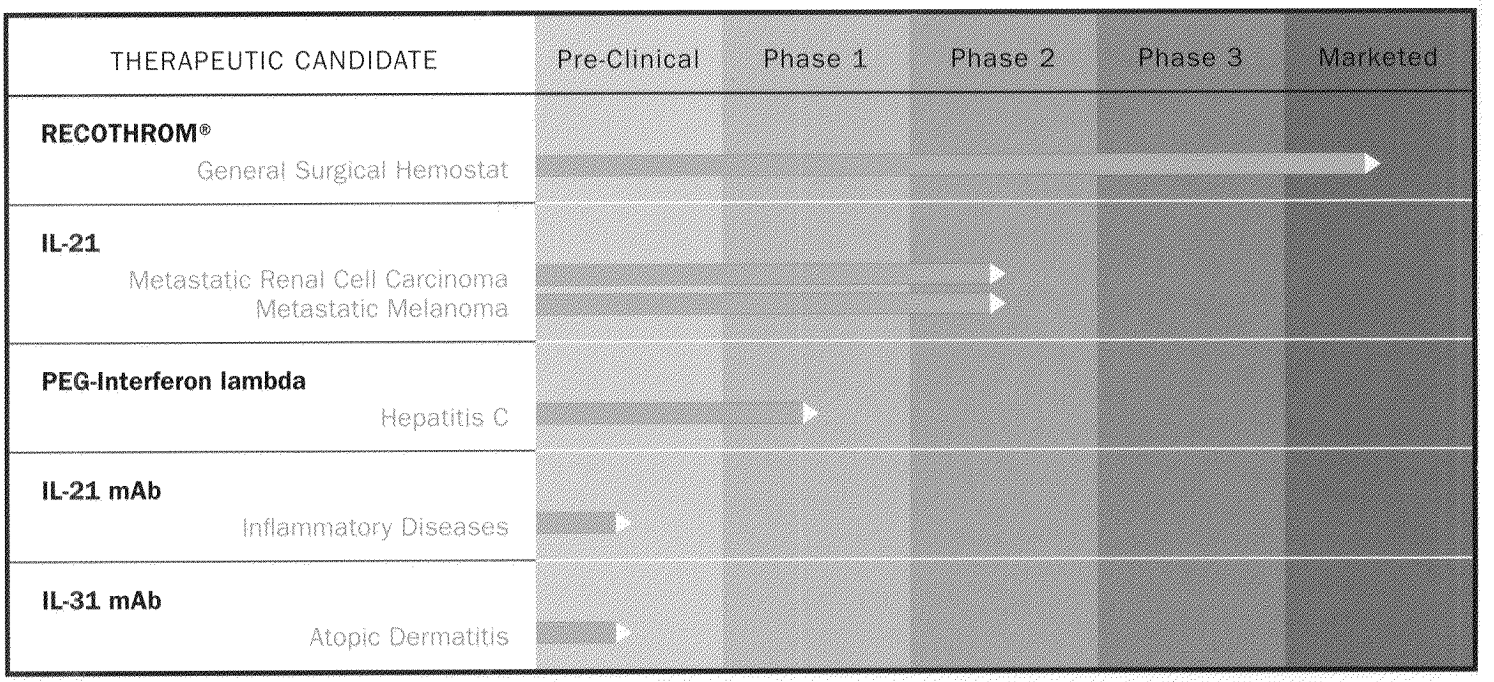
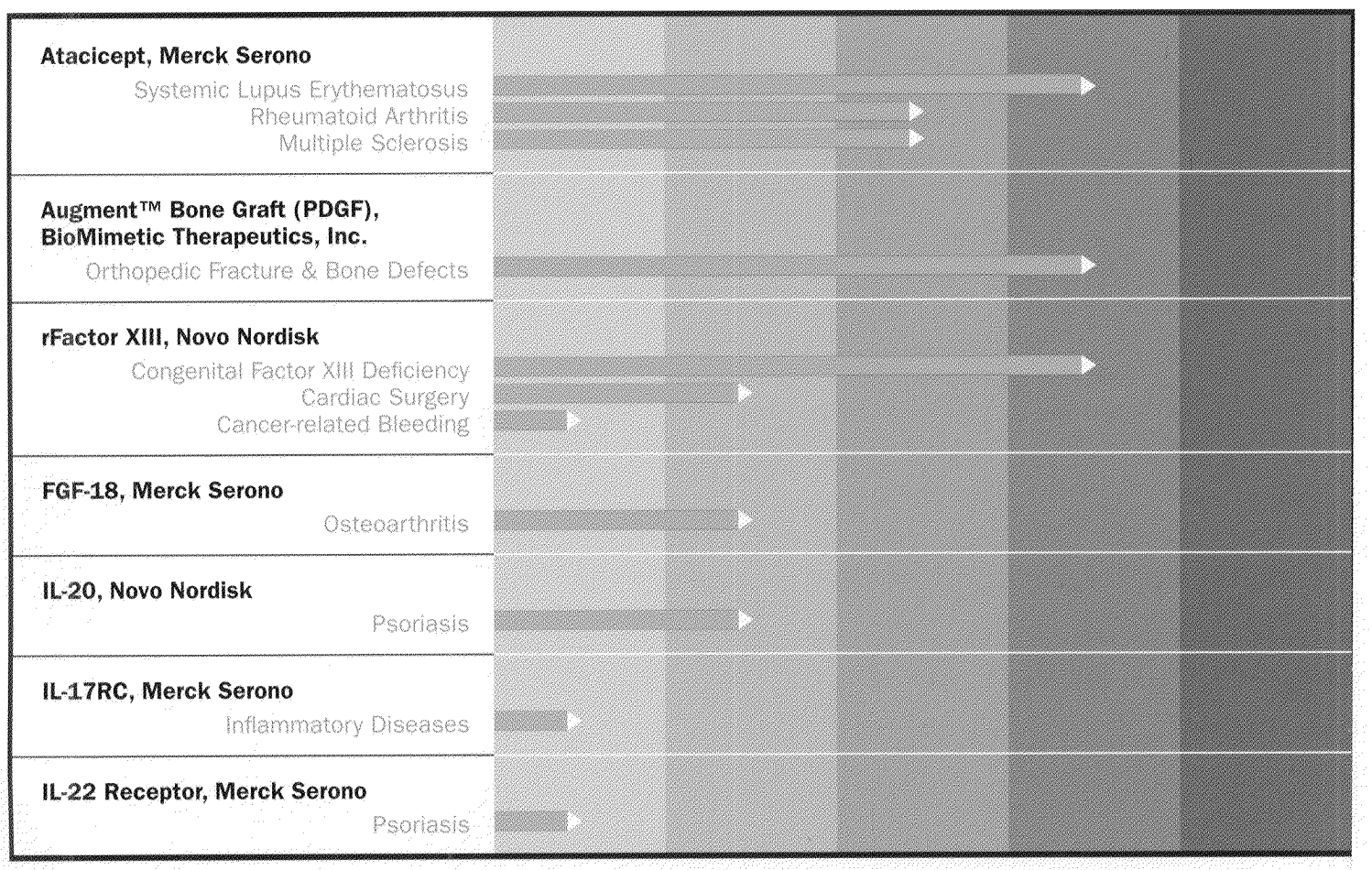
ZYMOGENETICS

2008 Annual Report

ZymoGenetics Pipeline



Out-Licensed Product Candidates



ZYMOGENETICS

Fellow Shareholders,

This letter is the first from me as the company's Chief Executive Officer. ZymoGenetics has passed through 2008 and entered 2009 as a very different organization from a year ago. Some of the events of 2008 were reasons to celebrate, such as the approval of our first product, RECOTHROM® Thrombin, topical (Recombinant). However, the year was for the most part unsatisfying, most certainly as judged by our share price performance. We are committed to unlocking the value in our company in 2009 and beyond through three key initiatives: making RECOTHROM a success in the marketplace, supporting PEG-Interferon lambda development with our partner Bristol-Myers Squibb, and significantly reducing our cash consumption to focus on a subset of our highest value opportunities. I'll expand on these three themes below.

Before we look forward to 2009, we should recognize the significant contributions of Bruce Carter. Bruce was with ZymoGenetics for over 20 years, starting as Vice President of Research before the acquisition by Novo Nordisk in 1988. It was his vision and drive that allowed ZymoGenetics to emerge as an independent company in 2000 and, as CEO, that launched ZymoGenetics into the public markets in 2002. Bruce worked tirelessly to create a great company and presided over the transition from research boutique to fully integrated commercial stage biopharmaceutical company. That's quite an accomplishment in seven years. Speaking personally, it has been a great pleasure to have Bruce as a colleague, friend and mentor, and I look forward to continuing to work with him in his role as non-executive Chairman.

Looking ahead to 2009, we have a lot of work to do to unlock the intrinsic value in ZymoGenetics. Our first priority is to make RECOTHROM a commercial success. During 2008, we received approvals for three separate product presentations and launched the product into the US market. Our partner Bayer Healthcare also took steps to gain approval for RECOTHROM in Europe by submitting a Marketing Authorization Application in August. Admittedly, the US launch has not proceeded to displace bovine thrombin as quickly as we had hoped. We took steps at the end of 2008 which we believe will provide greater sales momentum to build on in 2009. In addition, we recently announced the recruitment of a senior level executive, Stephen Zaruby, who has extensive hospital sales and marketing experience, to be our President and head up our RECOTHROM business. His mandate is simple: establish RECOTHROM as the leading topical surgical

hemostat and identify additional product line extensions and licensing opportunities to leverage our commercial infrastructure.

Our second major strategic objective for creating value in 2009 got off to a great start on January 12 when we announced a collaboration with Bristol-Myers Squibb for development and commercialization of PEG-Interferon lambda. This agreement could bring in up to $1.1 billion in fees and milestones over the course of the agreement, but importantly it provided for $105 million in license fees we received in March 2009 and for $95 million in additional milestones expected later this year related to our planned initiation of Phase 2 testing. Furthermore, the transaction secures substantial late stage commercial value in this asset by providing the right for ZymoGenetics to receive 40% of the profits and co-promote the product in the US, along with double digit royalties for ex-US sales. This collaboration reflects the alignment in how both Bristol-Myers Squibb and ZymoGenetics see PEG-Interferon lambda: as a highly differentiated drug candidate which could become an integral component in the regimens used to treat Hepatitis C. Bristol-Myers Squibb is an ideal partner for ZymoGenetics, and we are committed to working together to bring this drug to patients as quickly as possible.

The third and final major objective for us during 2009 is to significantly strengthen the company's financial position. The PEG-Interferon lambda collaboration is the first step in this direction; however, we also plan to take steps to generate additional partnership revenue and to reduce cash consumption by reducing operating costs. We believe that our current cash reserves, anticipated growth in RECOTHROM revenues, new partnering revenue, and cost cutting measures should provide sufficient capital for us to fund our operations well into the future.

By pursuing these major objectives, we expect to increase our focus on creating value from our most promising product opportunities and, over time, build a valuable and profitable biopharmaceutical company.

Thank you for your support. We look forward to 2009 as a year of substantial progress for ZymoGenetics.

Douglas E. Williams, Ph.D.
Chief Executive Officer

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2008

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

Commission File Number 0-33489

ZYMOGENETICS, INC.

(exact name of registrant as specified in its charter)

Washington	**91-1144498**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

1201 Eastlake Avenue East, Seattle, WA 98102
(Address of principal executive offices)

Registrant's telephone number, including area code (206) 442-6600

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, no par value	**The NASDAQ Stock Market**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark whether the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.
Yes ☐. No ☒.

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

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, and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒. No ☐.

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

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

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

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

The aggregate market value of the common equity held by non-affiliates computed by reference to the price at which the common equity was last sold as of June 30, 2008 was: $332,999,330.

Common stock outstanding at February 20, 2009: 68,797,832 shares.

DOCUMENTS INCORPORATED BY REFERENCE

(1) Portions of the Company's definitive Proxy Statement for the annual meeting of shareholders to be held on June 10, 2009 are incorporated by reference in Part III.

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ZYMOGENETICS, INC.

ANNUAL REPORT ON FORM 10-K

For the Year Ended December 31, 2008

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PART I

Item 1. Business

This Annual Report on Form 10-K contains, in addition to historical information, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties. This Act provides a "safe harbor" for forward-looking statements to encourage companies to provide prospective information about themselves. All statements other than statements of historical fact, including statements regarding company and industry prospects and future results of operations, financial position and cash flows, made in this Annual Report on Form 10-K are forward-looking. We use words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "future," "intend," "may," "potential," "seek," "should," "target" and similar expressions, including negatives, to identify forward-looking statements. Forward-looking statements reflect management's current expectations, plans or projections and are inherently uncertain. Our actual results could differ significantly from the results discussed in the forward-looking statements. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Factors that could cause or contribute to such differences include those discussed in "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," as well as those discussed elsewhere in this Annual Report on Form 10-K. We undertake no obligation to publicly release any revisions to these forward-looking statements that may be made to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. Readers are urged, however, to review the information provided in reports that we file from time to time with the Securities and Exchange Commission or otherwise make public.

Overview

Our company is focused on the discovery, development, manufacture and commercialization of therapeutic proteins for the treatment of human diseases. Our current programs target hemostasis, inflammatory and autoimmune diseases, cancer and viral infections. Our first internally developed product candidate, RECOTHROM® Thrombin, topical (Recombinant), was approved by the U.S. Food and Drug Administration (FDA) on January 17, 2008 for use as a topical hemostat to control moderate bleeding during surgical procedures and is now being marketed in the United States. Our portfolio of novel proteins, which we are developing on our own or in collaboration with partners, includes the following commercial product and product candidates in clinical development.

Commercial Product

- *RECOTHROM® (also referred to as rThrombin).* RECOTHROM, recombinant thrombin, is a topical hemostatic agent used for the control of moderate bleeding during surgical procedures, which was approved by the FDA on January 17, 2008. It is a recombinant version of a blood-clotting protein. Other thrombins are marketed in the United States in forms derived from bovine (cow) plasma or human plasma. Our product provides an effective and safe alternative to plasma-derived thrombin products. We are marketing RECOTHROM in the United States using our own commercial infrastructure, which includes a dedicated field force of sales people and medical scientific liaisons. We have retained all RECOTHROM rights in the United States. In June 2007, we entered into a license and collaboration agreement with Bayer Schering Pharma AG, under which Bayer Schering Pharma will develop and commercialize RECOTHROM outside of the United States. Simultaneously, we entered into a co-promotion agreement with Bayer HealthCare LLC, under which Bayer will co-promote RECOTHROM in the United States for up to four years following the RECOTHROM launch, ending in March 2012. In August 2008, Bayer Schering Pharma submitted the Marketing Authorization Application (MAA) to the European Medicines Agency (EMEA) for approval to market RECOTHROM as a topical aid to control surgical bleeding.

Product Candidates in Clinical Development

- *PEG-IFN-λ (formerly known as IL-29).* Interferon-λ1 (IFN-λ1) is a cytokine with potential applications for the treatment of viral infections and autoimmune diseases. Our product candidate, PEG-IFN-λ, is a pegylated version of the IFN-λ1 protein. We are conducting a Phase 1b trial to evaluate the safety and anti-viral activity of PEG-IFN-λ in patients with genotype 1 hepatitis C virus (HCV) infection who relapsed after the combination treatment of interferon-α and ribavirin. In November 2008, we presented positive interim study results at the American Association for the Study of Liver Diseases (AASLD) annual meeting. In January 2009, we entered into a global collaboration for PEG-IFN-λ with Bristol-Myers Squibb Company. Under the terms of the collaboration, the companies will co-develop PEG-IFN-λ in the United States and Europe. ZymoGenetics retains the option to co-promote and share profits on product sales in the United States and Bristol-Myers Squibb is responsible for commercializing the product outside the United States.

- *IL-21.* Interleukin-21 (IL-21) is a cytokine with potential use in the treatment of cancer. We have retained all rights to IL-21 in North America and recently reacquired rights in the rest of the world from Novo Nordisk A/S. We are conducting a Phase 2 clinical trial to test IL-21 in combination with the tyrosine kinase inhibitor Nexavar® (a product marketed by Bayer HealthCare AG and Onyx Pharmaceuticals, Inc.) in patients with metastatic renal cell carcinoma. Final results from the trial, including progression-free survival data, are expected in 2009. We are also conducting a Phase 2 clinical trial in collaboration with the National Cancer Institute of Canada to test IL-21 as a single agent in patients with metastatic melanoma. Results from this trial are also expected to be available in 2009.

In recent years, we have built a development organization with the skills and expertise necessary to design and implement successful clinical and regulatory strategies and commercial infrastructure to support the commercialization of RECOTHROM in the United States. We continue to leverage our resources by accessing complementary technologies, infrastructure and expertise through strategic partnerships. We have established product-related collaborations with Bayer for RECOTHROM and Bristol-Myers Squibb for PEG-IFN-λ. To preserve our cash and achieve greater operational efficiencies, while securing the value of our assets (atacicept, IL-31 mAb and IL-17RC), we restructured our relationship with Merck Serono, a division of Merck KGaA. In August 2008, we converted the development and commercialization agreement for atacicept into a worldwide royalty bearing license, under which Merck Serono will have exclusive worldwide development and commercialization rights for atacicept. In addition, we acquired exclusive worldwide rights to IL-31 mAb, while Merck Serono acquired exclusive worldwide rights to IL-17RC.

Over the past few years, our approach to discovery of new product candidates has evolved. In the mid-1990's, we developed an advanced bioinformatics platform and focused our research strategy on the discovery of novel genes and proteins within key protein families that had known members with demonstrated therapeutic potential or medically-relevant biological activity. These discovery efforts resulted in multiple product candidates that are currently a part of our clinical development portfolio (IL-21 and PEG-IFN-λ) or were out-licensed and are currently being developed by licensees (atacicept, FGF-18, IL-17RC, etc.). Recently, we shifted our early discovery efforts to antibodies and antibody-like molecules with inhibitory activity in validated biological pathways, where the biology suggests a straightforward approach to clinical development. We continue to develop our antibody capabilities to allow the development of single molecules that can target multiple biological pathways (i.e., bispecific molecules). We believe our bispecific platform provides a means to develop more efficacious therapeutics with potentially greater specificity. We have multiple bispecific molecules in various stages of research and preclinical development.

We file detailed patent applications with respect to our discoveries covering multiple patentable inventions, including composition of matter, method of making and method of use claims. We have issued patents or pending applications covering all of our internal product candidates in clinical development. In total, we have

more than 325 unexpired issued or allowed United States patents and over 280 United States patent applications pending. Outside of the United States, we have more than 670 issued or allowed foreign patents.

We have been active in the area of therapeutic proteins since our incorporation in the state of Washington in 1981. For 12 years we were a wholly owned subsidiary of Novo Nordisk, one of the world's largest producers of therapeutic proteins. We have contributed to the discovery or development of six recombinant protein products currently on the market. In November 2000, as part of a restructuring by Novo Nordisk, we became an independent company. In February 2002, we completed our initial public offering.

Commercial Product and Product Pipeline

Our current focus is the continued commercialization of our first product, RECOTHROM, and the development of PEG-IFN-λ in partnership with Bristol-Myers Squibb and other internal product candidates to treat a variety of serious diseases and medical conditions. We have out-licensed several product candidates that are outside of our core areas of interest or for which we could not justify the required capital investment. We are eligible to receive milestone payments and royalties related to these assets. Our track record in the field of therapeutic proteins includes contributions to the discovery or development of six recombinant protein products currently being marketed by Novo Nordisk or other companies. The following table summarizes our commercial product and product candidates that have been internally developed or co-developed, as well as out-licensed product candidates and commercial products.

	Commercial Product/ Product Candidate	Indication or Intended Use	Stage of Development	Ownership of Development/ Commercial Rights
Internal Commercial Product and Product Candidates	RECOTHROM® (also known as rThrombin)	General surgical hemostat	Marketed (U.S.) MAA filed (EU)	ZymoGenetics (U.S.); Bayer (outside U.S.)
	IL-21	Metastatic melanoma Metastatic renal cell carcinoma	Phase 2 Phase 2	ZymoGenetics
	PEG-IFN-λ	Hepatitis C virus infection Multiple sclerosis Hepatitis B virus infection	Phase 1b Preclinical Research	ZymoGenetics and Bristol-Myers Squibb (U.S.); Bristol-Myers Squibb (outside U.S.)
	IL-21 mAb	Inflammatory diseases	Pre-IND	ZymoGenetics (North America); Novo Nordisk (outside North America)
	IL-31 mAb	Atopic dermatitis Inflammatory diseases	Preclinical Research	ZymoGenetics(1)
Out-Licensed Product Candidates	Atacicept	Systemic lupus erythematosus Rheumatoid arthritis Multiple sclerosis	Phase 2/3 Phase 2 Phase 2	Merck Serono
	Augment™ Bone Graft/Augment™ Injectable Bone Graft (Platelet-derived Growth Factor)	Orthopedic fracture and other bone defects	Pivotal	BioMimetic Therapeutics, Inc.
	rFactor XIII	Congenital Factor XIII deficiency Cardiac surgery Cancer-related bleeding	Phase 3 Phase 1 Preclinical	Novo Nordisk
	FGF-18	Osteoarthritis	Phase 1	Merck Serono
	IL-17RC	Inflammatory diseases	Preclinical	Merck Serono
	IL-20	Psoriasis	Phase 1	Novo Nordisk
	IL-22 receptor	Psoriasis	Preclinical	Merck Serono
Out-Licensed Commercial Products	Novolin® (Insulin) and Insulin Analogs	Diabetes	Marketed	Novo Nordisk
	NovoSeven® (Factor VIIa)	Hemophilia	Marketed	Novo Nordisk
	Regranex® (Platelet-derived Growth Factor)	Wound healing	Marketed	Systagenix Wound Management (portfolio company of One Equity Partners LLC)
	GEM 21S® (Platelet-derived Growth Factor)	Periodontal defects	Marketed	BioMimetic Therapeutics, Inc.
	GlucaGen® (Glucagon)	Hypoglycemia; gastrointestinal motility inhibition	Marketed	Novo Nordisk
	Cleactor™ (tPA Analog)	Myocardial infarction	Marketed	Eisai Co., Ltd.

(1) Subject to certain opt-in rights granted to Merck Serono.

In the preceding table, "Research" refers to the stage in which we analyze the biology and therapeutic potential of newly discovered proteins using a variety of laboratory methods. "Preclinical" refers to the stage in which safety, pharmacology and proof of efficacy in non-human animal models of specific human disease are evaluated. "Pre-IND" refers to the stage in which investigational new drug enabling preclinical toxicology studies are performed and materials in support of the investigational new drug (IND) and clinical studies are manufactured. "Phase 1" refers to clinical trials designed primarily to determine safety and pharmacokinetics in healthy volunteers or a limited patient population. "Phase 1b" refers to clinical trials designed to demonstrate biomarker or clinical outcome that could be considered for proof of concept in a limited patient population. "Phase 2" refers to clinical trials designed to evaluate preliminary efficacy, further characterize safety and optimize dosing in a limited patient population. "Phase 2/3" refers to large-scale clinical trials designed to establish safety and confirm efficacy in comparison to standard therapies in a patient population large enough to

generate statistically significant results. "Phase 3" and "Pivotal" refers to clinical trials in a broad patient population with the intention of generating statistical evidence of efficacy and safety to support product approval.

Internal Commercial Product

RECOTHROM® (also referred to as rThrombin)

RECOTHROM Thrombin, topical (Recombinant) was approved by the FDA on January 17, 2008 for use as a general surgical hemostat. Net sales of RECOTHROM totaled $8.8 million during the year ended December 31, 2008. RECOTHROM is available in a 5,000 international unit (IU) vial, a 20,000 IU vial and a 20,000 IU vial co-packaged with the spray applicator kit. Three wholesalers, AmerisourceBergen Corporation, Cardinal Health, Inc. and McKesson Corporation, accounted for approximately 91% of U.S. sales in 2008. If any of these distributors ceased distributing RECOTHROM, other wholesalers already distributing RECOTHROM would likely absorb the incremental sales volume with minimal interruption to the business or we would sell directly to hospitals.

Thrombin is a specific blood-clotting enzyme that converts fibrinogen to fibrin, the primary protein contained in newly formed blood clots. Thrombin also promotes clot formation by activating Factor XIII, which cross-links the fibrin molecules and strengthens the newly forming clot. Plasma-derived thrombin is widely used to stop diffuse bleeding occurring during surgical procedures, when control of bleeding by standard surgical techniques, such as direct pressure, ligation, or cautery, is ineffective or impractical. Minimizing bleeding during surgical procedures is important to maintain visibility in the operating field, limit the use of transfused blood products and reduce peri- and post-operative complications. Thrombin is generally sold as a lyophilized powder stored at room temperature, which is dissolved in saline and absorbed onto a surgical sponge, embedded onto a hemostatic pad or sprayed directly for topical application to wounds. Prior to 2007, only bovine (cow) plasma-derived thrombin, Thrombin-JMI®, from King Pharmaceuticals, Inc. was available in the United States as a stand-alone product. In August 2007, the FDA approved human plasma-derived thrombin, Evithrom®, which is currently owned by Ethicon, Inc., a Johnson & Johnson Company. In December 2007, the FDA approved GELFOAM® Plus hemostasis kit, which contains GELFOAM® absorbable gelatin sponge from Pfizer, Inc. and human plasma-derived thrombin from Baxter Healthcare Corporation. The market for thrombin has grown since 2000, with the combined net sales of Thrombin-JMI, Evithrom and RECOTHROM estimated to be approximately $270 million in 2008. It has been estimated that thrombin is used in over a million surgical procedures annually in the United States.

We believe that there are several potentially important advantages to recombinant thrombin. Some patients may experience allergic reactions to plasma-derived products. Patients could also develop antibodies to bovine plasma-derived thrombin or to bovine Factor V or other protein impurities in the bovine plasma-derived product. In some cases, these antibodies can cross-react with analogous human proteins, creating a bleeding condition that can be difficult to manage and which has been fatal in patients who develop the most severe cases. Use of bovine plasma-derived thrombin in patients with pre-existing antibodies to bovine clotting factors may cause bleeding, thrombosis or other post-operative complications, which can result in increased treatment costs. The package insert for bovine plasma-derived thrombin contains a black box warning, the most serious form of warning the FDA can require for approved products, describing these potential risks. In addition, all human plasma-derived products carry an FDA warning addressing a potential risk of transmitting infectious and other diseases, including HIV, hepatitis, parvovirus, Creutzfeldt-Jakob disease (CJD) and variant CJD. RECOTHROM, which is recombinant thrombin, is inherently free from these potential risks and its package insert does not have a black box warning or any other warnings associated with the risk of transmitting blood-borne pathogens or infectious diseases. RECOTHROM is more convenient to handle and store as compared to Evithrom. RECOTHROM is available as a lyophilized powder, and is stored at room temperature, with a two-year shelf life. Evithrom must be stored frozen and thawed before use. Once thawed, it is stable in the refrigerator for only 30 days.

In June 2007, we entered into a license and collaboration agreement with Bayer Schering Pharma AG and a U.S. co-promotion agreement with Bayer HealthCare LLC. Under the license and collaboration agreement, Bayer

Schering Pharma will develop and commercialize RECOTHROM outside the United States. In addition, the two companies may collaborate to develop new presentations of RECOTHROM or product line extensions, in which rThrombin is combined with other passive or active hemostatic materials. Under the co-promotion agreement, Bayer HealthCare will provide sales people and medical science liaisons through at least March 2011 to support RECOTHROM commercialization in the United States. Depending on the level of sales in the first two years, Bayer may have an option to extend the co-promotion agreement for one additional year. In August 2008, Bayer Schering Pharma submitted the MAA to the EMEA for approval to market RECOTHROM Thrombin, topical (Recombinant) as a topical aid to control surgical bleeding. In November 2008, Bayer also filed a New Drug Submission (NDS) with Health Canada for marketing authorization of RECOTHROM Thrombin in Canada.

We have developed a patent-protected two-step process for the manufacture of recombinant thrombin. First, recombinant human prethrombin-1 (prethrombin-1) is produced in mammalian cells. Then, using an enzyme activation step, prethrombin-1 is converted to recombinant thrombin. A commercial-scale manufacturing process has been developed in collaboration with Abbott Laboratories, our commercial manufacturer of the RECOTHROM bulk drug substance.

General Surgical Hemostat. In September 2006, we completed a pivotal Phase 3 clinical study designed to evaluate the comparative efficacy of RECOTHROM and bovine thrombin, both administered with an absorbable gelatin sponge. The randomized, double-blind study was conducted at 34 sites in the United States and enrolled 411 patients in four surgical settings: spinal surgery, liver resection, peripheral artery bypass and arteriovenous graft construction. Both the primary and secondary endpoints of the study were met. RECOTHROM was shown to have comparable efficacy to bovine thrombin, as measured by the overall percentage of patients achieving hemostasis within 10 minutes. RECOTHROM also demonstrated a superior immunogenicity profile to bovine thrombin, based on a significantly lower incidence of post-treatment anti-product antibody development. Both treatments were well tolerated and exhibited similar adverse event profiles. The results from this study were published in the Journal of the American College of Surgeons in August 2007. Based on the pivotal Phase 3 study results, we received FDA approval on January 17, 2008 to market RECOTHROM as a general aid to control bleeding during surgery applied with an absorbable gelatin sponge. In May 2008, the FDA approved a Prior Approval Supplement (PAS) for a 20,000 IU vial of RECOTHROM in addition to a 5,000 IU vial.

In December 2008, we completed an open-label Phase 3b study designed to evaluate the safety and immunogenicity of RECOTHROM in subjects at increased risk for having anti-bovine thrombin product antibodies as a result of prior surgical history. The study enrolled 205 subjects, 16% of which had pre-existing antibodies to bovine thrombin. The study results demonstrated that no patients developed antibodies against RECOTHROM. Following a 29-day period after topical RECOTHROM application during a single spinal or vascular surgical procedure, the immunogenicity profile of RECOTHROM did not differ among subjects with or without pre-existing antibodies to bovine thrombin. RECOTHROM was well tolerated and observed adverse events were consistent with those commonly seen in post-surgical settings. In January 2009, as a part of our post marketing approval commitments, we initiated an open-label Phase 4 clinical study to evaluate the safety and immunogenicity of re-exposure to RECOTHROM in approximately 30 subjects who previously received RECOTHROM during our pivotal Phase 3 study. In addition, under the Pediatric Research Equity Act, we plan to initiate an open-label Phase 4 clinical study to evaluate the safety of RECOTHROM as an aid to hemostasis in a pediatric population in the first half of 2009.

Spray Applicator Kit. In August 2007, we completed an open-label, non-comparative Phase 2 clinical trial designed to evaluate safety and immunogenicity of RECOTHROM administered using a spray device in patients with burns undergoing autologous skin grafting. The study results, which demonstrated a safety and immunogenicity profile similar to that observed in the pivotal Phase 3 study, were presented at the American Burn Association annual meeting in April 2008. In January 2008, after the initial RECOTHROM regulatory approval, we submitted a PAS to the FDA for co-packaging of the RECOTHROM 20,000 IU vial with a spray applicator kit, which was approved in May 2008.

In January 2008, we launched RECOTHROM in the United States with a combined sales force of experienced sales professionals from ZymoGenetics and our co-promotion partner Bayer HealthCare. The ZymoGenetics sales force consists of six regional business directors and 48 surgical sales managers, fully dedicated to promoting RECOTHROM. Currently, the combined sales force includes more than 100 sales professionals. We also established the supply chain for RECOTHROM, from sourcing of critical raw materials and manufacturing to distribution to end customers, and built sufficient commercial inventories to meet expected market demand and provide what we believe are sufficient levels of safety stock.

In June 2008, we entered into a financing arrangement with Deerfield Management (Deerfield) whereby we can borrow up to $100 million in four draws of $25 million each until January 2010. Each $25 million draw entitles Deerfield to a royalty equal to 2% of RECOTHROM net sales in the United States.

We own issued United States and foreign patents directed to certain recombinant human thrombin, a genetically engineered thrombin precursor termed "prethrombin-1", methods of producing recombinant human thrombin from prethrombin-1, formulations, and methods of activation and therapeutic use of the protein.

Internal Product Candidates

PEG-IFN-λ

IFN-λ1 (formerly known as IL-29) is a type III interferon that belongs to the 4-helical-bundle cytokine family. IFN-λ1 is generated in response to a viral infection and exhibits broad anti-viral activity similar to type I interferons, such as interferon-alpha. However, IFN-λ1 signals through a receptor that is distinct from the one for type I interferons and has a more selective expression pattern compared to the widely expressed receptor for type I interferons. The difference in the receptor tissue distribution suggests that IFN-λ1 may serve as an alternative to interferon-alpha based therapy for viral infection by providing antiviral activity with potentially fewer side effects.

In vitro studies have shown that IFN-λ1 has antiviral activity against human hepatitis C virus (HCV) in the sub-genomic HCV replicon model. Additionally, we have demonstrated that IFN-λ1 induces antiviral gene expression similar to interferon-alpha in primary human hepatocytes. IFN-λ1 has also been shown to enhance viral antigen presentation, which may promote an immune response against the virus. Combined with the significant expression of the receptor for IFN-λ1 in liver samples from HCV positive individuals, these data provided the rationale for selecting HCV infection as our first clinical indication.

Chronic infection with HCV is a leading cause of cirrhosis, liver failure, and hepatocellular carcinoma worldwide. It is estimated that there are over 170 million people worldwide infected with hepatitis C virus. In the United States, an estimated 4.0 million people have been exposed to HCV, and approximately 3.1 million have chronic HCV infection. HCV is associated with an estimated 10,000-12,000 deaths per year and is the main indication for liver transplantation in the United States. The current standard of care for chronic HCV infection involves treatment with the combination of pegylated interferon-alpha and ribavirin. Interferon-alpha based therapy has been associated with a number of significant side effects, including flu-like symptoms, anorexia, depression, hemolytic anemia and myelosuppression, which continue to be a treatment-limiting factor. With a response rate to the current standard treatment for the most common form of HCV – genotype 1 HCV – in the United States of only 40%, there remains a need for better tolerated and more effective therapy for HCV infection. Our product candidate, PEG-IFN-λ, is a pegylated version of the IFN-λ1 protein. Pegylation extends the *in vivo* half-life of the protein, potentially allowing for convenient dose scheduling, such as once per week.

In January 2009, we entered into an exclusive global collaboration with Bristol-Myers Squibb for PEG-IFN-λ. Under the terms of the collaboration, the companies will co-develop PEG-IFN-λ in the United States and Europe, sharing development costs. We will conduct the ongoing Phase 1 and certain Phase 2 clinical trials. We will have the option to co-promote PEG-IFN-λ and to share profits on product sales in the United States, while receiving royalties on sales in the rest of the world. We may opt out of the co-development,

co-promotion and profit sharing arrangement in the United States, in which case we would receive royalties on worldwide product sales.

In 2007, we completed a randomized, placebo-controlled, dose-escalation Phase 1a clinical trial in healthy volunteers to evaluate the safety, tolerability and pharmacokinetics of a single dose of PEG-IFN-λ administered subcutaneously. The study enrolled 20 subjects who were randomized to four dose levels of PEG-IFN-λ, ranging from 0.5 to 7.5 mcg/kg, or placebo. The results from this study demonstrated that administration of a single dose of PEG-IFN-λ was associated with dose-related pharmacokinetic and pharmacodynamic effects, with evidence of biological activity, including up-regulation of interferon response markers, being observed at dose levels of 1.5 mcg/kg and above. No fever or hematologic effects, which are typically seen with interferon-alpha, were observed at all tested dose levels in this study.

In December 2007, we initiated a two-part Phase 1b study to evaluate the safety and antiviral effect of repeat dosing of PEG-IFN-λ in patients with genotype 1 HCV infection who have relapsed after combination treatment of interferon-alpha and ribavirin. In Part 1 of this study, PEG-IFN-λ is administered subcutaneously as a single agent weekly and bi-weekly over a four-week period at biologically active dose levels of 1.5 and 3.0 mcg/kg. Enrollment in Part 1 was completed in January 2009. A total of 24 patients were enrolled in 4 cohorts, consisting of 6 patients each. In Part 2, PEG-IFN-λ is being administered weekly in combination with ribavirin over a four-week period. Enrollment in Part 2 is ongoing. Interim results from 18 patients in Part 1 demonstrated anti-viral activity at all tested dose levels, with the best anti-viral effect observed at a dose of 1.5 mcg/kg administered weekly. All six patients treated in this cohort showed a two log or greater decrease in viral load after four weeks. PEG-IFN-λ was also well tolerated at all dose levels, with no discontinuations due to toxicity, no treatment-related fever, no signs of hematological toxicity and no meaningful changes in hematological parameters. These interim results were presented at the American Association for the Study of Liver Diseases (AASLD) annual meeting. Final results from Part 1 and Part 2 of the Phase 1b study are expected to be available in 2009. Together with our partner Bristol-Myers Squibb, we plan to move PEG-IFN-λ into Phase 2 development in 2009.

We own issued patents for IFN-λ1 polypeptides, polynucleotides, expression vectors, cells, methods of treating a hepatitis infection, and a method of producing IFN-λ1. We have filed patent applications for IFN-λ1 polypeptides, IFN-λ1 fusion proteins, antibodies, methods of expressing and purifying IFN-λ1, methods of using IFN-λ1 alone and in combination with other therapeutic agents to treat various viral diseases, cancers and autoimmune disorders. We will continue to file patent applications as new inventions are made. As part of our agreement with Bristol Myers Squibb, we will assign to Bristol Myers Squibb a one-half ownership interest in each core patent relating to PEG-IFN-λ filed outside the United States.

IL-21

IL-21 is a protein belonging to a family of cytokines that modify the function of cells in the immune system. We have shown that IL-21 activates several types of immune cells thought to be critical in eliminating cancerous or virally infected cells from the body. More specifically, IL-21 enhances the activity of mature natural killer (NK) cells; it has multiple effects on cytotoxic T lymphocyte cells (CTL), including increased activation and proliferation, extended longevity in circulation and improved ability to kill cancerous cells; and it enhances B-cell antibody production.

Preclinical studies have indicated that our recombinant version of IL-21 is an effective therapy in a number of animal models of cancer. In an animal model of metastatic melanoma, IL-21 was associated with significant anti-tumor activity. Animals in this model develop aggressive metastases to the lung, which can be readily measured. Treatment with IL-21 led to a significant reduction in the number of lung metastases relative to controls. IL-21 also was found to have potent inhibitory activity in other animal models of cancer, especially renal cell cancer. These models demonstrated that the *in vivo* effects of IL-21 were mediated through the activation of CTL and NK cells, which contribute to rejection of the tumors in the animal models. Moreover, this led to establishment of immunological memory, which protected animals from rechallenge with the parent tumor.

We believe that IL-21 could represent a potentially better tolerated and more efficacious immunotherapeutic agent than other cancer immunotherapies, such as interleukin-2 (IL-2) and interferon-alpha. In clinical practice, IL-2 is an effective therapy producing durable responses in a very small percentage of patients with metastatic melanoma and metastatic renal cell carcinoma. Accompanying this relatively low level of efficacy are significant toxicities, including vascular leak and the release of pro-inflammatory cytokines, which profoundly limit the utility of IL-2 in treating disease. These side effects can be so severe that many patients are either hospitalized or stop the therapy before completion of the treatment program. Although somewhat better tolerated, interferon-alpha therapy is associated with significant chronic toxicities limiting its administration and produces a lower overall response rate with fewer complete responses compared to IL-2.

We own worldwide rights to our product candidate, IL-21 protein. Previously we retained only the North American rights to IL-21, including the IL-21 protein, and out-licensed rest of the world rights to IL-21, including the IL-21 protein, to Novo Nordisk. In January 2009, subsequent to a strategic decision by Novo Nordisk to exit all of its oncology development programs, we reacquired rest of the world rights to the IL-21 protein. Simultaneously, we and Novo Nordisk terminated the collaborative data sharing and cross-license agreement, which provided the framework for sharing data and coordinating clinical development activities, and the manufacturing agreement, under which Novo Nordisk was supplying clinical materials. As part of this termination, we acquired rights to all data generated and clinical product manufactured by Novo Nordisk. We expect the transfer to be completed during the first half of 2009. The reacquisition agreements do not require any upfront payment to Novo Nordisk. However, we will owe milestone payments and royalties to Novo Nordisk upon commercialization of IL-21.

We are pursuing metastatic melanoma and metastatic renal cell carcinoma as initial indications for IL-21. There are an estimated 62,000 new cases of melanoma per year in the United States, with over 8,000 deaths per year attributed to this disease. Metastatic melanoma is essentially an incurable cancer with no established standard of care. There are an estimated 54,000 new cases of renal cell carcinoma per year in the United States, with over 13,000 deaths per year attributed to this disease. In the past several years, three new products were approved by the FDA for the treatment of advanced renal cell carcinoma: two oral tyrosine kinase inhibitors (TKIs) – Nexavar® (a product marketed by Bayer HealthCare AG and Onyx Pharmaceuticals, Inc.) and Sutent® (a product marketed by Pfizer, Inc.) – and one mammalian target of rapamycin (mTOR) inhibitor administered via intravenous infusion – Torisel® (a product marketed by Wyeth Pharmaceuticals Inc.). While these products extend the time during which patients live without evident tumor progression, the disease remains incurable. In October 2005, the FDA granted IL-21 orphan drug status for the treatment of melanoma patients with advanced or aggressive disease.

In 2006, we completed a Phase 1 clinical trial in patients with metastatic melanoma or metastatic renal cell carcinoma and Novo Nordisk completed a Phase 1 study in patients with metastatic melanoma. The combined results from the Phase 1 studies demonstrated that IL-21 had a favorable safety profile and can be used in an outpatient setting. We also observed preliminary evidence of anti-tumor activity in both metastatic renal cell carcinoma and melanoma patients.

Metastatic Renal Cell Carcinoma. Our development strategy for IL-21 in metastatic renal cell carcinoma is focused on a combination approach with TKIs. We have shown that IL-21 in combination with TKIs has additive anti-tumor effect *in vivo* in preclinical model(s). We are conducting an open-label Phase 1/2 clinical trial of IL-21 in combination with Nexavar in patients with advanced renal cell carcinoma, with the Phase 1 part of the study completed in December 2007 and Phase 2 initiated in January 2008. In Phase 1 of the study, we established the maximum tolerated dose (MTD) of IL-21 in combination with Nexavar at 30 mcg/kg. The ongoing Phase 2 study is designed to evaluate the safety, pharmacokinetics and anti-tumor activity of the combination therapy at the MTD. Study endpoints are overall response rate and progression-free survival. Interim Phase 2 results, which were presented at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in October 2008, provided further evidence of anti-tumor activity of the combination therapy, including partial responses in five of 18 patients. The combination of IL-21 with Nexavar was also

associated with side effects that are manageable in an outpatient setting. A total of 33 patients were enrolled in the Phase 2 study. Final study results, including progression-free survival data, are expected to be available in 2009.

Metastatic Melanoma. Based on Phase 1 results, we are continuing development of IL-21 in metastatic melanoma as a single agent. Novo Nordisk completed an open-label Phase 2 clinical trial in Australia in December 2007. That study was designed to confirm the IL-21 activity at a dose level of 30 mcg/kg. In December 2007, we initiated an open-label Phase 2 clinical trial of IL-21 in previously untreated patients with metastatic melanoma. This study is being run by the National Cancer Institute of Canada and will evaluate two dose levels of IL-21 (30 and 50 mcg/kg) in approximately 50 patients. The study will investigate if a higher dose of IL-21 (50 mcg/kg) can be tolerated as an outpatient treatment and result in greater anti-tumor activity. Results from this trial are expected to be available in 2009.

Other Indications. We have explored the use of IL-21 in combination with monoclonal antibodies, particularly those like Rituxan® (a product marketed by Genentech, Inc. and Biogen Idec Inc.) that function via antibody-dependent cellular cytotoxicity, a process enhanced by IL-21. In January 2008, we completed a two-part open-label Phase 1 clinical trial of IL-21 in combination with Rituxan in patients with relapsed low-grade B-cell lymphoma. Part 1 of the study, which included nine patients, evaluated three dose levels of IL-21 (30, 100 and 150 mcg/kg) in combination with Rituxan. A dose of 100 mcg/kg was identified as safe and well tolerated in combination with Rituxan. Part 2 of the study evaluated the safety and anti-tumor effects of the combination of IL-21 at 100 mcg/kg and Rituxan in 12 additional patients. A total of 15 patients were treated at a 100 mcg/kg dose of IL-21. Final Part 2 results demonstrated that the combination of IL-21 at 100 mcg/kg with Rituxan was well tolerated and provided evidence of anti-tumor activity in this heavily pre-treated population, including one confirmed complete response, one unconfirmed complete response and three partial responses. Final study results were presented at the ASCO annual meeting in May 2008.

We own issued patents for IL-21 polypeptides, polynucleotides and methods of using IL-21 to stimulate immune responses, particularly in tumor-bearing subjects as well as to the cell lines and methods of producing the recombinant IL-21 clinical product. We have filed patent applications for IL-21 antibody compositions, additional compositions, IL-21 fusion proteins and other methods of using IL-21 for the treatment of disease. We have additional patent applications relating to IL-21 directed to methods for expressing and purifying recombinant IL-21; methods of treating specific cancers and viral diseases; combination therapies for IL-21 and monoclonal antibodies and IL-21 and TKIs; and antagonist IL-21 ligands. We will continue to file patent applications as new inventions are made.

IL-21 mAb

IL-21 monoclonal antibody (IL-21 mAb) is a fully human monoclonal antibody derived from the Medarex mouse system that binds to and neutralizes human IL-21 with high affinity. IL-21 is a T-cell derived cytokine that exerts multiple effects on both T-cell and B-cell responses. In particular, IL-21 is a key regulator of two types of T cells: Th17 cells and T follicular helper (TFH) cells. Th17 cells are known to be involved in inflammation. By blocking IL-21 with IL-21 mAb, we expect to reduce inflammation in a number of diseases that share this pathway, such as psoriasis, Crohn's disease and rheumatoid arthritis. TFH cells are specialized types of T cells that promote antibody responses from B cells. By blocking IL-21's effect on B cells, we expect to have an impact on human diseases that are driven by antibody responses, such as systemic lupus erythematous (SLE). Murine models of psoriasis, Crohn's disease (colitis), rheumatoid arthritis and SLE have demonstrated that inhibition of IL-21 leads to significant reductions in disease scores and pathology.

We have retained all rights to IL-21 mAb within North America and, pursuant to an option and license agreement, Novo Nordisk has licensed certain rights to IL-21 antibodies outside North America. IL-21 mAb is currently in the pre-IND stage and we intend to evaluate it as a treatment for inflammatory diseases.

In addition to patents and patent applications related to IL-21, we have filed several patent applications relating to anti-IL-21 monoclonal antibodies and their use in disease, including autoimmune and inflammatory diseases. We currently own worldwide rights to all such antibody patents and patent applications, subject to Novo Nordisk's license to certain of them. We will continue to file patent applications as new inventions are made.

IL-31 mAb

IL-31 is a cytokine derived from T cells, which we discovered. Analysis of IL-31 and IL-31 receptor levels in human and murine disease tissues suggests that IL-31 could play a role in atopic dermatitis (AD) and other inflammatory disorders. Transgenic animals expressing the IL-31 gene develop a severe skin phenotype that resembles human AD, resulting from a chronic scratch response to itch induced by over-expression of IL-31. Itch is a characteristic of human AD and the scratch response to itch is thought to be a major contributor to the severity of disease. Treatment of animals in a murine model of AD with a neutralizing antibody against IL-31 results in the reduction of the incidence of the scratch response. Additionally, analysis of peripheral blood T cells from human atopic dermatitis patients provides an association between IL-31 and skin-homing T cells, suggesting that cutaneous diseases, such as AD, should be considered as a leading therapeutic area for inhibition of IL-31.

We own worldwide rights to IL-31, including protein products that target IL-31 such as monoclonal antibodies, subject to certain opt-in rights held by Merck Serono. Previously, Novo Nordisk licensed the rights to IL-31 outside North America pursuant to an option and license agreement. Subsequently, under our strategic alliance with Merck Serono, we entered into a co-development and co-promotion agreement for IL-31 within the United States and granted Merck Serono an exclusive license to IL-31 in Mexico and Canada. In June 2008, Novo Nordisk terminated its license to IL-31. In August 2008, as a part of restructuring our strategic alliance with Merck Serono, we acquired exclusive worldwide development and commercialization rights to IL-31, subject to certain opt-in rights granted to Merck Serono. Our product candidate is a humanized anti-IL-31 monoclonal antibody (IL-31 mAb), which was developed jointly by Novo Nordisk, Merck Serono and ZymoGenetics, and is currently in preclinical development for AD.

We have issued patents to IL-31. We also have filed several patent applications relating to IL-31 and IL-31 antagonists on a worldwide basis, which cover protein products that target IL-31, including monoclonal antibodies, and will continue to file new patent applications as new inventions are made.

Out-licensed Product Candidates

Atacicept (formerly known as TACI-Ig)

TACI is a member of the tumor necrosis factor receptor family of proteins. Atacicept is a soluble form of the TACI receptor that binds to two ligands, BLyS and APRIL, that are implicated in B-cell survival, maturation and antibody production. We believe that atacicept could represent a more specific immunosuppressive agent with less off-target activities, making it more potent and less toxic than current therapies for the treatment of autoimmune diseases. Such diseases include systemic lupus erythematous (SLE), rheumatoid arthritis (RA) and multiple sclerosis (MS).

Until August 2008, atacicept was developed jointly by us and Merck Serono S.A. pursuant to a collaborative development and marketing agreement established in 2001. Effective August 28, 2008, we converted this agreement to a worldwide royalty license, granting Merck Serono exclusive worldwide development and commercialization rights for atacicept. We discontinued our co-development and co-funding obligations, while Merck Serono assumed full responsibility for the program's cost. By converting to a royalty position, we will avoid a major capital commitment, reduce operating expenses and preserve cash over the next several years, while maintaining the value of our atacicept asset. Merck Serono is currently developing atacicept in three indications: SLE, RA and MS.

Systemic Lupus Erythematosus. Based on positive data from animal models, SLE was selected as one of the initial clinical indications for atacicept. The cause of this disease remains unknown, but there is substantial evidence suggesting that B-cell hyperactivity resulting in the secretion of autoantibodies is fundamental to its development. It is estimated that approximately 1.5 million people in the United States suffer from some form of lupus. The number of diagnosed cases of SLE in the United States is estimated to be approximately 358,000, with at least 30% of them involving lupus nephritis (LN), a severe form of SLE that is characterized by inflammation of the kidneys. There are believed to be approximately 484,000 treated patients with SLE in major markets, with approximately 323,000 of these in the United States. No new FDA-approved treatment for SLE has been introduced in the last 40 years. Current therapies, including immunosuppressive agents and corticosteroids, have limited efficacy and are associated with severe and debilitating toxicities. We believe that patients diagnosed with moderate to severe SLE would be candidates for treatment with atacicept. Merck Serono is conducting a randomized, double-blind, placebo-controlled Phase 2/3 clinical trial of atacicept in patients with general SLE. The study is being conducted under a Special Protocol Assessment (SPA) agreement with the FDA. In October 2008, Merck Serono discontinued a Phase 2/3 study in patients with lupus nephritis. The study was discontinued due to the observation of the increased risk of severe infection, possibly resulting from significant underlying disease activity and the concomitant use of several immunosuppressive agents.

Rheumatoid Arthritis. Rheumatoid arthritis is one of the most prevalent chronic inflammatory diseases, afflicting an estimated 1% of the population in industrialized countries, including approximately five million patients in North America, Europe and Japan. Although the underlying cause of RA is unknown, considerable data indicate a major role of B cells in this disease. RA has been an attractive therapeutic area for drug development because of its large market size and robust measures of disease activity. As a consequence, several drugs have been developed and a large number of drugs are currently being developed. Atacicept represents a novel mode of treatment that could alleviate the symptoms of RA associated with pathogenic B cells. Moreover, the apparent lack of side effects and mode of action of atacicept strengthens its potential as an add-on therapy to existing drugs. In the second half of 2008, Merck Serono completed enrollment in two ongoing Phase 2 studies. Both studies are randomized, double-blind, placebo-controlled Phase 2 clinical trials evaluating atacicept in different patient populations: one in RA patients with inadequate response to TNF inhibitor therapy and another in RA patients who have not previously received TNF inhibitor therapy. In addition, Merck Serono initiated a third Phase 2 clinical trial to evaluate safety and efficacy of atacicept in combination with Rituxan® (a product marketed by Genentech, Inc. and Biogen Idec Inc.) in 2008.

Multiple Sclerosis. Multiple sclerosis is a chronic inflammatory disease that affects the central nervous system. While the annual number of new cases of MS is small, the long clinical course of the disease results in a relatively large patient population. In 2005, approximately 260,000 people were affected by this disease in the United States, with a predicted annual growth rate of 0.9% through 2010. MS is typically treated with immunotherapies, which have modest efficacy, inconvenient administration and unfavorable side effect profiles. There is a scientific and medical rationale that B-cell depletion may provide an effective mode of therapy in this disease. Merck Serono is conducting two studies in MS. The first study is a placebo-controlled Phase 2 clinical trial, which will evaluate reduction in central nervous system inflammation in patients with relapsing MS. The second study is a placebo-controlled exploratory trial evaluating the neuroprotective effect of atacicept in patients with optic neuritis, an inflammation of the optic nerve which in some patients may be the first manifestation of MS.

Other Out-licensed Product Candidates

Augment™ Bone Graft (formerly GEM-OS1™)/Augment™ Injectable Bone Graft (formerly GEM-OS2™). Augment Bone Graft/Augment Injectable Bone Graft is a combination of platelet-derived growth factor (PDGF-BB) and a synthetic bone matrix. PDGF-BB is a growth factor that stimulates the growth of a variety of cell types, including bone forming cells. We have out-licensed this protein to BioMimetic Therapeutics, Inc. for the treatment of bone defects. BioMimetic is developing Augment Bone Graft for the treatment of fractures in open surgical settings and Augment Injectable Bone Graft for the treatment of fractures

in closed surgical settings and for prophylactic bone augmentation. BioMimetic has completed a pivotal trial in Canada and is conducting pivotal trials in the United States and Europe to evaluate Augment Injectable Bone Graft for use in foot and ankle fusion procedures. Other clinical studies are also being conducted to evaluate Augment Injectable Bone Graft for fracture repair.

rFactor XIII. rFactor XIII is a recombinant version of a protein that is involved in blood clotting, and is being developed for the treatment of bleeding disorders. Novo Nordisk acquired rights to this protein in October 2004 after we completed several Phase 1 clinical trials in healthy volunteers and in patients with congenital Factor XIII deficiency. Novo Nordisk is conducting a Phase 3 study of rFactor XIII in patients with congenital Factor XIII deficiency and is planning to begin a Phase 2 study in patients undergoing cardiac surgery in 2009.

Fibroblast growth factor-18 (FGF-18). FGF-18 is a novel member of the fibroblast growth factor family of proteins. Our preclinical data suggest that FGF-18 may be useful for healing cartilage damaged by injury or disease. We out-licensed this protein to Merck Serono in October 2004 in conjunction with the strategic alliance. In late 2007, Merck Serono initiated a Phase 1 clinical trial of FGF-18 for the treatment of osteoarthritis.

IL-17 receptor C (IL-17RC). IL-17RC is a soluble receptor that binds to both IL-17A and IL-17F, the two most closely related cytokines in the IL-17 family. Both cytokines are highly expressed in a variety of inflammatory and autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis and transplant rejection. We hypothesize that use of IL-17RC to neutralize the pro-inflammatory properties of IL-17A and IL-17F could have a beneficial therapeutic effect in any or all of these diseases. In August 2008, as part of the restructuring of our relationship, Merck Serono acquired an exclusive development and commercialization license to IL-17RC worldwide. The product candidate is currently in preclinical development.

IL-20. IL-20 is a member of the IL-10 cytokine family. In September 2001, Novo Nordisk licensed the rights to IL-20 outside North America pursuant to the option and license agreement. In March 2004, they licensed the rights to IL-20 in North America under a separate agreement. Our preclinical data suggest that IL-20 may play an important role in the regulation of cutaneous inflammation and the pathology of psoriasis, and therefore is a potential target for the treatment of psoriasis.

IL-22 receptor subunit alpha (IL-22RA). IL-22RA is a cytokine receptor that signals both IL-20 and IL-22 activities and which is a potential target for the treatment of psoriasis. We out-licensed this protein to Merck Serono in October 2004 as part of the strategic alliance.

Out-licensed Commercial Products

We have participated in the discovery or development of six recombinant protein products marketed by other companies.

Novolin® (insulin) and insulin analogs. Novolin and insulin analogs are marketed by Novo Nordisk worldwide for the treatment of diabetes. In collaboration with Novo Nordisk, we developed a process for the production of recombinant human insulin in yeast that is used by Novo Nordisk.

NovoSeven® (recombinant Factor VIIa). NovoSeven is a protein involved in the generation of blood clots, marketed worldwide by Novo Nordisk for the treatment of hemophilia patients. We cloned the gene that codes for human Factor VII and developed the process for the production of activated recombinant human Factor VII, or recombinant Factor VIIa, which led to the establishment of the manufacturing process that Novo Nordisk currently uses to produce this protein.

Regranex® (platelet-derived growth factor). Regranex, until recently a product of Ethicon, Inc., a Johnson & Johnson company, is a growth factor approved for the treatment of non-healing diabetic ulcers. In December 2008, One Equity Partners LLC announced the acquisition of Regranex from Ethicon Inc., which will

be marketed and distributed by Systagenix Wound Management, a new company created by One Equity Partners LLC. We cloned the gene that codes for platelet-derived growth factor and demonstrated the importance of this protein in stimulating wound healing.

GEM 21S® (platelet-derived growth factor). GEM 21S is a combination of a platelet-derived growth factor with a synthetic bone matrix, developed by BioMimetic Therapeutics, Inc. and marketed by Osteohealth Company, a division of Luitpold Pharmaceuticals, Inc. for the treatment of bone loss and gum tissue recession associated with advanced periodontal disease. We cloned the gene that codes for platelet-derived growth factor, the active agent in GEM 21S.

GlucaGen® (glucagon). GlucaGen is a protein marketed by Novo Nordisk, Bedford Laboratories and Eisai Co., Ltd. (Eisai) for use as an aid for gastrointestinal motility inhibition and for the treatment of severe hypoglycemia in diabetic patients treated with insulin. In collaboration with Novo Nordisk, we developed a process for the production of this protein that is currently used by Novo Nordisk in the manufacture of GlucaGen.

Cleactor™ (tPA analog). Cleactor is a modified form of the protein tissue plasminogen activator, marketed in Japan by Eisai for the treatment of myocardial infarction, or heart attacks. In collaboration with Eisai, we developed this modified protein, which has enhanced properties that allow it to be given as a single injection.

We have earned royalties on sales of some of these products. In the aggregate, from sales of these products and other technology licenses, we earned royalties of $6.3 million, $6.3 million and $6.9 million for the years ended December 31, 2008, December 31, 2007 and December 31, 2006, respectively.

Commercialization

To commercialize RECOTHROM in the United States, we established our own dedicated commercial operations team with sales and sales operations, marketing, and supply chain and inventory management functions. While we believe that the thrombin market, with its concentrated customer base, can be addressed with a relatively small sales force and that our recombinant technology gives us a competitive advantage in the current market, we entered into a co-promotion agreement with Bayer HealthCare to further facilitate conversion and maximize penetration of RECOTHROM in the United States market. Currently, the combined sales force includes more than 100 sales professionals. Our dedicated sales force consists of six regional business directors and 48 surgical sales managers. The combined sales force has been actively working to convert the top bovine thrombin accounts to RECOTHROM, by focusing on key surgeons, clinical pharmacists, operating room nurses and Pharmacy and Therapeutics (P&T) committee members within each account. Our strategy in the surgical hemostasis area includes potential RECOTHROM line extension products and other complimentary products, which we would develop internally and/or in-license and which we would market and sell through our commercial operation.

With our other product candidates, we may pursue commercialization in North America internally, through co-development/co-commercialization or out-licensing strategies. We will only consider independently developing and commercializing products in North America that we believe could be successfully developed with our current infrastructure or with limited additions. In most situations, we expect to pursue co-development, with cost sharing and potential for co-commercialization in North America, or out-licensing.

Research and Development

We have developed a fully integrated therapeutic protein research and development infrastructure that draws upon a broad range of skills and technologies, including scientific computing, molecular and cellular biology, animal models of human disease, protein chemistry, antibody generation and engineering, pharmacology and toxicology, clinical development, medical and regulatory affairs, drug formulation, process development and protein manufacturing. We believe that this comprehensive approach gives us a competitive advantage, enabling us to effectively expand our diverse pipeline of therapeutic proteins.

Our discovery and research activities span from identifying proteins with potential therapeutic value through designing and/or selecting a product candidate and testing it in animal models of human diseases. We are pursuing several approaches to generating biologic product candidates for the treatment of diseases in the areas of autoimmunity, inflammation and oncology, allowing us to impact a wide variety of biological pathways in ways that have therapeutic relevance. Our expertise includes the discovery and development of protein ligands, soluble receptors and conventional antibodies as therapeutic candidates. Our clinical development candidates (IL-21 and PEG-IFN-λ) and preclinical candidates (IL-21 mAb and IL-31 mAb) exemplify these approaches. We have recently implemented strategies to allow for the development of single molecules that can target multiple biological pathways (i.e., bispecific molecules). We believe that our bispecific platform provides a means to develop more efficacious therapeutics with potentially greater specificity. We have multiple bispecific molecules in various stages of research and preclinical development.

To evaluate a protein's biological function and its potential as a therapeutic candidate, we go through several stages of research activities. Potential product candidates begin in the exploratory phase, during which we conduct an intensive literature review and, if necessary, perform experiments to support the development of a biological hypothesis as to the candidate's biological function. Once a biological hypothesis is developed, the candidate moves to the investigational phase, during which we conduct an in-depth evaluation of the competitive landscape and, if required, complete more extensive experiments to confirm the biological hypothesis and to establish a medical hypothesis. A medical hypothesis involves the identification of specific diseases or conditions, for which we believe the candidate might have therapeutic importance. If the competitive landscape is favorable and a solid medical hypothesis can be established, the candidate moves to the lead development phase. During this phase, a lead therapeutic molecule is produced and tested in a variety of animal models, where we try to learn which diseases or conditions show promise for treatment, test dosing regimens and examine systemic effects of the product candidate. Assuming positive results, both in terms of efficacy and toxicology, we may decide to move the product candidate into development. At this stage, a commercial hypothesis for the product candidate is developed that requires the identification of a market opportunity and a preliminary determination that it will be economically feasible to manufacture the product candidate and administer it to patients.

In recent years, we have built a development organization with the skills and expertise to design and implement clinical trials for multiple product candidates and to file license applications with the FDA and other regulatory agencies. Our in-house development resources include a clinical development group responsible for designing, conducting and analyzing clinical trials. The group includes clinical research, clinical operations, biometrics, medical writing and drug safety. Our preclinical development group provides support in the areas of bioanalytical research and development, pharmacology, toxicology, pathology and pharmacokinetics. Our regulatory affairs group develops regulatory strategies and manages communications and submissions to regulatory agencies.

For additional details for research and development activities, refer to the Operating Expenses section under "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations Overview".

Manufacturing

RECOTHROM® (also referred to as rThrombin)

In preparation for the RECOTHROM launch in the United States, we established a commercial supply chain, which relies on single-source vendors. We have entered into a long-term manufacturing agreement with Abbott Laboratories for commercial-scale production of recombinant thrombin (rThrombin), the bulk active drug substance in RECOTHROM. Under the agreement, Abbott manufactures rThrombin using mammalian cells, according to specifications developed and agreed upon by both companies. Abbott has committed to supply each year up to a maximum amount, which we believe is sufficient to meet our projected market demand and provide adequate safety stock. The agreement will terminate in 2018. To obtain raw material for manufacture of rThrombin bulk drug substance, we have entered into long-term supply agreements with the supplier of snake

protein and the manufacturer of immobilized prothrombin activator (PTA), which is used to activate prethrombin-1, the precursor for rThrombin. We have also entered into a long-term manufacturing services agreement with Patheon, Inc. for fill and finish of rThrombin. In addition, we have entered into agreements with Anderson Packaging, Inc., a division of AmerisourceBergen Corp., as our secondary packaging vendor and Cardinal Health SPS, Inc. as our third party logistics and distribution partner. Under the terms of a license and collaboration agreement with Bayer Schering Pharma AG, we will supply vials of rThrombin for up to five years from June 18, 2007, the effective date of the agreement. Thereafter, we will supply rThrombin bulk drug substance throughout the term of the license and collaboration agreement.

IL-21

Our initial clinical supply of IL-21, which is made in *E. coli*, was manufactured by Avecia Limited using a process developed at ZymoGenetics. Subsequently, Novo Nordisk manufactured clinical materials for Phase 2 and initial Phase 3 development under a manufacturing agreement established in 2007. In January 2009, Novo Nordisk terminated the agreement, but we acquired all rights to the manufacturing processes and product already manufactured.

Other

We have established internal manufacturing capabilities to supply various products for toxicology studies and early-stage clinical trials. We intend to transfer manufacturing to a collaborative partner or third party contractor for late-stage clinical and commercial production runs. Our pilot-scale GMP manufacturing facility gives us the capability to manufacture products using bacterial and mammalian cell production systems. In 2007, we continued production of PEG-IFN-λ clinical supplies, using a high-yield internally developed *E. coli* process. We believe that we have produced sufficient supplies of PEG-IFN-λ to support clinical development though Phase 2. Bristol-Myers Squibb will be responsible for all future manufacturing of PEG-IFN-λ, including product for Phase 3 clinical trials and commercial sale, under the terms of our co-development and co-promotion agreement. We also plan to use our internal facility to produce our antibody and antibody-like product candidates, which are manufactured using mammalian cell culture recombinant technology. Our first antibody product candidate – IL-21 mAb – is currently being manufactured in this facility.

Collaborative Relationships

Bayer License and Collaboration Agreement for rThrombin and U.S. Co-Promotion Agreement for RECOTHROM®

In June 2007, we executed a license and collaboration agreement with Bayer Schering Pharma AG and a U.S. co-promotion agreement with Bayer HealthCare LLC. Pursuant to the license and collaboration agreement, Bayer Schering Pharma will develop and commercialize the initial presentations of rThrombin outside the United States. Pursuant to the co-promotion agreement, Bayer HealthCare will contribute sales people and medical science liaisons for the first three years following the launch of RECOTHROM in the United States. Depending on the level of sales in the first two years, Bayer may have an option to extend the co-promotion agreement for one additional year. In addition, the license and collaboration agreement includes provisions through which the two companies may collaborate to develop subsequent presentations or line extensions of rThrombin, which we will commercialize within the United States and Bayer will commercialize outside the United States.

As part of these agreements, Bayer receives:

- Development and commercialization rights to rThrombin outside the United States.
- A tiered commission of up to 20% on RECOTHROM sales in the United States during a three-year co-promotion period, which may be extended by one additional year at Bayer's option. For two years following the end of the co-promotion period, a sales commission will be paid at a reduced rate, subject to an annual maximum.

- Up to $20.0 million in sales bonus payments upon achievement of certain sales levels of RECOTHROM in the United States.
- An option to co-develop or opt into our development of new presentations or line extensions of rThrombin and commercialize them outside the United States.

In return, we received:

- A $30.0 million upfront payment.
- A $40.0 million milestone payment upon the approval of RECOTHROM in the United States.
- $6.5 million in milestone payments upon the submission of RECOTHROM approval applications to the EMEA and Canada.

In addition, we may receive:

- Up to approximately $120.0 million in additional development and sales-based milestone payments based on Bayer Schering Pharma's development and sales of rThrombin products outside the United States.
- Tiered royalties based on annual sales of rThrombin products outside the United States.

Under the license and collaboration agreement, each party is free to research and develop new presentations or line extensions of rThrombin provided that it proposes the new presentation to the other party within a specified period prior to filing an IND for the new presentation. The other party may then opt to co-develop and commercialize the new presentation by co-funding the past and future development cost provided that the cost of certain territory-specific activities is not shared. The co-development activities would be governed by a steering committee with equal representation from the two companies. Within the United States, we would have exclusive commercial rights to any new presentation that we co-developed with Bayer Schering Pharma or which we proposed and Bayer Schering Pharma declined to co-develop. However, we would have no rights to any new presentation proposed by Bayer Schering Pharma that we declined to co-develop. Outside the United States, Bayer Schering Pharma would have exclusive commercial rights to any new presentation that it co-developed with us or which it proposed and we declined to co-develop, and would pay us a royalty on product sales. There is an opt-in right wherein the declining party can opt-in at a later time by paying a premium to the developing party. Under no circumstances may we commercialize a presentation of rThrombin outside the United States nor, except for the role of Bayer HealthCare under the co-promotion agreement, may Bayer Schering Pharma commercialize a presentation of rThrombin within the United States.

Bristol-Myers Squibb Co-Development and Co-Promotion Agreement for PEG-IFN-λ

In January 2009, we entered into a co-development/co-promotion and license agreement with Bristol-Myers Squibb Company focused on product candidates derived from the type-3 interferon family. During the term of the agreement, we will work exclusively with Bristol-Myers Squibb to develop biopharmaceutical products based on the type-3 interferon family, which includes our development candidate PEG-IFN-λ. The ongoing co-development of PEG-IFN-λ in Hepatitis C is pursuant to this agreement.

As part of the co-development/co-promotion and license agreement, Bristol-Myers Squibb receives an exclusive worldwide license to the core patents relating to the type-3 interferon family and a co-ownership interest in all core patents relating to the type-3 interferon family filed outside of the United States. In addition, Bristol-Myers Squibb receives a non-exclusive license to other intellectual property rights relating to the licensed products. We will be responsible for funding the first $100 million of development costs in the United States and Europe, which we expect to incur during Phase 1b and Phase 2 clinical testing, and 20% of all further development costs in the United States and Europe.

In return, we receive:

- $85.0 million in March 2009.
- $20.0 million additional license fee in March 2009.
- Additional payments of up to $430 million based on pre-defined development and regulatory milestones for PEG-IFN-λ in Hepatitis C, of which $95 million is related to initiation of Phase 2 activities that are expected to occur in 2009; up to $287 million in development and regulatory milestones for other potential indications; and up to $285 million based on pre-defined annual sales milestones.
- 40% of the profits from the co-commercialization of any type-3 interferon family product within the United States. We will also be responsible for 40% of any loss from the co-commercialization of any product within the United States; provided that a portion of our share of losses incurred through the initial launch phase will be deferred, and deferred losses will subsequently be deducted from milestones, royalties and our share of profits.
- Royalties on product sales outside the United States for PEG-IFN-λ.

The research and development activities are governed by a steering committee made up of an equal number of representatives from each company. Bristol-Myers Squibb is responsible for all future manufacturing of PEG-IFN-λ , including product for Phase 3 clinical trials and commercial sale.

We have the right to co-promote or co-fund PEG-IFN-λ in the United States, and must exercise this right within 30 days after acceptance by the FDA of a Biologics License Application (BLA) filing, in which case we will share any United States profits or losses. In certain circumstances, we may opt out of co-promotion or co-funding in the United States, in which case we will share any United States profits or losses. We have the right to discontinue co-promotion and co-funding in the United States, in which case we would be eligible to receive royalties on product sales in the United States. Under certain restricted circumstances, Bristol-Myers Squibb may terminate our right to co-promote in the United States, provided that, in certain of these circumstances, we will retain the option to co-fund and share product profits and losses. If Bristol-Myers Squibb terminates our co-promotion right and we do not have the option to co-fund or choose not to exercise that option, we would receive royalties on product sales instead of sharing profits and losses in the United States.

Royalties on sales vary based on annual sales volume and the degree of patent protection provided by the licensed intellectual property. Royalty payments may be reduced if Bristol-Myers Squibb is required to license additional intellectual property from one or more third parties in order to commercialize a product or, in certain circumstances, if a product suffers from competition. Royalty obligations under the agreement continue on a country-by-country basis until the date on which no valid patent claims relating to a product exist or, if the product is not covered by a valid patent claim, eleven years after the date of first sale of the product in that country.

The term of the agreement began on February 26, 2009 and will continue for as long as a type-3 interferon product is the subject of an active development project or there is an obligation to pay royalties under the agreement.

Merck Serono Strategic Alliance Agreement

In October 2004, we executed a strategic alliance agreement with Serono S.A. to research, develop and commercialize product candidates, including protein and antibody therapeutics, based on a specific portfolio of our proprietary genes. Following the acquisition of Serono in 2007 by Merck KGaA, Serono's rights under this agreement have been held by Merck Serono S.A., an affiliate of Merck KGaA. In August 2008, we executed a first amended and restated strategic alliance agreement. The restated strategic alliance agreement retains the same five-year term, with a maximum three-year research period for each product candidate that may extend beyond the five-year term on a product candidate-by-product candidate basis.

As part of the restated strategic alliance, Merck Serono received:

- An option to acquire an exclusive worldwide, royalty bearing license to product candidates based on a specific portfolio of our proprietary genes, where the product candidate results from research that Merck Serono performs without us.
- An alternating option to acquire an exclusive worldwide, royalty bearing license to product candidates based on a specific portfolio of our proprietary genes, where the product candidate results from research that Merck Serono performs jointly with us. Under this alternating option arrangement, we and Merck Serono take turns having the first right to obtain exclusive rights to the relevant product candidates.
- Upfront fees and potential milestone payments related to development progress, regulatory submissions and approvals for product candidates resulting from joint research under the restated strategic alliance that we exclusively license.
- Royalties on worldwide sales of licensed products, where the product results from joint research under the restated strategic alliance that we exclusively license.

In return, we receive:

- Upfront fees and potential milestone payments related to development progress, regulatory submissions and approvals for every product candidate exclusively licensed by Merck Serono.
- Royalties on worldwide sales of licensed products derived from product candidates based on a specific portfolio of our proprietary genes, where the product candidate results from any research under the restated strategic alliance agreement.

An exclusive license to a product candidate resulting from joint research under the restated strategic alliance will provide that if the licensee (whether us or Merck Serono) seeks a partner for the applicable product candidate, the licensor will have the right to opt in to co-develop and co-commercialize the product candidate on pre-negotiated terms, including retroactive and prospective cost sharing, royalties and milestone fees. In addition to its co-development and co-commercialization rights within the United States, Merck Serono will have an exclusive license outside of the United States whether Merck Serono opts in to develop a product candidate of ours or we opt in to develop a product candidate of Merck Serono.

During the research stage of the collaboration, the two companies will work together for five years (expiring October 2009) to identify new product candidates from the specific portfolio of our proprietary genes. Upon the generation of a medical hypothesis by either company for a product candidate, Merck Serono has a specified amount of time to make a decision whether or not to co-fund continued research on the product candidate. If Merck Serono declines to continue, all rights to the product candidate revert to us. If Merck Serono decides to collaborate, it will fund the majority of the research costs if we decide to participate, or 100% of the costs if we decline.

The research collaboration for a product candidate can continue for up to three years or until the product candidate reaches the point of being designated a candidate for development. At this time, Merck Serono has an option to obtain rights to the product candidate. The option will be exclusive or alternating with our own depending on whether the Merck Serono bore the research costs alone or the parties shared such costs. Merck Serono has a specified amount of time in which to exercise this option.

At the time of the original agreement, we executed agreements granting Merck Serono exclusive worldwide licenses to two preclinical candidates, FGF-18 and IL-22RA, and entered into a co-development agreement relating to IL-31. Subsequently, we licensed to Merck Serono the rights to IL-17RC, which was designated as a candidate for development in June 2007. In connection with the original agreement we received:

- A $20.0 million upfront option fee.

- $11.25 million in license fees for FGF-18, IL-22RA and IL-31.

In addition, Merck Serono purchased approximately 3.2 million shares of our common stock for a total of $50.0 million, and entered into a related lockup agreement and a standstill agreement.

In connection with the amendment of the strategic alliance agreement, we amended and restated the co-development agreements for IL-31 and IL-17RC to provide for exclusive licenses to, in the case of IL-31, ZymoGenetics and, in the case of IL-17RC, Merck Serono. The terms of these exclusive licenses are comparable to those under the amended and restated strategic alliance agreement.

Merck Serono Development and Marketing Agreement for Atacicept

In August 2001, we entered into a collaborative development and marketing agreement with Ares Trading S.A., a wholly owned subsidiary of Serono S.A., focused on product candidates derived from two cellular receptors (designated TACI and BCMA) that are involved in the regulation of the human immune system. Following the acquisition of Serono by Merck KGaA in 2007, Serono's rights under this agreement have been held by Merck Serono S.A. In August 2008, we entered into an amended and restated development and marketing agreement. Pursuant to the original collaborative development and marketing agreement, the parties had been co-developing atacicept in autoimmune diseases and cancer. Merck Serono now has exclusive worldwide rights to develop, market and sell products developed under the agreement, for which we will be entitled to receive milestone fees and royalties on worldwide net sales. By converting to a royalty position, we will avoid a major capital commitment, reduce operating expenses and preserve cash over the next several years, while maintaining the value of our atacicept asset.

We granted Merck Serono an exclusive license to our intellectual property relating to TACI, BCMA and certain other related technologies to make, use, have made, sell, offer to sell and import products based on TACI and BCMA. Merck Serono is required to pay royalties on sales, which vary based on annual sales volume and the degree of patent protection provided by the licensed intellectual property. Royalty payments may be reduced if Merck Serono is required to license additional intellectual property from one or more third parties in order to commercialize a product or, in certain circumstances, if a product suffers from competition. Royalty obligations under the agreement continue on a country-by-country basis until the date on which no valid patent claims relating to a product exist or, if the product is not covered by a valid patent claim, 15 years from the date of first sale of the product in that country.

The agreement will continue for as long as a TACI or BCMA product is the subject of an active development project or there is an obligation to pay royalties under the agreement. The agreement provides for an initial fee and milestone payments to be paid by Merck Serono in connection with the development and approval of products, up to an aggregate of $52.5 million of which $15.5 million has been received to date.

Novo Nordisk Data Sharing and Cross-License Agreement for IL-21

In 2001, Novo Nordisk initially licensed the rights to various embodiments of IL-21 in territories outside of North America and is obligated to make milestone payments based on the achievement of development milestones and royalties on sales of any resulting products. Royalty obligations under the agreement continue on a country-by-country basis until the date on which no valid patent claims relating to a product exist or, if the product is not covered by a valid patent claim, 12 years from the date of first sale of the product in that country.

In 2005, we entered into a collaborative data sharing and cross-license agreement with Novo Nordisk to develop and execute a joint global clinical development plan for the IL-21 protein to achieve regulatory approval of a common product in the companies' respective territories.

In January 2007, the parties also entered into a manufacturing agreement whereby Novo Nordisk agreed to supply us with IL-21 protein for use in clinical trials.

In January 2009, the parties restructured their relationship as it relates to IL-21. As part of the restructuring, the parties:

- Amended and restated the license agreement such that it no longer covers the IL-21 protein. However, Novo Nordisk will continue to be responsible for developing other embodiments of IL-21, including antibodies to IL-21, outside North America. Novo Nordisk will continue to be obligated to pay development milestones and royalties on any products developed by Novo Nordisk.
- Entered into a license and transfer agreement whereby we receive an exclusive license outside North America to the intellectual property rights that Novo Nordisk developed relating to the IL-21 protein. and are obligated to make milestone payments based on approval and sales and pay single digit royalties on sales of any resulting products. In addition, ZymoGenetics will pay Novo Nordisk a portion of any third party license fees above a certain threshold.
- Terminated the collaborative data sharing and cross-license agreement. However, ZymoGenetics' exclusive license in North America to the intellectual property rights that Novo Nordisk developed relating to the IL-21 protein survives termination.
- Terminated the manufacturing agreements and Novo Nordisk will transfer to us all manufacturing processes developed and its existing stock of IL-21 protein.

As a result of this restructuring, we now have worldwide development and commercialization rights for products based on the IL-21 protein.

Patents and Proprietary Rights

We seek appropriate patent protection for our proprietary technologies and product candidates by filing patent applications in the United States. We have more than 325 unexpired issued or allowed United States patents, and over 280 pending United States patent applications. When appropriate, we also seek foreign patent protection and to date have more than 670 issued or allowed foreign patents.

Our patents and patent applications are primarily directed to therapeutic protein-based products. We commonly seek claims directed to compositions of matter for genes and proteins, including antibodies, methods of using and methods of making. When appropriate, we also seek claims to related technologies, such as reagents used in release assays and formulations. We maintain patents and prosecute applications, worldwide, for technologies that we have outlicensed. Similarly, for development projects that are partnered, we work closely with our development partners to coordinate patent efforts, including filings, prosecution, term extension, defense and enforcement. As our development product candidates advance through research and development, we seek to diligently identify and protect new inventions, such as combinations, improvements to methods of manufacturing or purification, and methods of treatment. We also work closely with our researchers to identify and protect new inventions that could eventually add to our research and development pipeline.

Patents expire, on a country by country basis, at various times depending on various factors, including the filing date of the corresponding patent application(s), the availability of patent term extension and supplemental protection certificates, terminal disclaimers, etc. For our commercial product and each of our product candidates, we have filed or expect to file multiple patent applications and expect to obtain multiple patents. The table below provides expected dates for the first patent expiration in patent portfolios for our commercial product, RECOTHROM, and product candidates in our development pipeline. Each expiration date may be subject to patent term extension, where the length of term extension would not exceed five years under current law and depends on factors such as the amount of time taken by the FDA to review the first marketing approval application of a drug covered by the patent.

Commercial Product/Product Candidate	First Patent Expiration Date
RECOTHROM (rThrombin)	December 2012; expected to extend until July 2015 under patent term extension
IL-21	March 2020
PEG-IFN-λ	September 2021
IL-21 mAb	March 2020
IL-31 mAb	January 2023

We require our research personnel to maintain laboratory notebooks and other research records in accordance with our policies, which are designed to strengthen and support our patent efforts. In addition to our patented intellectual property, we also develop and seek to protect unpatented technology, trade secrets and confidential information, including our genetic sequence database, bioinformatics algorithms, research, preclinical and clinical data, development and manufacturing strategies. Our policy is to require our employees, consultants and advisors to execute a confidentiality and proprietary information agreement before beginning their employment, consulting or advisory relationship with us. These agreements generally provide that the individual must keep confidential and not disclose to other parties any confidential information developed or learned by the individual during the course of their relationship with us except in limited circumstances. These agreements also generally provide that we shall own all inventions conceived by the individual in the course of rendering services to us. These agreements, however, may not provide effective protection of our technology, confidential information or, in the event of unauthorized use or disclosure, may not provide adequate remedies.

As part of our business strategy, we work with third parties in our research and development activities. Accordingly, disputes may arise about inventorship, ownership and corresponding rights to know-how and inventions resulting from the joint creation or use of intellectual property by us and our corporate partners, licensors, scientific collaborators and consultants. In addition, other parties may circumvent any proprietary protection we do have. These parties may independently develop equivalent technologies or independently gain access to and disclose substantially equivalent information, and confidentially agreements and material transfer agreements we have entered into with them may not provide us with effective protection.

Refer to "Item 1A. Risk Factors" for additional information relating to our patents and proprietary rights.

Government Regulation

Regulation by government authorities in the United States, Europe, Japan and other countries is a significant consideration in our ongoing research and product development activities and in the manufacture and marketing of our potential products. The FDA and comparable regulatory bodies in other countries currently regulate therapeutic proteins and related pharmaceutical products as biologics. Biologics are subject to extensive pre- and post-market regulation by the FDA, including regulations that govern the collection, testing, manufacture, safety, efficacy, potency, labeling, storage, record keeping, advertising, promotion, sale and distribution of the products. The time required for completing testing and obtaining approvals of our product candidates is uncertain but will take several years. Any delay in testing may hinder product development. In addition, we may encounter delays in product development or rejections of product applications due to changes in FDA or foreign regulatory laws or policies during the period of product development and testing. Failure to comply with regulatory requirements may subject us to, among other things, civil penalties and criminal prosecution; restrictions on product development and production; suspension, delay or withdrawal of approvals; and the seizure or recall of products. The lengthy process of obtaining regulatory approvals and ensuring compliance with appropriate statutes and regulations requires the expenditure of substantial resources. Any delay or failure, by us or our corporate partners, to obtain regulatory approvals could adversely affect our ability to commercialize product candidates, receive royalty payments and generate sales revenue.

The nature and extent of the governmental pre-market review process for our potential products will vary, depending on the regulatory categorization of particular products. The necessary steps before a new biological product may be marketed in the United States ordinarily include:

- nonclinical laboratory and animal tests;
- compliance with product manufacturing requirements including, but not limited to, current Good Manufacturing Practices (GMP) regulations;
- submission to the FDA of an IND application, which must become effective before clinical trials may commence;
- completion of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of a BLA; and
- FDA review and approval of the BLA prior to any commercial sale or shipment of the product.

Nonclinical tests include laboratory evaluation of the product, as well as animal studies to assess the potential safety concerns and efficacy of the product. Nonclinical safety tests must be conducted by laboratories that comply with current Good Laboratory Practices regulations. The results of nonclinical tests, together with extensive manufacturing information, analytical data and proposed clinical trial protocols, are submitted to the FDA as part of an IND application, which must become effective before the initiation of clinical trials. The IND application will automatically become effective 30 days after receipt by the FDA unless the FDA indicates that the application does not contain sufficient information to permit initiation of the clinical studies. If the FDA raises any concerns related to the clinical program, it is possible that these concerns will not be resolved quickly, if at all. In addition, the FDA may impose a clinical hold on a proposed or ongoing clinical trial if, for example, safety concerns arise, in which case the trial cannot commence or recommence without FDA authorization under terms sanctioned by the agency.

Clinical trials involve the administration of the product to healthy volunteers or to patients under the supervision of a qualified principal investigator. Clinical trials are conducted in accordance with current Good Clinical Practices regulations under protocols that detail the objectives of the trial, inclusion and exclusion criteria, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Protocols for each phase of the clinical trials are submitted to the FDA as part of the original IND application or as an amendment to the IND application. Further, each clinical trial must be reviewed and approved by an independent institutional review board at each institution. The institutional review board will consider, among other things, ethical factors, the safety of human subjects and the possibility of liability of the institution conducting the trial. An institutional review board may require changes in a protocol, and the submission of an IND application does not guarantee that a trial will be initiated or completed.

Clinical trials generally are conducted in three sequential phases that may overlap. In Phase 1, the initial product is administered to healthy human subjects or patients, or both, to assess safety, metabolism, pharmacokinetics and pharmacological actions associated with increasing doses. Phase 2 usually involves trials in a limited patient population to evaluate the efficacy of the potential product for specific, targeted indications, to determine dosage tolerance and optimum dosage, and to further identify possible adverse reactions and safety risks. If a compound appears to be effective and to have an acceptable safety profile in Phase 2 evaluations, Phase 3 trials may be undertaken to evaluate further clinical efficacy in comparison to standard therapies, generally within a broader patient population at geographically dispersed clinical sites. Phase 3 protocols are reviewed with the FDA to establish endpoints and data handling parameters. Phase 1, Phase 2 or Phase 3 testing may not be completed successfully within any specific period of time, if at all, with respect to any of our potential products. Furthermore, we, an institutional review board, the FDA or other regulatory bodies may suspend a clinical trial at any time for various reasons, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The results of pharmaceutical development, nonclinical studies and clinical trials are submitted to the FDA in the form of a BLA for approval of the manufacture, marketing and commercial shipment of the biological product. A BLA contains extensive manufacturing information, and each manufacturing facility and quality system must be inspected and approved by the FDA before a BLA can be approved. The inspection and approval process is likely to require substantial time, effort and resources, and necessary approvals may not be granted on a timely basis, if at all. The FDA may deny a BLA if applicable regulatory criteria or clinical endpoints have not been met. The FDA may also require additional testing of the product or other information, or require post-market testing and surveillance to monitor the safety or efficacy of the product. In addition, after marketing approval is granted, the FDA may require post-marketing clinical trials, which typically entail extensive patient monitoring and may result in restricted marketing of an approved product for an extended period of time.

Some of our product candidates may qualify as orphan drugs under the Orphan Drug Act of 1983. This act generally provides incentives to manufacturers who undertake development and marketing of products to treat relatively rare diseases, defined as those diseases that affect fewer than 200,000 persons in the United States. Orphan drug status is granted for a product within a specific indication; therefore, it is possible for more than one product to receive orphan drug designation for the same indication. A product that receives orphan drug designation by the FDA is entitled to various advantages, including a seven-year exclusive marketing period in the United States for that product claim and certain tax credits. The FDA granted IL-21 orphan drug status for the treatment of melanoma patients with advanced or aggressive disease. However, it is possible that in the future none of our other product candidates will be designated as an orphan drug by the FDA. Orphan drug designation may or may not have a positive effect on our revenues.

The FDA has very broad enforcement authority under the Federal Food, Drug and Cosmetic Act and the Public Health Services Act. This authority extends to compliance with product manufacturing requirements, including current GMP regulations. Prior to approval of a BLA, all third parties, domestic or foreign, that are involved in manufacturing, testing or release of our products must pass an FDA inspection of their facility and quality systems. The facilities are inspected for compliance with applicable requirements, including current GMP guidelines, and must submit to continued periodic inspection by the FDA. Failure to comply with these requirements can result in civil and criminal penalties, including the issuance of a warning letter directing us to correct deviations from FDA standards. In addition, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceutical and biologic products and medical devices, including, among others, standards and regulations for direct-to-consumer advertising, off-label promotions, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. Failure to abide by these regulations can result in civil and criminal penalties, as well as a requirement that future advertising and promotional materials be pre-cleared by the FDA.

FDA marketing approval is only applicable in the United States. Marketing approval in foreign countries is subject to the regulations of those countries. The approval procedures vary among countries and can involve additional testing. The time required to obtain approval outside of the United States may differ from that required for FDA approval. There are centralized procedures for filings in the European Union (EU) countries, which allow submission of a single marketing authorization application to obtain approval in the approximately 25 countries of the EU. Outside of the EU, most countries generally have their own procedures and requirements, and compliance with these procedures and requirements may be expensive and time-consuming. Accordingly, there may be delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed, if approvals are ultimately received at all.

We are also subject to various federal, state and local laws, regulations, industry guidelines and recommendations relating to employment practices; safe working conditions; laboratory and manufacturing practices; the experimental use of animals; the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents; product liability; and unfair competition, including advertising and other promotional efforts. Government regulations that might result from future legislation or administrative action, including additions or changes to environmental laws, may materially affect our business operations and revenues.

Competition

We currently face competition from a range of biotechnology and pharmaceutical companies as well as academic and research institutions. We compete with these entities to discover and obtain proprietary rights to new genes and their corresponding proteins and to commercialize the products we develop from these genes and proteins. Some of our competitors have greater resources and experience than we have in discovering, developing, manufacturing and selling protein-based products. We expect that competition in our field will continue to be intense.

RECOTHROM, which was approved in January 2008 by the FDA for use as a topical hemostat in the United States, faces substantial competition in the topical hemostat market. In addition to RECOTHROM, there are two stand-alone thrombin products currently available in the United States: Thrombin-JMI, a bovine plasma-derived thrombin from King Pharmaceuticals, Inc., and Evithrom, a pooled human plasma-derived thrombin, from Ethicon, Inc., a Johnson & Johnson Company. Also, a number of other hemostatic agents are currently available on the market, including topical hemostats and fibrin sealants from Johnson & Johnson Wound Management, a division of Ethicon, Inc. and the BioSurgery business unit of Baxter BioScience. Furthermore, new products and technologies could be developed in the future to limit or control bleeding during surgeries.

We anticipate that our other product candidates currently in research or development will face intense competition in their respective therapeutic areas from gene- or protein-based products as well as other therapies. In our efforts to research and develop new therapeutic proteins we will compete with other entities that are involved in the research and development of therapeutic proteins, including Genentech, Inc., Human Genome Sciences, Inc., Medarex, Inc. and Biogen Idec Inc., among others. We also will face competition from large pharmaceutical and other companies that develop other types of products related to particular diseases.

Although we believe that we are well positioned to compete effectively with respect to our existing and potential competitors, our ability to compete successfully in the future will depend on many factors, including our ability to:

- successfully maintain and expand as appropriate RECOTHROM commercial infrastructure, including the product supply and sales force, and establish commercial infrastructure for other product candidates as necessary;
- develop products that are safer, more efficacious or more convenient to administer than other products in the marketplace;
- leverage our established collaborations and enter into new collaborations to support the development of our products;
- obtain timely regulatory approvals;
- manufacture our products in a cost-effective manner in quantities sufficient to meet market demands;
- obtain adequate reimbursement from government health administration authorities, private health insurers and health maintenance organizations;
- identify new product candidates through our internal discovery efforts or through in-licensing; and
- obtain and enforce adequate patent protection for our genes, proteins and technologies.

Employees

As of December 31, 2008, we had 530 full-time employees, including 383 employees dedicated to research and development and 68 employees dedicated to sales and marketing. Each of our employees had signed confidentiality and intellectual property agreements, and no employees are covered by a collective bargaining agreement. We have never experienced employment-related work stoppages and consider our employee relations to be good.

Website Access to Our SEC Reports

Our Internet address is www.zymogenetics.com. We make our periodic SEC reports (Form 10-Q and Form 10-K), current reports (Form 8-K) and amendments to these reports available free of charge through our website as soon as reasonably practicable after they are filed electronically with the SEC. We may from time to time provide important disclosures to investors by posting them in the investor relations section of our website, as allowed by SEC rules.

Item 1A. Risk Factors

You should carefully consider the following risk factors before you decide to invest in our Company because these risk factors may have a significant impact on our business, operating results, financial condition, and cash flows. However, the risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. If any of the following risks actually occur, our business, operating results, financial condition, and cash flows could be materially and adversely affected.

Risks Related to Our Business

Our near-term success is highly dependent on the commercialization of RECOTHROM® recombinant thrombin.

Prior to the launch of RECOTHROM in the United States in January 2008, we had never sold or marketed a product. Our ability to generate product sales in the foreseeable future will depend solely on the commercialization of this product. The successful commercialization of RECOTHROM will depend on many factors, including the following:

- successfully maintaining a product supply chain to meet demand;
- successfully maintaining a commercial infrastructure, including a sales force;
- competition from products that are already marketed or are being developed;
- our ability to penetrate the existing thrombin market and develop line extensions or complementary products;
- product demand within the medical community; and
- approval and product demand in countries outside the United States.

If we are unable to successfully commercialize RECOTHROM, or if we are significantly limited in doing so, our business will be materially harmed.

We may be unable to successfully commercialize RECOTHROM® in the face of substantial competition.

We may not be able to compete successfully in the marketplace and generate market demand for RECOTHROM. RECOTHROM faces substantial competition from alternative topical hemostats. In the United States, stand-alone plasma-derived thrombin products on the market include Thrombin-JMI, a bovine plasma-derived thrombin sold by King Pharmaceuticals, Inc., and Evithrom, a pooled human plasma-derived thrombin sold by Ethicon, Inc., a division of Johnson & Johnson. In addition, Baxter International, Inc. markets the Gelfoam Plus Hemostasis Kit, which is Pfizer Inc.'s Gelfoam sterile sponge co-packaged with human plasma-derived thrombin. Further, a number of companies, including Johnson & Johnson and Baxter International, Inc., currently market other hemostatic agents that may compete with RECOTHROM, including passive agents such as gelatin and collagen pads, as well as fibrin sealants and tissues glues. Many of these alternative hemostatic agents are inexpensive and have been widely used for many years. Consequently, physicians and medical decision-makers may be hesitant to adopt RECOTHROM. Despite the potential advantages of RECOTHROM, we may be unsuccessful in competing against these companies and hemostatic agents.

Further, even if our promotional efforts are successful, many hospitals will evaluate the entire product category in which RECOTHROM falls using their pharmacy and therapeutic committees or formulary processes, including performing comparisons between RECOTHROM and its competitors, including price comparisons. The review cycle will vary among hospitals and could delay the uptake of RECOTHROM.

Prior to the launch of RECOTHROM, the price of bovine plasma-derived thrombin increased significantly over several years; however, subsequent to our launch, King Pharmaceuticals has lowered the price of bovine plasma-derived thrombin. We may not be able to compete effectively if this price competition were to intensify. Furthermore, price competition would likely reduce the value of the overall thrombin market, which would impair our business prospects.

RECOTHROM also must compete with the promotion of other types of products in order to be noticed by healthcare practitioners and our potential customers. The level of promotional effort in the pharmaceutical, biopharmaceutical and medical device markets is substantial. Market acceptance of RECOTHROM will be affected by the level and effectiveness of promotional effort that we are able to provide compared with others in this business. The level and quality of our promotional efforts depends on our ability to train, deploy and retain an effective sales and marketing organization. We cannot assure you that the level of promotional effort that we will be able to provide for RECOTHROM will be sufficient to generate market demand for RECOTHROM.

RECOTHROM® may not achieve market acceptance or generate significant revenues.

If RECOTHROM fails to achieve market acceptance, our product sales, our ability to maintain current levels of research, development and commercialization activities, and our ability to become profitable in the future, will be adversely affected. Many factors may affect the rate and level of market acceptance of RECOTHROM, including:

- the effectiveness of our product differentiation, marketing, promotion, distribution, sales and pricing strategies and programs, and those of our competitors;
- our ability to provide acceptable evidence of the product's safety, efficacy, cost-effectiveness and convenience compared to that of competing products;
- the perception of physicians and other members of the healthcare community of the product's safety, efficacy, cost-effectiveness and convenience compared to that of alternative or competing products;
- the level of satisfaction with the product among healthcare providers;
- clinical practice or other guidelines regarding topical hemostats published by professional organizations or specialty groups;
- any publicity concerning the product or similar products;
- new data or adverse event information relating to the product or any similar products and any resulting regulatory action;
- regulatory constraints on our promotional materials and programs;
- the results of clinical studies conducted by us, or by our competitors;
- regulatory developments relating to the development, manufacture, commercialization or use of the product;
- the introduction, availability and acceptance of alternative or competing treatments, including lower-priced products;
- the ability to gain formulary acceptance and favorable formulary positioning in a timely fashion or at all;
- our ability to supply RECOTHROM to meet demand;

- the continued availability of third parties to manufacture and distribute the product on acceptable terms, and the continued ability to manufacture commercial-scale quantities of the product successfully and on a timely basis; and
- the outcome of patent, product liability or other litigation, if any, related to the product.

The approved product labeling and FDA restrictions on promotional communications may adversely affect market acceptance of RECOTHROM®.

The approved product labeling for RECOTHROM will have a direct and significant impact on our marketing, promotional and sales programs and could adversely affect market acceptance. The label contains warnings and contraindications that are typical for thrombin and recombinant products, as well as some that are unique to RECOTHROM. While we hope customers will prefer the inherent properties of a recombinant product to plasma-derived alternatives, the label does not state that RECOTHROM has demonstrated superior safety or efficacy to competing thrombin products. Customers may be not be familiar with the labeling approved for competing products and may be unaware of side effects or other conditions associated with competitive products. We may be restricted in our ability or success in raising awareness of these issues. If potential purchasers or those influencing purchasing decisions, such as physicians and pharmacists, react negatively to our product because of their perception of the approved product labeling, or if they do not believe our product offers advantages over competing products, it may result in lower product acceptance and lower product revenues. Our competitors may seek and obtain approval of labeling containing fewer or less severe warnings and contraindications than required for our product.

In addition to approving product labeling, the FDA typically reviews and provides advisory comments regarding core promotional materials for a pharmaceutical product. The FDA reviewed our core promotional materials in connection with the launch of RECOTHROM, and we must submit all additional promotional materials to the FDA at the time of their first use. If the FDA raises concerns regarding our promotional materials or messages, we may be required to modify or discontinue using them, and in some cases we may be required to provide corrective information to healthcare practitioners. Our promotional materials or messages may not allow us to effectively differentiate and promote RECOTHROM. For example, the approved product labeling states that in the pivotal clinical trial we observed a lower incidence of immunogenicity of RECOTHROM compared with that of bovine plasma-derived thrombin, but that there is no demonstrated correlation of this finding to clinical outcome. Various laws and regulations prevent us from making statements that imply that our product offers superior efficacy or safety compared with competitive products, including bovine plasma-derived thrombin. Accordingly, we may be unable to address all potential questions and concerns regarding our product or its label, or our competitors' products, which could result in lower product demand and lower product sales.

A lack of familiarity with RECOTHROM® and our company may adversely affect market acceptance of RECOTHROM®.

We may be hampered in our promotional efforts by a lack of familiarity with RECOTHROM and our company among healthcare practitioners. Because RECOTHROM is our first product introduced commercially, there is limited, if any, awareness and goodwill associated with our company's name. Even though we co-promote the product with Bayer HealthCare, we may not benefit from customer recognition of that company's name or goodwill. Healthcare providers may prefer products from companies with which they have long-standing relationships. Any or all of these factors may result in less market demand and lower sales of RECOTHROM.

If Bayer HealthCare, upon whom we rely to co-promote RECOTHROM® and provide additional medical science liaisons, fails to perform, our business may be adversely affected.

Under a 2007 agreement, Bayer HealthCare LLC co-promotes RECOTHROM and provides additional medical science liaisons in the United States for a limited time. Our success in selling RECOTHROM depends in

part on the efforts of Bayer HealthCare. Collaboration with Bayer HealthCare involves certain risks, including, but not limited to, risks that Bayer HealthCare will:

- not effectively co-promote RECOTHROM;
- not provide effective medical science liaisons; or
- not devote adequate resources or effort to co-promote RECOTHROM according to our plans.

In addition, we must ensure that our own promotional and sales activities are coordinated with those of Bayer HealthCare. Any such failure by Bayer HealthCare or in the coordination of our efforts may result in decreased product sales and negatively affect our reputation and that of RECOTHROM, which would harm our business.

If we or others identify previously unknown side effects of RECOTHROM® or product manufacturing problems occur, our business would be adversely affected and could lead to a significant decrease in the sales of RECOTHROM® or to the FDA's withdrawal of marketing approval.

If we or others identify previously unknown side effects, or detect unexpected safety signals, for RECOTHROM or any products perceived to be similar to RECOTHROM, or if serious product manufacturing problems occur, then in any of these circumstances:

- sales of RECOTHROM may decrease significantly;
- regulatory approvals for RECOTHROM may be restricted or withdrawn;
- we may decide to, or be required to, send product warning letters or field alerts to physicians, pharmacists and hospitals;
- reformulation of the product, additional preclinical or clinical studies, changes in labeling or changes to or re-approvals of manufacturing facilities may be required;
- our reputation in the marketplace may suffer; and
- government investigations and lawsuits, including class action suits, may be brought against us.

Any of the above occurrences would harm or prevent sales of RECOTHROM, increase our expenses and impair our ability to successfully commercialize RECOTHROM.

Furthermore, now that RECOTHROM is approved in the United States, it is being used in a wider population and in a less rigorously controlled fashion than in clinical studies. It is expected that some patients exposed to RECOTHROM will become sick or die suddenly, that in some or even many of these cases there will not be sufficient information available to rule out RECOTHROM as a contributing factor or cause of sickness or mortality, and that safety reporting from physicians or from us to regulatory authorities may link RECOTHROM to death or other serious adverse effects. As a result, regulatory authorities, healthcare practitioners, third party payers or patients may perceive or conclude that the use of RECOTHROM is associated with death or other serious adverse effects, any of which could mean that our ability to commercialize RECOTHROM could be adversely affected and our business could be impaired.

In addition, our competitors and others are free to generate new data regarding RECOTHROM, which they may publish in the scientific literature or otherwise publicize, without our consent or control.

Distribution of RECOTHROM® is highly concentrated among a small group of wholesale drug distributors on whom we rely for crucial functions.

We distribute RECOTHROM through a small number of large wholesale drug distributors, primarily AmerisourceBergen Corporation, Cardinal Health, Inc. and McKesson Corporation, which control a significant

share of the pharmaceutical market in the United States. Our ability to distribute RECOTHROM and to recognize revenues on a timely basis substantially depends on our ability to maintain commercially reasonable agreements with each of these wholesale distributors and the extent to which these distributors, over which we have no control, comply with such agreements. Unless other distributors absorb the incremental sales volume or we are able to sell directly, the loss or bankruptcy of any of these distributors would materially and adversely affect our future results of operations, financial condition and our ability to distribute RECOTHROM.

Further, we rely on our distributors to provide us with accurate and timely information regarding their inventories and complaints about RECOTHROM. If they fail to provide this information, or if they provide incomplete, faulty or untimely information, our ability to forecast product demand will be hindered and our business may be significantly harmed.

Guidelines, recommendations and other literature published by various organizations, including competitors, may affect the use of RECOTHROM®.

In addition to government agencies, whose regulations may restrict our promotion and sales of RECOTHROM, various professional societies, practice management groups, private health/science foundations, and organizations periodically publish guidelines, recommendations and other literature to the healthcare and patient communities. These publications may relate to such matters as product usage, labeling and packaging, dosage, route of administration, and use of related or competing products. These organizations have in the past made recommendations about RECOTHROM or products that compete with RECOTHROM, such as the treatment guidelines of the Society of Thoracic Surgeons. Competitors may also conduct and publish the results of clinical trials aimed at diminishing concerns about their own products, or indicating advantages over RECOTHROM. These types of publications could result in negative perceptions about or decreased use of RECOTHROM. In addition, such publications could also negatively impair the perception of our Company by the investment community or shareholders and could adversely affect the market price of our stock.

Codes, guidelines and policies published by the Pharmaceuticals Research and Manufacturers of America and similar organizations may affect our ability to effectively promote RECOTHROM®.

The Pharmaceuticals Research and Manufacturers of America or "PhRMA" is an influential industry trade association that encourages self-policing measures by pharmaceutical and biopharmaceutical companies to prevent improper promotional practices and improper interactions with health care providers. Over the past several years, there has been increasing scrutiny of pharmaceutical promotional activities by government agencies, professional organizations, patient advocacy groups and pharmaceutical competitors, which has resulted in substantial, well-publicized fines, and has terminated or altered some long-standing promotional practices. State and federal agencies may adopt or rely on PhRMA's codes and recommendations when establishing new legal requirements or evaluating our promotional practices for compliance with existing laws and industry standards. The company is committed to promoting its products in an ethical and appropriate manner. Principles and guidelines promulgated by PhRMA, including the recent revisions to the PhRMA Code on Interactions with Health Care Professionals (HCPs), may limit our ability to effectively gain access to and communicate with potential customers. Among other things, the revised PhRMA Code narrowly limits the provision of meals for HCPs and restricts the involvement of industry sponsors with the conduct and content of continuing medical education, support of education and professional meetings, and use of speaker programs. The restrictions imposed by codes established by PhRMA and similar organizations could limit our ability to interact with customers and promote RECOTHROM, and any failure to follow such codes could harm our reputation and could increase the risk of government investigations or other actions against us.

RECOTHROM® has not been approved for sale outside of the United States, and may never receive foreign marketing approval.

Under a 2007 agreement, our ex-US licensee Bayer Schering Pharma AG agreed to seek applicable government approvals for and develop and market RECOTHROM outside the United States. During 2008, Bayer

Schering Pharma filed applications in Europe and Canada; however, we and Bayer Schering Pharma do not know whether foreign regulatory authorities will grant marketing approval to RECOTHROM. In the United States, RECOTHROM was approved by the FDA on the basis of clinical studies showing non-inferiority to bovine plasma-derived thrombin. The European Medicines Agency, Health Canada and other regulatory authorities may require other clinical trials having a different comparator or study design prior to, or after, approval, especially because bovine plasma-derived thrombin is not currently approved in Europe or Canada. In addition, the foreign regulatory authorities may not be satisfied with the safety and efficacy data submitted in support of the foreign applications, which could result in either non-approval or a requirement of additional clinical trials or further analysis of existing data. Furthermore, as an element of the foreign approval process, the applicable regulatory authority must be satisfied with the processes and facilities for all stages of the manufacture, packaging and distribution of RECOTHROM, which may include physical inspections of many or all relevant facilities. Any conclusion that there are shortcomings in the processes, facilities, quality control or oversight of contract manufacturers, or other quality assurance procedures related to manufacture, packaging and distribution of the drug could result in a significant delay in or failure to receive foreign approval. Lack of or limited marketing approval in a particular country could prevent or limit Bayer Schering Pharma from selling RECOTHROM in that country, which could significantly harm our business.

We will be dependent on the efforts of Bayer Schering Pharma to market and promote RECOTHROM® in countries outside the United States where RECOTHROM® may receive approval and we may otherwise be limited due to our relationship with Bayer.

Under our license and collaboration agreement with Bayer Schering Pharma, we will be dependent solely on Bayer Schering Pharma to promote and market RECOTHROM in countries outside the United States where RECOTHROM is approved. We have limited ability to direct Bayer Schering Pharma in its promotion of RECOTHROM in foreign countries. Bayer Schering Pharma may not have sufficient experience to promote topical hemostat products in foreign countries and may fail to devote appropriate resources to this task. No form of thrombin is currently sold in Europe or Canada, and, therefore, Bayer Schering Pharma will have to create a new market for RECOTHROM, an endeavor in which it may fail. If Bayer Schering Pharma fails to effectively promote RECOTHROM in foreign countries, we may be unable to obtain any meaningful remedy against Bayer Schering Pharma. In addition, Bayer Schering Pharma has the right to terminate the license and collaboration agreement for its own convenience and upon its own election, even if we are in full compliance with our obligations under the agreement. If Bayer Schering Pharma were to fail to perform, or to terminate the agreement, sales of RECOTHROM in foreign countries may be harmed, which would negatively impact our business.

Further, pursuant to the license and collaboration agreement, we granted to Bayer Schering Pharma certain license rights to other potential products containing recombinant thrombin. We retained the right to co-develop such other products and the exclusive right to commercialize them in the United States, however, Bayer Schering Pharma has the ability to license the full rights to these products outside the United States, and even if it does not elect to do so, we will not be permitted to commercialize other products containing recombinant thrombin outside of the United States.

Overall, our agreement with Bayer Schering Pharma may:

- limit the financial benefits we derive from products containing recombinant thrombin by precluding us from markets outside the United States;
- limit the financial benefits we may derive from products containing recombinant thrombin by allowing Bayer Schering Pharma to license them in exchange for predetermined payments and royalties and with predetermined cost-sharing arrangements, which payments and royalty rates may be less than, and which cost-sharing arrangements may be less favorable to us than, terms we might otherwise obtain in collaborative or licensing arrangements with other parties;

- result in a delay in developing one or more products containing recombinant thrombin due to Bayer Schering Pharma's internal decisions, procedures or development strategies; and
- prevent us from collaborating with or licensing a product candidate containing recombinant thrombin to another company that, by virtue of its particular skills and capabilities, may be a more desirable collaborator or licensing partner for that particular product candidate than Bayer Schering Pharma.

We have limited composition of matter patent protection for RECOTHROM®.

While we hold patents to the manufacture of RECOTHROM, our composition of matter patent protection is limited to a key intermediate in the production of recombinant thrombin. Accordingly, we may not be able to prevent other parties from developing alternate methods of manufacturing recombinant thrombin or from selling recombinant thrombin. If a third party sold recombinant thrombin manufactured using an alternate method of manufacturing, it could significantly impair our business. In addition, after FDA approval of RECOTHROM, we filed an application for patent term extension of our relevant US patents, but thus far, we have not received confirmation from the US Patent and Trademark Office that the extension will be granted to the extent we requested, or at all. If we are unable to obtain the requested term extension of our RECOTHROM patents, it could limit our ability to stop competitors and could impair our business.

Certain third parties hold patents relating to thrombin.

We are aware of certain United States and European patents and patent applications held by third parties relating to thrombin and to methods of manufacture of thrombin and other recombinant proteins. Our analyses of these patents lead us to conclude that we do not and will not infringe these patents and that many of the claims of these patents are invalid or unenforceable; however, the patent holders, courts or other governmental or legal entities may conclude that our products, processes and/or actions in developing, manufacturing or selling RECOTHROM do infringe one or more patents. We may seek licenses to such patents if, in our judgment, such licenses are needed. If any licenses are required, we may not be able to obtain any such licenses on commercially favorable terms, if at all. If these licenses are not obtained, we might be prevented from selling RECOTHROM or from using certain of our technologies for the manufacture of RECOTHROM. Our failure to obtain a license to any technology that we may require may severely harm our business.

We rely on third parties to manufacture commercial supplies of RECOTHROM® and our product candidates and, therefore, we may not be able to effectively control production or obtain adequate supplies, which could cause delays in product manufacturing, subject us to product shortages or reduce product sales.

The manufacture and delivery of sufficient quantities of pharmaceutical products and devices is a time-consuming and complex process. Except for limited capabilities to produce protein product candidates for clinical trials, we currently have no internal manufacturing capabilities. In order to successfully commercialize our products, including RECOTHROM, and continue to develop our product candidates, including line extensions for RECOTHROM, and PEG-IFNλ, we need to contract or otherwise arrange for the necessary manufacturing. For example, we have entered into an agreement with Abbott Laboratories for commercial-scale production of bulk drug substance recombinant thrombin and an agreement with Patheon Italia S.p.A., Inc. for fill and finish of the dosage form of RECOTHROM. We have also entered into agreements with several suppliers of critical raw materials, manufacturing process intermediates and components for RECOTHROM, some of which are located outside the United States. For our PEG-IFNλ product candidate, we will rely on our collaborative partner Bristol-Myers Squibb to manufacture supplies for late-stage clinical trials and, if approved, commercial sales.

Reliance on third-party manufacturers, other vendors and collaborators limits our control regarding many aspects of the manufacturing and delivery processes and therefore exposes us to a variety of significant risks relating to:

- our ability to commercialize our products or conduct clinical trials (including, for example, due to contractual provisions allocating supplies in the event of a shortage);
- reliance on third parties for legal and regulatory compliance and quality assurance;
- third-party refusals to supply on a long-term basis;
- third-party insistence on minimum and/or maximum levels of supply and related restrictions on our ability to increase or decrease supply;
- problems with the manufacturing facilities used by third parties, including problems leading to production delays, unanticipated expenses and withdrawal of facilities approvals by regulatory authorities;
- breach of agreements by third-parties; and
- termination, price increases, or non-renewal of agreements by third-parties, based on other business priorities, at times that are costly or inconvenient for us.

Furthermore, the manufacturing facilities of our contract manufacturers and collaborators will be periodically inspected by the FDA. A manufacturer's failure to satisfy regulatory requirements may result in withdrawal of FDA approval for that facility, including those used in the production of RECOTHROM and our clinical product candidates. In complying with FDA regulations, we and our contract manufacturers will be obligated to expend time, money and effort in production, record keeping and quality assurance to assure that our products meet applicable requirements.

If any of these risks occur, our product supply could be interrupted resulting in lost or delayed revenues, delayed clinical trials, and significant increase in production costs and cost of goods.

In addition, if, for any reason, we are required to engage an additional, second-source or replacement manufacturer or other vendor, the investment of funds and management time could be significant. For example, we could be required to engage a replacement manufacturer if our current manufacturers are adversely impacted by the current global economic crisis. The cost and time to establish and license these new manufacturing facilities would be substantial. As a result, using a new manufacturer or other vendor could disrupt our ability to market our products, subject us to product shortages, reduce product sales, and/or reduce our profit margins. Further, any delay or disruption in the manufacturing of bulk product, the dosage form of our products or other product components, including spray applicators for delivery of RECOTHROM, could also harm our reputation in the medical community.

Overall, while we believe that business relations between us and our manufacturers and other supply chain vendors are generally good, we cannot predict whether any of the manufacturers and other vendors that we may use will continue to meet our requirements for quality, quantity or timeliness for the manufacture of RECOTHROM, its intermediates or components or for our other product candidates.

There are limited numbers of potential manufacturers and other vendors on whom we could rely to supply RECOTHROM® and our other product candidates.

There are a limited number of manufacturers and other vendors that operate under the FDA's cGMP regulations capable of manufacturing for us, and we have not established backup manufacturers and suppliers for RECOTHROM or any of our product candidates. Accordingly, if we are not able to maintain third-party manufacturing on commercially reasonable terms, or if we lose a significant supplier used for RECOTHROM, its line extensions, if any, or for our other product candidates, we may not be able to market our products, meet

certain contractual supply obligations or complete development of our product candidates on a timely basis, if at all. For example, under our agreements with Bayer, we are required to provide Bayer with RECOTHROM and may be in breach of the agreement if we cannot make the required deliveries on time.

In addition, some of the inventions and patents licensed to us were initially developed at universities or other not-for-profit institutions with funding support from an agency of the United States government. In accordance with federal law, our licensees or we may be required to manufacture in the United States products covered by those patents, unless we can obtain a waiver from the government on the basis that such domestic manufacture is not commercially feasible. We have not attempted to secure any such waivers from the government, and do not know if they would be sought or available if sought. If we are not able to obtain such waivers, if requested, on a timely basis, we might be forced to seek manufacturing arrangements at higher prices, or on otherwise less favorable terms, than might be available to us in the absence of this domestic manufacturing requirement.

Failure to effectively manage the RECOTHROM® supply chain could result in inventory shortages, supply interruptions or inventory obsolescence.

Our supply chain for RECOTHROM, its intermediates and components, is particularly complex and involves a number of third parties on several continents. In addition to coordinating the efforts of these third party contractors, we must navigate the laws and regulations of multiply jurisdictions, including tax laws, and our failure to do so effectively may negatively impact our business.

In addition, our contract manufacturers and other vendors have not produced RECOTHROM, its intermediates or components, for commercial use for a sustained period of time. As such, unforeseeable risks may be encountered as we, together with our manufacturers and other vendors, continue to develop familiarity and experience with regard to manufacturing RECOTHROM, its intermediates and components. Failure to adequately manage our supply chain could result in inventory shortages or other supply interruptions that could negatively impact RECOTHROM sales and, consequently, negatively impact product revenue.

We have limited expiration dating for RECOTHROM. Consequently, if we are unable to sell at forecasted levels we may have excess RECOTHROM inventory, resulting in inventory obsolescence, increased costs of product sales and ineffective use of our financial resources.

As we progress from a primarily research and development company to a company increasingly involved in commercialization of products, we may encounter difficulties in managing our growth and expanding our operations.

As we commercialize RECOTHROM and continue to advance product candidates through clinical trials and on to commercialization, we may need to expand our development and commercial operations capabilities. If we are not able to provide these capabilities internally, we may need to rely on collaborative partners or other third parties to provide these services for us. Expanded operations would add significant complexity to our business and responsibilities to certain members of our management and key personnel. We may need to manage relationships with an increasing number of collaborative partners, suppliers and third-party contractors. If we are unable to successfully provide the required infrastructure, either internally or through third parties, and successfully manage an increasing number of relationships, we will have difficulty growing our business.

We have rapidly expanded our field force operations, including sales personnel and medical science liaisons, and any difficulties managing these functions or the related growth could disrupt our operations.

Prior to launch of RECOTHROM in the United States, we rapidly expanded and developed our field force operations, including sales personnel and medical science liaisons, which included, for the first time, hiring employees based outside of our Washington State headquarters. We increased expenditures in these areas, hiring

additional employees and expanding the scope of our operations. Since the launch of RECOTHROM, we have had limited opportunity to test our field force operations, and our ability to manage them. If we are unable to effectively manage our field force operations, or if our capabilities prove to be inadequate, we may not be able to effectively implement or sustain our business plan.

We may be unable to satisfy the rigorous government regulations relating to the development and marketing approval of our product candidates.

The successful commercialization of IL-21, PEG-IFN-λ or any of our other product candidates will depend on obtaining marketing approval from the applicable regulatory authorities in each market in which we or our collaborators or our licensees intend to market the product candidates. Any failure to receive the marketing approvals necessary to commercialize our product candidates could severely harm our business. The FDA regulates, among other things, the collection, testing, manufacturing, safety, efficacy, potency, labeling, storage, record keeping, quality systems, advertising, promotion, sale and distribution of therapeutic products. If our potential products are marketed abroad, they will also be subject to extensive regulation by foreign governments. Except for RECOTHROM in the United States, none of our product candidates has been approved for sale in any country, and our experience in filing and pursuing applications necessary to gain regulatory approvals is limited.

The regulatory review and approval process of governmental authorities, which includes nonclinical studies and clinical trials of each product candidate, is lengthy, expensive and uncertain. For example, securing FDA approval requires the submission of extensive nonclinical and clinical data and supporting information to the FDA for each indication to establish the product candidate's safety and effectiveness, including significant information regarding the chemistry, manufacturing and controls or the product. The approval process typically takes many years to complete and may involve ongoing requirements for post-marketing clinical studies or other risk management measures. In addition, we may not achieve governmental approval, including that of the FDA, of a product candidate even if we have met our internal safety and efficacy criteria and completed clinical trials. Also, any regulatory approval of any of our product candidates, once obtained, may be withdrawn. Government regulation may result in:

- prohibitions or significant delays in the marketing of potential products;
- recalls and discontinuation of the marketing of potential products; and
- limitations of the indicated uses for which potential products may be marketed.

If we fail to comply with the laws and regulations pertaining to our business, in each applicable country, we may be subject to sanctions, including the temporary or permanent suspension of operations, product recalls, marketing restrictions and civil and criminal penalties. In addition, some of our product candidates may be approved for use in combination with other products that are not our own. Failure by any of these products to comply with the laws and regulations pertaining to their business, resulting in potential product restrictions or recalls, may materially harm our ability to successfully commercialize and generate revenues from our products used in combination regimens.

Clinical trials may fail to demonstrate the safety and effectiveness of our product candidates, which could prevent or significantly delay their regulatory approval.

Clinical trials involving IL-21, PEG-IFN-λ or any of our other product candidates may reveal that those candidates are ineffective, are insufficiently effective given their safety profile, have unacceptable toxicity or safety profiles or have other unacceptable side effects. In addition, data obtained from tests are susceptible to varying interpretations, which may delay, limit or prevent regulatory approval. Likewise, the results of preliminary studies do not predict clinical success, and larger and later-stage clinical trials may not produce the same results as earlier-stage trials. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. Similarly, clinical trial results

may vary between different arms of a clinical trial for reasons that we cannot adequately explain. In addition, clinical trials of potential products often reveal that it is not practical or feasible to continue development efforts.

We may be required to defend lawsuits and pay damages in connection with alleged or actual harm caused by our products and product candidates.

The design, testing, manufacture and sale of therapeutic products involve an inherent risk of product liability claims and associated adverse publicity, even if the claims arise from use of the product in a manner inconsistent with label or other instructions. In addition, RECOTHROM is and will be used on patients undergoing surgery, where there are significant risks to patients. Further, our marketing and promotional efforts for RECOTHROM could increase the risk of litigation based on claims by our competitors or others of unfair competition or unfair advertising. We may incur significant expenses if any of these lawsuits against us were to be successful. Even if such lawsuits are without merit or otherwise unsuccessful, they could cause adverse publicity, divert management attention and be costly to respond to, and, therefore, could have a material adverse effect on our business, including negatively impacting our share price. Although we maintain product liability and general insurance, our coverage may not be adequate to cover such claims. We do not know if we will be able to maintain existing or obtain additional product liability insurance on acceptable terms or with adequate coverage against potential liabilities. This type of insurance is expensive and may not be available on acceptable terms or at all. If we are unable to obtain or maintain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to continue to develop or commercialize RECOTHROM or any other product candidates. Any product liability claims, whether or not ultimately successful, could have a material negative effect on our reputation, stock price, the market acceptance and sales of products and our financial condition and results.

Our use of collaborations to leverage our capabilities may not be successful.

We have entered into collaboration arrangements with partners to co-develop and co-commercialize products and will continue to evaluate similar opportunities. To be successful, we must identify and attract partners whose competencies and priorities complement ours. We must enter into collaboration agreements on terms beneficial to us and integrate and coordinate their processes, resources and capabilities with our own on a continuing basis. We may be unsuccessful in entering into collaboration agreements with acceptable partners or negotiating favorable terms in these agreements or maintaining such relationships so as to reap benefits from them over time. Also, we may be unsuccessful in integrating the resources, processes, capabilities or priorities of these collaborators on a continuing basis. In addition, our collaborators may prove difficult to work with or less skilled than we originally expected. If we are unsuccessful in our collaborative efforts, our ability to develop and market product candidates could be severely limited.

We have very recently initiated our collaborative efforts with Bristol-Myers Squibb for the development of PEG-IFN-λ. This collaboration will require close and frequent communications between several different teams within the respective companies, technology transfer, and in general a collaborative sharing of responsibilities for clinical studies and all other development activities. While we are hopeful that we will be able to integrate our processes with our counterparts at Bristol-Myers Squibb, we have limited experience with them and are unable to accurately predict our ultimate ability to collaborate with them. Difficulties in collaboration could result in lower than expected revenue, delays in development, loss of market opportunities, and significant deterioration in the value of this product candidate and our company.

We may not be able to generate any revenue from product candidates developed by collaborators or licensees if they do not successfully develop those candidates.

We may be unable to derive any value from product candidates developed by collaborators or licensees, including Novo Nordisk, Merck Serono, Bayer Schering Pharma and Bristol-Myers Squibb. Our ability to generate revenues from existing or future collaborations and license arrangements is subject to numerous risks, including:

- the possibility that our collaborators or licensees lack sufficient financial, technical or other capabilities to develop these product candidates;
- the possibility that our collaborators or licensees choose to scale back or discontinue their development activities due to changes in their strategies, restructuring, mergers or acquisitions;
- the length of time that it takes for our collaborators or licensees to solve technical problems or achieve various clinical development and regulatory approval milestones;
- differences in opinion about development, clinical and regulatory strategies and timeframes;
- the inability of collaborators or licensees to successfully address any regulatory or technical challenges they may encounter; and
- the possibility that these product candidates may not be effective or may prove to have undesirable side effects, unacceptable toxicities or other characteristics that preclude regulatory approval or prevent or limit commercial use.

Because we will depend on third parties to conduct certain laboratory tests and clinical trials, we may encounter delays in or lose some control over our efforts to develop product candidates.

We commonly rely on third parties to conduct laboratory tests and clinical trials for us, especially to the extent clinical trials include sites outside the United States. If we are unable to obtain these services on acceptable terms, we may not be able to complete our product development efforts in a timely manner. Also, to the extent we will rely on third parties for laboratory tests and clinical trials, we may lose some control over these activities or be unable to manage them appropriately, or may become too dependent on these parties. These third parties may not complete the tests or trials on our schedule, and the tests or trials may be methodologically flawed, may not comply with applicable laws or be otherwise defective. Any delays or difficulties associated with third-party laboratory tests or clinical trials may delay and increases the risks and costs of the development of our product candidates.

We have shifted our discovery efforts to therapeutic antibodies with which we have limited experience and face competition.

We have shifted our discovery efforts to focus on developing therapeutic antibodies. We have limited experience developing antibodies and may not be successful in these efforts. In addition, there is a great deal of competition in the field of antibody products. Our competitors include multinational pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions. A number of our largest competitors, including Genentech, Inc., Amgen Inc., AstraZeneca PLC and Human Genome Sciences, Inc., are pursuing the development or marketing of pharmaceuticals that address the same diseases that we are pursuing, and it is possible that the number of companies seeking to develop products and therapies for these diseases will increase.

We may be unable to commercialize antibody products.

We may not be successful in obtaining adequate, if any, patent coverage for our discoveries and therapeutic antibody products. In addition, third parties may own key technology or target patents or dominating patents that may prevent us from developing, manufacturing or commercializing therapeutic antibodies. For example, we are

aware of broad patents owned by others relating to the discovery, development, manufacture, use and sale of recombinant humanized antibodies, recombinant humanized single chain antibodies, recombinant human antibodies, and recombinant human single chain antibodies and other technologies. Many of our product candidates may use or include such technologies. While we have entered into agreements with certain third parties in order to gain access to their technology, often the technology is made available on a target-by-target basis upon submission of specific targets and payment of a fee. We have no assurance that a license to a particular target will be available until it is submitted as part of such a process. We are also aware that third parties own patents related to the target molecules with which our antibody products are designed to interact. Even if we are successful at obtaining patent protection for our antibody product candidates, these antibody product candidates may infringe such third party patents covering the targets. We may not be able to obtain necessary rights to such targets, or to key technologies needed for the discovery, development, production or commercialization of therapeutic antibodies through licensing agreements on terms attractive to us, if at all. If these licenses are not obtained, we might be prevented from developing antibodies aimed at such targets or from using certain of our technologies for the generation and development of our new discoveries. If we are unsuccessful in our efforts to obtain needed licenses, our ability to develop and commercialize antibody product candidates could be severely limited. Any patent infringement or other legal claims that might be brought against us may cause us to incur significant expenses, enjoin our development or commercialization of such products, divert the attention of our management and key personnel from other business concerns and, if successfully asserted against us, require us to pay substantial damages.

If our research and development programs fail to result in additional product candidates, our potential to generate revenue will be substantially limited.

Potential product candidates from our research and development programs are at relatively early stages and will require significant research, development, preclinical and clinical testing, manufacturing scale-up activities, regulatory approval and/or commitments of significant resources before commercialization. We cannot predict whether our efforts will lead to the development of any additional product candidates that could generate revenues for us.

The failure to attract or retain key management or other personnel could decrease our ability to discover, develop and commercialize potential products.

We depend on our senior executive officers as well as key scientific, management and other personnel. Only a small number of our key personnel are bound by employment agreements, and those with employment agreements are bound only for a limited period of time. Further, we have not purchased key-person life insurance policies for any of our executive officers or key personnel. Competition for scientists and other qualified employees is intense among pharmaceutical and biotechnology companies, and the loss of qualified employees, or an inability to attract, retain and motivate the additional highly skilled employees required for the expansion of our activities, could hinder our ability to discover, develop and commercialize potential products.

We may expand our business through the acquisition of companies or businesses or in-licensing product candidates that could disrupt our business and harm our financial condition.

We may in the future seek to expand our products and capabilities by acquiring one or more companies or businesses or in-licensing one or more product candidates. Acquisitions and in-licenses involve numerous risks, including:

- substantial cash expenditures;
- potentially dilutive issuance of equity securities;
- incurrence of debt and contingent liabilities, some of which may be difficult or impossible to identify at the time of acquisition;
- difficulties in assimilating the operations of the acquired companies;

- diverting our management's attention away from other business concerns;
- entering markets in which we have limited or no direct experience; and
- potential loss of our key employees or key employees of the acquired companies or businesses.

Historically, we have not expanded our business through acquisition or in-licensing and, therefore, our experience in making acquisitions and in-licensing is limited. We cannot assure you that any acquisition or in-license will result in short-term or long-term benefits to us. We may incorrectly judge the value or worth of an acquired company or business or in-licensed product candidate. In addition, our future success would depend in part on our ability to manage the rapid growth associated with some of these acquisitions and in-licenses. We cannot assure you that we would be able to make the combination of our business with that of acquired businesses or companies or in-licensed product candidates work or be successful. Furthermore, the development or expansion of our business or any acquired business or company or in-licensed product candidate may require a substantial capital investment by us. We may not have these necessary funds or they might not be available to us on acceptable terms or at all. We may also seek to raise funds by selling shares of our stock, which could dilute our current shareholders' ownership interest, or securities convertible into our stock, which could dilute current shareholders' ownership interest upon conversion.

Our patents and patent applications may not result in meaningful protection against competitors, provide us with any competitive advantage, or provide adequate protection or rights for new discoveries, and our competitors may commercialize the discoveries we patent or attempt to patent.

We own (or in the case of certain foreign patents related to PEG-IFNλ, co-own with Bristol-Myers Squibb) or hold exclusive rights to many issued United States and foreign patents and pending patent applications related to the development and commercialization of our products and product candidates. These patents and applications cover composition-of-matter for genes, proteins, and antibodies, medical indications, methods of use, methods of making, formulations, technologies and other inventions related to therapeutic proteins and antibodies. Our success will depend in part on our ability to obtain and maintain patent protection for our products and product candidates in the United States and other countries.

Although we diligently seek to identify and protect our important discoveries and inventions, we may fail to file timely patent applications. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Our pending and future patent applications covering products and product candidates may not meet the statutory requirements for patentability, meaning that our applications may not result in the issuance of any patents, and, if issued, such patents may not be valid or enforceable. Our rights under any patents may not provide us with sufficient protection against competitive products or otherwise cover commercially valuable products or processes. In addition, because patent applications in the United States are maintained in secrecy for eighteen months after the filing of the applications, and publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we cannot be sure that the inventors of subject matter covered by our patents and patent applications were the first to invent or the first to file patent applications for these inventions.

Our patents may not provide us with any competitive advantage. Although we have a number of issued patents, the discoveries or technologies covered by these patents may not have any value. These issued patents may not provide commercially meaningful protection against competitors, nor may they provide all rights necessary to commercialize our products or product candidates. In addition, we may not be able to or allowed to obtain patent term extension or restoration on patents covering our products in a manner that would provide commercially meaningful protection against competitors.

Other parties may have a dominating or blocking patent position covering a composition of matter, or methods of making or using our products or product candidates. In addition, other parties may be able to design around our issued patents or independently develop products having attributes or uses similar or identical to our

patented product candidates. The business model of some companies is to "design around" patented marketed protein-based products by altering the amino acid sequence of the marketed product, thereby avoiding the patent, but maintaining functional equivalence. Similarly, it may be easier to develop equivalent versions of monoclonal antibodies and soluble receptors than to develop equivalent versions of the proteins with which they interact because there is often more than one antibody or receptor that can have the same therapeutic effect. Consequently, any of our existing or future patents that cover monoclonal antibodies or soluble receptors may not provide any meaningful protection against competitors. In addition, other parties may discover uses for genes or proteins that are different from the uses described in our patents, and these other uses may be separately patentable. If another party holds a patent on the use of a gene or protein, then even if we hold the patent covering the composition of matter of the gene or protein itself, that party might prevent us from promoting and selling any product directed to such use. Also, other parties may have patents covering the composition of matter of genes or proteins for which we have patents covering only methods of use or methods of manufacture. Furthermore, our patents on recombinant proteins or their precursors or methods of manufacturing such proteins, such as our patents covering the precursor to RECOTHROM and its method of manufacture, may not prevent competitors from developing other precursors or methods of manufacturing these proteins.

Third parties may challenge the validity or enforceability of our patents.

The issuance of a patent is not conclusive as to its scope, validity or enforceability. Third parties, including our competitors and licensees, may initiate proceedings to limit the scope, validity or enforceability of our patents, including but not limited to *inter-partes* re-examination proceedings in the United States Patent and Trademark Office, opposition proceedings in patent authorities outside of the United States, declaratory judgment proceedings in United States courts, or in the event a third party independently makes an invention similar to ours, interference proceedings in the United States Patent and Trademark Office to determine priority of invention. Likewise, we may initiate *inter-partes* proceedings to challenge the scope, validity or enforceability of third party patents. The outcome of any such proceeding is uncertain and could result in judicial determinations that our patents are invalid, limited in scope, not infringed, and/or unenforceable, which would impair our business. Participating in such proceedings or other challenges, whether initiated by us or by third parties may require significant expenditures and divert the attention of our management and key personnel from other business concerns, which may also impair our business.

Third parties may infringe our patents.

Competitors and other third parties may infringe our patents, or use inventions described in our patent applications. It may be difficult or impossible for us to police third party activities and detect such infringement, for example, we may be unable to discover a competitor's manufacturing process to determine whether it infringes a patent claims to a method of manufacture. Patent litigation is very expensive and time-consuming and is a distraction to management and personnel who are needed to supply evidence and support to litigation efforts. Enforcing our patents against third parties may require significant expenditures regardless of outcome. We may incur substantial expenditures in such patent litigation and the outcome of any lawsuit is uncertain.

Further, challenges raised in patent infringement litigation initiated by us or by third parties may result in determinations that our patents have not been infringed or that they are invalid, unenforceable or otherwise subject to limitations. Consequently, third parties, including licensees, may be able to use the discoveries or technologies claimed or described in our patents without paying licensing fees or royalties to us, which could significantly diminish the value of our intellectual property.

We may be subject to patent infringement claims, which could result in substantial costs and liability and prevent us from commercializing our products and product candidates.

Third parties may claim that our products or product candidates, or processes or related technologies infringe their patents. The risk of infringement claims filed against us is likely to increase as we commercialize

products or move product candidates closer to commercialization. Furthermore, we may not have identified or analyzed all United States and foreign patents that pose a risk of our infringement.

Any patent infringement or other legal claims that might be brought against us may cause us to incur significant expenses, divert the attention of our management and key personnel from other business concerns and, if successfully asserted against us, require us to pay substantial damages. In addition, as a result of a patent infringement suit, we may be forced to stop or delay developing, manufacturing or selling products or product candidates that are claimed to infringe a third party's patent unless that party grants us rights to use its intellectual property. We may be unable to obtain these rights on terms acceptable to us, if at all. Even if we are able to obtain rights to a third party's patented intellectual property, these rights may be non-exclusive, allowing our competitors to obtain access to the same intellectual property. Ultimately, we may be unable to commercialize our potential products or may have to cease some of our business operations, which could severely harm our business.

Patent protection for protein-based therapeutic products and other biotechnology inventions is subject to a great deal of uncertainty, and if patent laws or the interpretation of patent laws change, our competitors may be able to develop and commercialize products based on our discoveries.

Patent protection for protein-based therapeutic products is highly uncertain and involves complex legal and factual questions. In recent years, there have been significant changes in patent law, including the legal standards that govern the scope of protein and biotechnology patents. Standards for patentability of full-length and partial genes, and their corresponding proteins, are changing. Also, there is substantial uncertainty regarding the patentability of proteins without known function or specific correlation with diseases. Recent court decisions have made it more difficult to obtain patents, by making it more difficult to satisfy the requirement of non-obviousness, have decreased the availability of injunctions against infringers, have decreased the likelihood of proving willfulness, and have increased the likelihood of challenging the validity of a patent through a declaratory judgment action. Taken together, these decisions make it more difficult and costly for us to obtain, license and enforce our patents. In addition, in recent years, several members of the United States Congress have made numerous proposals to change the patent statute. These proposals include measures that, among other things, would expand the ability of third parties to oppose United States patents, introduce the "first to file" standard to the United States patent system, and limit damages an infringer is required to pay. If the patent statute is changed, the scope, validity and enforceability of our patents may be significantly decreased.

There also have been, and continue to be, policy discussions concerning the scope of patent protection awarded to biotechnology inventions. Social and political opposition to patents on genes and proteins may lead to narrower patent protection, or narrower claim interpretation, for genes, their corresponding proteins and inventions related to their use, formulation and manufacture. Patent protection relating to biotechnology products is also subject to a great deal of uncertainty outside the United States, and patent laws are evolving and undergoing revision in many countries. Changes in, or different interpretations of, patent laws worldwide may result in our inability to obtain or enforce patents, and may allow others to use our discoveries to develop and commercialize competitive products, which would impair our business.

We expect to incur significant expenses in applying for patent protection and prosecuting our patent applications.

Our success depends significantly on the establishment of patent protection for the products and product candidates and related technologies. Consequently, we intend to continue our substantial efforts in applying for patent protection and prosecuting pending and future patent applications and maintaining patents. These efforts have historically required the expenditure of considerable time and money, and we expect that they will continue to require significant expenditures. We may fail to secure meaningful patent protection relating to any of our existing or future product candidates, discoveries or technologies despite the expenditure of considerable resources. In addition, future changes in United States or foreign patent laws may complicate or hinder our efforts to obtain patent protection and may significantly increase the costs associated with patent prosecution.

We may be unable to protect our unpatented proprietary technology and information.

In addition to our patented intellectual property, we also rely on trade secrets and confidential information. We may not be able to effectively protect our rights to such proprietary technology or information. Other parties may independently develop or gain access to equivalent technologies or information and disclose it for others to use. Disputes may arise about inventorship and corresponding rights to know-how and inventions resulting from the joint creation or use of intellectual property by us and our corporate partners, licensees, scientific and academic collaborators and consultants. In addition, confidentiality agreements and material transfer agreements we have entered into with these parties and with employees and advisors may not provide effective protection of our proprietary technology or information or, in the event of unauthorized use or disclosure, may not provide adequate remedies.

Environmental and health and safety laws may result in liabilities, expenses and restrictions on our operations.

State and federal laws and regulations and those of foreign jurisdictions regarding environmental protection, hazardous substances and human health and safety may adversely affect our business. The use of hazardous substances in our operations exposes us to the risk of accidental releases. If our operations, including those of our strategic partners, result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and fines. Future changes to environmental and health and safety laws could cause us to incur additional expenses or restrict our operations. In addition, the site where our principal headquarters and facilities are located has been listed as a contaminated property by the State of Washington due to its previous use by the City of Seattle as an electricity generating plant. The City of Seattle has agreed to defend us against and indemnify us for any claims that arise from this pre-existing contamination, except to the extent that we caused the claim through our negligence or intentional fault, or to the extent that we contributed to the contamination that is the subject of the claim, caused an increase in the clean-up costs or failed to comply with our obligations under our agreement with the City of Seattle. This indemnity may be insufficient and we may be subject to environmental liabilities or be prohibited from using or occupying some or all of the property as a result of environmental claims.

Natural or man-made disasters may impair our ability to conduct our business.

While our headquarters and principal research and development operations are in Seattle, Washington, we also have partners, manufacturers, suppliers and distributors in various parts of the United States, Europe and Australia. Our facilities and those of our partners, manufacturers, suppliers or distributors may be subject to natural or man-made disasters. A natural or man-made disaster could cause damage to our facility, personnel or equipment, which in turn, could cause us to cease or curtail operations. Our business and financial position may also be affected by disasters affecting the operations of one of our partners, manufacturers, suppliers or distributors. Disasters may include, but are not limited to earthquakes, volcanic eruptions, tsunamis, fires, floods, power loss, communication failures and other similar events, including the effects of war or acts of terrorism. If any disaster were to occur, our ability to operate our business could be seriously or completely impaired. Although we maintain insurance coverage for many of these types of risks, it may not be adequate to cover our losses resulting from disasters or other business interruptions.

Financial and Market Risks

We anticipate incurring additional losses and may not achieve profitability.

As of December 31, 2008, we had an accumulated deficit of $762 million. We expect to continue to incur significant losses over the next several years, and we may never become profitable. Although we began generating RECOTHROM sales revenue in 2008, it will be a number of years before we generate revenues from sales of other potential products, if ever. Our revenues from the sales of RECOTHROM and existing collaborative and licensing arrangements are currently insufficient to cover our operating expenses, and we may

never generate revenues sufficient to cover these expenses. In addition, we will continue to incur substantial expenses relating to our research, development and commercialization efforts. The development and commercialization of our product candidates will require significant further research, development, testing, regulatory approvals and sales and marketing activities, including, in the immediate future, pursuing the commercialization of RECOTHROM. We may not be able to complete such development or succeed in developing and commercializing products that will generate revenues that will justify the costs of development and commercialization. We may incur substantial operating losses for at least the next few years as we continue to expand our commercial function in the immediate future for RECOTHROM and our research and development activities for the other product candidates in our development pipeline. These losses have had and will have an adverse effect on our shareholders' equity and working capital. Even if we become profitable in the future, we may not remain profitable.

If we do not obtain substantial additional funding on acceptable terms, we may not be able to continue to grow our business or generate enough revenue to recover our investment in research and development.

Our business does not currently generate the cash needed to finance our operations, and we do not expect it to in the near future. We anticipate that we will continue to expend substantial funds on our research and development programs, the amount of which may increase in the future. We expect to seek additional funding through public or private financings, including equity financings, or through other arrangements, including collaborative and licensing arrangements. Poor financial results, unanticipated expenses or unanticipated opportunities that require financial commitments could give rise to additional financing requirements sooner than we expect. However, financing may be unavailable when we need it or may not be available on acceptable terms, especially in light of the current global economic crisis. If we raise additional funds by issuing equity or convertible debt securities, the percentage ownership of our existing shareholders will be diluted, and these securities may have rights superior to those of our common stock. If we are unable to raise additional funds when we need them, we may be required to delay, scale back or eliminate expenditures for some of our research or development or commercialization programs. We may also be required to grant rights to third parties to develop, commercialize and market products and product candidates that we would prefer to develop, commercialize and market internally, and such rights may be granted on terms that are not favorable to us. If we were required to grant such rights, the ultimate value of these products or product candidates to us would be reduced. In addition, if our cash and cash equivalents drop below a certain level it may constitute an event of default under our June 28, 2008 Facility Agreement with Deerfield Private Design Fund, L.P., Deerfield Private Design International, L.P. and Deerfield ZG Corporation.

Our operating results are subject to fluctuations that may cause our stock price to decline.

Our operating results have fluctuated in the past and are likely to continue to do so in the future. Our revenues have been unpredictable and could fluctuate due to slow or erratic uptake of RECOTHROM sales or the timing of licensing fees or the achievement of milestones under new or existing licensing and collaborative arrangements. In addition, our expenses may fluctuate from quarter to quarter due to the timing of expenses, particularly with respect to collaborative cost-sharing, contract manufacturing and clinical and nonclinical testing.

Accordingly, we believe that period-to-period comparisons of our past operating results are not good indicators of our future performance and should not be relied on to predict our future operating results. It is possible that in the future our operating results in a particular quarter or quarters will not meet the expectations of securities analysts or investors, causing the market price of our common stock to decline, perhaps substantially.

We are exposed to risks related to foreign currency exchange rates.

Some of our costs and expenses are denominated in foreign currencies and, even if they are not as a matter of contract, vendors may seek concessions in the event that their anticipated economic return is impaired by

exchange rate fluctuations. Most of our existing foreign expenses are associated with the manufacture of RECOTHROM, sharing of development costs with foreign partners or our global clinical studies. We are primarily exposed to changes in exchange rates with Europe. When the United States dollar weakens against other currencies, the dollar value of the foreign-currency denominated expense increases, and when the dollar strengthens against other currencies, the dollar value of the foreign-currency denominated expense decreases. Consequently, changes in exchange rates, and in particular a weakening of the United States dollar, may adversely affect our results of operations. We currently do not hedge against our foreign currency risks.

Risks Related to Our Industry

Many of our competitors have substantially greater capabilities and resources than we do and may be able to develop and commercialize products before we do or more effectively than we do.

We may be unable to compete successfully against our current or future competitors. We expect that competition in our field will continue to be intense. RECOTHROM and its line extensions, if any, will face substantial competition in the topical hemostat market from the current well-established participants, including King Pharmaceuticals, Inc., Ethicon, Inc. and Baxter International, Inc., as well as any future entrants into this market. For our product candidates in development, we face competition from other entities involved in the research and development of therapeutic proteins, including Genentech, Inc., Human Genome Sciences, Inc., Medarex, Inc. and Biogen Idec Inc., among others. We also face competition from entities developing other types of products related to particular diseases or medical conditions, including other biotechnology and pharmaceutical companies. Furthermore, our potential products, if approved and commercialized, may compete against well-established existing therapeutic protein-based products, many of which may be currently reimbursed by government health administration authorities, private health insurers and health maintenance organizations.

Many of our existing and potential competitors have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we do. As a result, these competitors may:

- succeed in identifying genes or proteins, or developing therapeutic protein-based products, earlier than we do;
- obtain approvals for products from the FDA or other regulatory agencies more rapidly than we do;
- obtain patents that block or otherwise inhibit our ability to develop and commercialize our product candidates;
- develop treatments or cures that are safer or more effective than those we propose to develop;
- devote greater resources to marketing or selling their products;
- introduce or adapt more quickly to new technologies or scientific advances, which could render our discovery technologies obsolete;
- introduce products that make the continued development of our potential products uneconomical;
- withstand price competition more successfully than we can;
- more effectively negotiate third-party collaborative or licensing arrangements; and
- take advantage of acquisitions or other opportunities more readily than we can.

Because of these potential disadvantages, we may not be able to compete effectively with these competitors.

Our products and product candidates, even if approved by the FDA or foreign regulatory agencies, may not achieve market acceptance among hospitals, insurers or patients.

Our products and product candidates, even if approved by the FDA or foreign regulatory agencies, may fail to achieve market acceptance, which would impair our ability to become profitable. We believe that market acceptance of our products and product candidates will depend on:

- our ability to provide acceptable evidence of safety, efficacy and limited side effects;
- our ability to provide these products and product candidates at reasonable prices;
- the availability of third-party reimbursement for these products and product candidates;
- our ability to differentiate our products and compete effectively, including with products that are considered to be the standard of care; and
- the effectiveness of our sales and marketing capabilities.

If the healthcare system, reimbursement policies or any other healthcare related regulations change, the prices of our products and product candidates may fall or our potential sales may decline.

In recent years, officials have made numerous proposals to change the healthcare system in the United States. These proposals include measures that would limit or prohibit payments for certain medical procedures and treatments or subject the pricing of pharmaceuticals to government control. Government and other third-party payers increasingly have attempted to control healthcare costs by limiting both coverage and the level of reimbursement of newly approved healthcare products. Increasingly, third-party payors have been challenging the prices charged for products. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted marketing approval. The government may adopt future legislative proposals, such as price controls on prescription drugs, and federal, state or private payors for healthcare goods and services may take further action to limit payments for healthcare products and services. In addition, in certain foreign countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control with many of the same types of challenges as in the United States. Any of these factors could limit our ability to successfully commercialize our potential products.

We may face increased competition from lower priced products re-imported into the United States from Canada and other countries. The current law, enacted in December 2003, allows the importation of drugs from Canada, but only if the Secretary of Health and Human Services certifies that importation will pose no additional risk to the public's health and safety. To date, no such certifications have been given. Legislative proposals have been made to change the law to allow importation without any certification. If this or other new legislation or regulations were passed allowing the reimportation of drugs, it could adversely affect the prices of our potential products.

In addition, there has been much discussion regarding the creation of laws permitting "follow-on" or "generic" versions of biologics. While there is not currently an abbreviated approval pathway for biologics as there is with branded drugs, Congress and the FDA are studying the issue and there is increasing interest from the public. An abbreviated pathway for "follow-on" biologics may permit the FDA to rely on clinical data submitted by innovator developers like ourselves when evaluating applications filed by sponsors of follow-on biologics and may not require full or any clinical trials, significantly lowering the risks and financial barriers to entry. The approval of "follow-on" biologics could result in new and increased competition, including competition prior to expiration of our patents covering our products, and related litigation. Product liability litigation could become more complex and problematic for us as courts may permit purchasers and users of follow on biologic products to pursue product liability claims against innovator companies, such as us, as has recently happened in the context of generic small molecule drugs.

Negative public opinion and increased regulatory scrutiny of genetic and clinical research may limit our ability to conduct our business.

Ethical, social and legal concerns about genetic and clinical research could result in additional regulations restricting or prohibiting some of our activities or the activities of our suppliers and collaborators. In recent years, federal and state agencies, congressional committees and foreign governments have expressed interest in further regulating the biotechnology industry. More restrictive regulations could delay or complicate nonclinical studies or clinical trials, or prevent us from obtaining regulatory approvals or commercializing any products. In addition, animal rights activists may protest our use of animals in research and development and may attempt to disrupt our operations, which could cause us to incur significant expenses and distract our management's attention from other business concerns.

The marketing and sale of pharmaceutical products and biologics is subject to extensive regulation and aggressive government enforcement, and our corporate compliance program cannot guarantee that we are in compliance with all relevant laws and regulations.

Our activities relating to the sale and marketing of our products will be subject to extensive regulation under the U.S. Federal Food, Drug and Cosmetic Act and other federal statutes and associated regulations. These laws and regulations limit the types of marketing claims and other communications we can make regarding marketed products. We are also 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 prohibit payments of any kind intended to induce physicians or others either to purchase or arrange for or recommend the purchase of healthcare products or services, including the selection of a particular prescription drug. These laws make certain business practices that are relatively common in other industries illegal in our industry. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment to third-party payors, including Medicare and Medicaid, claims for reimbursed drugs or services that are false or fraudulent. The government has asserted very broad interpretations of these laws against pharmaceutical manufacturers, even though these manufacturers did not directly submit claims for reimbursement to government payors. In addition, regulation is not static and regulatory authorities, including the FDA, evolve in their staff, interpretations and practices and may impose more stringent requirements than currently in effect, which may adversely affect our sales and marketing efforts. Violations of the above 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. Many pharmaceutical and biotechnology companies have in recent years been the target of lawsuits and investigations alleging violations of government regulation, including claims asserting violations of the federal False Claims Act, the federal anti-kickback statute, and other violations in connection with off-label promotion of products, pricing, and government price reporting. While we will strive to comply with these complex requirements, the interpretation of these laws as applied to particular sales and marketing practices continues to evolve, and it is possible that our sales and marketing practices might be challenged. Further, although we have taken measures to prevent potential challenges, including through our corporate compliance program, we cannot guarantee that such measures will protect us from future challenges, lawsuits or investigations. Even if such challenges are without merit, they could cause adverse publicity, divert management attention and be costly to respond to, and thus could have a material adverse effect on our business, including impact on our stock price. In addition, our strategic partners and licensees are required to comply with comparably complex requirements in jurisdictions outside the United States.

In order to sell RECOTHROM to federal institutions, such as military hospitals and the Veterans Administration, we must satisfy the requirements of listing on the Federal Supply Schedule and we are required to periodically report product pricing-related information. The calculations used to generate the pricing-related information are complex. If we fail to accurately and timely report product pricing-related information or to comply with any of these or any other laws or regulations, various negative consequences could result, including criminal and/or civil prosecution, substantial criminal and/or civil penalties, exclusion of the approved product from coverage under governmental healthcare programs (including Medicare and Medicaid), costly litigation and

restatement of our financial statements. In addition, our efforts to comply with this wide range of laws and regulations are, and will continue to be, time-consuming and expensive.

Risks Related to Ownership of Our Stock

Our stock price is volatile.

The market price of our common stock may fluctuate significantly in response to many factors beyond our control, including:

- changes in the recommendations of securities analysts or changes in their financial estimates of our operating results;
- recommendations or opinions of journalists, media personalities or market commentators;
- failures in meeting performance expectations of securities analysts or investors;
- changes in the political climate and uncertainties about federal and state legislation, policies, and programs affecting health care and pharmaceuticals;
- fluctuations in the valuations of companies perceived by securities analysts or investors to be comparable to us; and
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares.

Furthermore, the stock markets have experienced significant price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. In particular, there have been high levels of volatility in the market prices of securities of biotechnology companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of our common stock.

We are at risk of securities class action litigation due to our expected stock price volatility.

In the past, shareholders have often brought securities class action litigation against a company following a decline in the market price of its securities. This risk is especially acute for us, because biotechnology companies have experienced greater than average stock price volatility in recent years, which increases the risk of substantial declines in stock price. As a result, biotechnology companies have been subject to, on average, a greater number of securities class action claims than companies in other industries. We may in the future be the target of securities class action litigation. Securities litigation could result in substantial costs, could divert management's attention and resources, and could seriously harm our business, financial condition and results of operations.

Certain of our shareholders have significant control of our management and affairs, which they could exercise against other shareholders' best interests.

Novo Nordisk, together with Warburg Pincus Equity Partners, L.P., beneficially owned an aggregate of approximately 45% of our outstanding common stock as of December 31, 2008. Representatives of these shareholders hold four out of nine seats on our board of directors pursuant to a shareholders agreement. These shareholders, acting together, have the ability to significantly influence our management and affairs and matters requiring shareholder approval, including the election of directors and approval of corporate strategy, significant corporate transactions, such as mergers, consolidations or the sale of substantially all of our assets. Consequently, these shareholders, acting together, may be able to cause a change in control, as well as delay or prevent a change in control. They may also discourage a potential acquirer from making a tender offer or otherwise attempting to effect a change in control, even if such a change in control would benefit our other shareholders.

Provisions in Washington law, our charter documents and executive employment agreements we have entered into may prevent, discourage or delay a change of control.

We are subject to the Washington anti-takeover laws regulating corporate takeovers, which, with limited exceptions, prohibit a "target corporation" from engaging in certain "significant business transactions" for a period of five years after the share acquisition by an acquiring person, unless (i) the prohibited transaction or the acquiring person's purchase of shares was approved by a majority of the members of the target corporation's board of directors prior to the acquiring person's share acquisition or (ii) the prohibited transaction was both approved by the majority of the members of the target corporation's board and authorized at a shareholder meeting by at least two thirds of the outstanding voting shares (excluding the acquiring person's shares) at or subsequent to the acquiring person's share acquisition. An "acquiring person" is defined as a person or group of persons that beneficially owns 10% or more of the voting securities of the target corporation. Such prohibited transactions include, among other things:

- certain mergers or consolidations with, dispositions of assets to, or issuances of stock to or redemptions of stock from, the acquiring person;
- termination of 5% or more of the employees of the target corporation as a result of the acquiring person's acquisition of 10% or more of the shares;
- allowing the acquiring person to receive any disproportionate benefit as a shareholder; and
- liquidating or dissolving the target corporation.

After the five-year period, certain "significant business transactions" are permitted, as long as they comply with certain "fair price" provisions of the statute or are approved by a majority of the outstanding shares other than those of which the acquiring person has beneficial ownership. A corporation may not "opt out" of this statute.

As such, these laws could prohibit or delay mergers or a change of control and may discourage attempts by other companies to acquire us.

In addition, our articles of incorporation and bylaws contain provisions, such as undesignated preferred stock and prohibitions on cumulative voting in the election of directors, which could make it more difficult for a third party to acquire us without the consent of our board of directors. Also, our articles of incorporation provide for a staggered board, removal of directors generally only for cause and certain requirements for calling special shareholder meetings. Further, our bylaws require advance notice of shareholder proposals and nominations and impose restrictions on the persons who may call special shareholder meetings. These provisions may have the effect of preventing or hindering any attempts by our shareholders to replace our current board of directors or management.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We are headquartered in Seattle, Washington, where we lease space in several buildings in close proximity to one another. We lease a total of 271,000 square feet in these buildings, as shown in the following table.

Property	Square Feet	Use	Lease Expiration Dates
Lake Union Steam Plant	106,000	Laboratories and offices	May 2019
Earl Davie Building	98,000	Laboratories, manufacturing and offices	May 2019
1144 Eastlake Building	67,000	Offices	April 2019

Effective March 2008, we consolidated the existing lease and sublease agreements for the 1144 Eastlake Building into a single lease, under which the lease term was extended to April 2019. We believe that our existing facilities, together with available, planned and potential expansion space, will be adequate to fulfill our needs for the foreseeable future.

For additional details on our headquarter lease, refer to "Note 7. Lease Obligation" under Notes to Consolidated Financial Statements.

Item 3. Legal Proceedings

None.

Item 4. Submission of Matters to a Vote of Security Holders

No matters were submitted to a vote of our shareholders during the fourth quarter of our fiscal year ended December 31, 2008.

PART II

Item 5. Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities

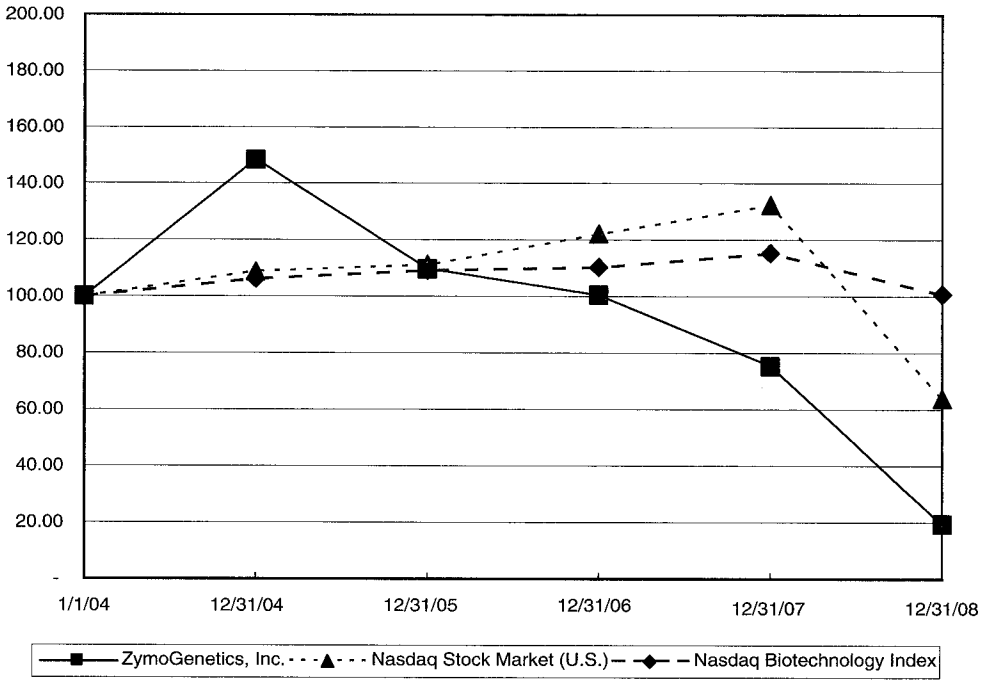
Our common stock began trading on the NASDAQ Stock Market under the symbol ZGEN on February 1, 2002. As of January 30, 2009, we had 88 shareholders of record and approximately 9,100 beneficial holders of our stock. We have never paid cash dividends and do not anticipate paying them in the foreseeable future.

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

	High	Low
Year Ended December 31, 2008		
1st Quarter	$13.05	$ 8.57
2nd Quarter	10.50	7.64
3rd Quarter	9.10	6.66
4th Quarter	6.42	2.29
Year Ended December 31, 2007		
1st Quarter	$16.32	$14.26
2nd Quarter	16.42	14.61
3rd Quarter	14.73	11.19
4th Quarter	14.85	11.67

The graph on the next page compares the cumulative total shareholder return on our common stock with the cumulative total shareholder return of the CRSP Total Return Index for The NASDAQ Stock Market (U.S. Companies) and the NASDAQ Biotechnology Index, for the period beginning January 1, 2004 and ending on December 31, 2008 (assuming the investment of $100 in our common stock and in each of the other indices on January 1, 2004 and reinvestment of all dividends).

The comparisons in the graph below are based on historical data and are not intended to forecast the possible future performance of our common stock.



	1/1/04	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08
ZymoGenetics, Inc.	$100.00	$148.39	$109.74	$100.45	$ 75.29	$ 19.35
NASDAQ Stock Market (U.S.)	100.00	108.84	111.16	122.11	132.42	63.80
NASDAQ Biotechnology Index	100.00	106.13	109.14	110.25	115.30	100.75

Item 6. Selected Financial Data

The following selected financial data should be read in conjunction with the financial statements and notes to the financial statements and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained elsewhere in this Form 10-K.

	Years Ended December 31,				
	2008	2007	2006	2005	2004
	(in thousands, except per share data)				
Statement of Operations Data:					
Revenues	$ 73,989	$ 38,477	$ 25,380	$ 42,909	$ 35,694
Costs and expenses:					
Costs of product sales	5,672	—	—	—	—
Research and development[1]	126,678	142,340	128,450	99,615	99,089
Selling, general and administrative[2]	60,238	46,890	33,224	23,321	23,500
Total costs and expenses	192,588	189,230	161,674	122,936	122,589
Loss from operations	(118,599)	(150,753)	(136,294)	(80,027)	(86,895)
Other income (expense)	2,358	2,609	6,292	2,000	(1,861)
Net loss	$(116,241)	$(148,144)	$(130,002)	$ (78,027)	$ (88,756)
Basic and diluted net loss per share	$ (1.69)	$ (2.17)	$ (1.94)	$ (1.28)	$ (1.64)
Weighted-average shares used in computing basic and diluted net loss per share	68,696	68,156	66,917	60,928	54,157
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 89,887	$ 170,941	$ 258,408	$366,311	$324,998
Working capital	75,988	118,822	239,432	343,459	297,361
Total assets	210,046	263,081	347,004	453,353	412,184
Total shareholders' equity	23,359	114,830	235,684	333,663	278,550

(1) The years ended December 31, 2008, 2007, 2006, 2005 and 2004 include noncash stock-based compensation expense of $13,572, $13,591, $12,102, $2,394 and $4,802, respectively.

(2) The years ended December 31, 2008, 2007, 2006, 2005 and 2004 include noncash stock-based compensation expense of $7,700, $7,286, $6,813, $519 and $4,493, respectively.

Statement of Financial Accounting Standards No. 123(R) *Share-Based Payment*, was adopted effective January 1, 2006.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing therapeutic protein-based products for the treatment of human diseases. The process for taking one of our discoveries to the marketplace is long, complex and very costly. It is difficult to predict the time it will take to reach the market with any given product candidate, but it would not be unusual to span ten years or more and cost hundreds of millions of dollars. It is also a business of attrition; it is expected that, for the industry as a whole, less than 20% of the drug candidates entering human clinical trials will actually make it to the marketplace. For the products that do make it, particularly for those that address previously unmet medical needs, the markets can be significant, with a number of successful products selling in excess of $1 billion per year.

In late 2006, we began preparations for the commercial launch of our first product, RECOTHROM®, which was approved by the FDA on January 17, 2008. In June 2007, we entered into a global collaboration with Bayer for development and commercialization of RECOTHROM. Bayer has agreed to commercialize RECOTHROM in countries outside the United States and will co-promote the product with us in the United States for up to four years. We have hired approximately 60 field personnel and additional headquarters-based personnel to support the commercial operations that are necessary for selling RECOTHROM. We are incurring substantial marketing costs to support the selling effort. We are also building significant levels of inventory to meet the expected demand for the product and minimize the risk of product shortages. These commercialization activities are utilizing substantial cash resources until such time as RECOTHROM sales reach a level, if ever, that will cover our related costs. We recorded net sales revenue of $8.8 million in 2008, and we anticipate significantly higher revenue generation from RECOTHROM sales over time; however, we cannot be certain of the future rate of market penetration or when, if ever, our revenues will exceed our related costs.

An important element of our business strategy is that we intend to maintain a significant share of the commercial value for certain of our products under development. As a result, we will be required to pay a significant portion of the development and commercialization costs for these products. Even if we decide to license a product candidate to another company, we will generally be required to pay research and development costs up to the point of licensing. Another important element of our strategy is that we maintain fully integrated research and development operations to enable us to discover new product candidates and advance them to the point where we can demonstrate clinical proof of concept. These operations, although critical to our long-term business strategy, are expensive to maintain and the level of output is uncertain. Substantial funding is required on an ongoing basis to maintain these operations.

Generating the funding necessary to operate our business is challenging. There are a number of potential sources of revenues and cash that we pursue in order to address our funding needs, including the following:

- sales of RECOTHROM, which were $8.8 million in 2008, net of all related discounts and allowances;
- research, development and commercialization collaborations, such as the ones we have entered into with Bayer for RECOTHROM and Bristol-Myers Squibb for PEG-Interferon lambda (PEG-IFN-λ), which provide revenues while also enabling us to reduce our ongoing research and development expenses;
- licensing of technologies or product candidates, such as atacicept and recombinant Factor XIII, to other companies, which typically provide license fees and potential milestone payments and royalties on sales;
- issuance of equity or equity-based securities;
- debt financing, such as the $100 million financing arrangement we entered into with Deerfield Management in June 2008; and
- investment income on our cash reserves.

We expect that it will be at least several years before we can generate enough product-related revenues for our company to reach net income or cash flow breakeven, and we expect to continue to invest significant amounts of cash in developing our business. We intend to pursue additional collaboration and license transactions as a means of generating additional cash and reducing our ongoing expenses. These transactions may involve our product candidate IL-21, currently in Phase 2 clinical trials, and our earlier stage candidates that have not yet begun clinical testing. In addition, we expect to continue our efforts to reduce our operating cost structure.

In addition, it is possible that we will look for opportunities to raise capital by issuing equity or equity-related securities, to help fund our company over the next several years. These opportunities may arise at any time, depending on things such as overall market conditions; dynamics in the biotechnology sector of the market; investor appetite for certain types of companies; and fundamental characteristics of our business. At other times, it may be difficult to raise capital on terms favorable to our company, if at all, especially in light of the current global economic crisis. Accordingly, we would expect to raise capital when it is available, not when there is an immediate need. We believe this strategy is important to minimize the financial risks to our company and our shareholders.

Results of Operations

Revenues

Product sales. The FDA granted marketing approval of RECOTHROM on January 17, 2008 for the 5,000 IU vial configuration and on May 27, 2008 for the 20,000 IU vial configuration, both with and without a spray kit. Sales of RECOTHROM are recognized as revenue when the product is shipped and title and risk of loss have passed. Product sales are recorded net of provisions for estimated discounts, rebates, chargebacks and returns. We recognized net product sales revenue of $8.8 million in 2008. We expect sales of RECOTHROM to increase over the next several years as we penetrate the market further.

Royalties. We earn royalties on sales of certain products subject to license agreements with other companies. Royalties decreased slightly year-to-year in 2008, 2007 and 2006 primarily due to insulin and glucagon patent expiration in most countries. Most of the effects of reduced insulin and glucagon royalties were offset by increasing minimum royalties earned on GEM 21S, a product of BioMimetic Therapeutics, Inc. Royalties are expected to be substantially less in 2009 as royalties from sales of GEM 21S decrease, due to the discontinuation of minimum royalty obligations, and the expiration of our patent related to BeneFIX, a product of Wyeth Pharmaceuticals, Inc., in December 2008.

Collaborations and licenses. We enter into various collaborative agreements that may generate significant license, option or other upfront fees with subsequent milestone payments earned upon completion of development milestones. Where we have no continuing performance obligations under an arrangement, we recognize these fees and payments as revenue when contractually due and payment is reasonably assured, as these payments represent the culmination of a separate earnings process. Where we have continuing performance obligations under an arrangement, revenue is recognized using one of two methods. Where we are able to estimate the total amount of costs we will incur under the arrangement, revenue is recognized using a proportional performance model. Costs incurred to date compared to total expected costs are used to determine proportional performance, as this is considered to be representative of the delivery of outputs under the arrangement. Revenue recognized at any point in time is limited to cash received and amounts contractually due. Changes in estimates of total expected performance are accounted for prospectively as a change in estimate. Where we cannot estimate the total amount of service that is to be provided, a time-based method is used to recognize revenue. Under the time-based method, revenue is recognized over the arrangement's estimated performance period, starting with the contract's commencement, but not before the removal of any contingencies for each milestone. Revenue recognition is determined based on the elapsed time compared to the total estimated performance period. Revenue recognized at any point in time is limited to the cash received and amounts contractually due. From period to period, license fees and milestone payments can fluctuate substantially based

on the completion of new licensing or collaborative agreements and the achievement of development-related milestones.

On August 28, 2008, we amended the Strategic Alliance Agreement with Serono S.A. (Merck Serono) and simultaneously exercised our right under the atacicept Collaborative Development and Marketing Agreement to discontinue our co-development and co-funding obligations and convert our position to an exclusive milestone and royalty bearing license. Based on these actions, our responsibility for funding atacicept product development costs ended June 1, 2008 and all significant continuing obligations under the agreements will end in October 2009. Since the agreements were negotiated in tandem, we are considering them as a single agreement for revenue recognition purposes. We have recorded our share of the collaboration expenses from January 1, 2008 to August 28, 2008 of $24.7 million as research and development expense. Additionally, as part of the amended agreements with Merck Serono, we do not have to pay for $9.8 million of development costs that were previously required to be reimbursed to Merck Serono under the prior agreements. These development costs were expensed as research and development costs in the period June 1, 2008 to August 28, 2008. The forgiveness of these expenses was determined to be consideration for the licenses granted to Merck Serono and therefore we have considered the $9.8 million to be incremental revenue which is being deferred and recognized as license fee revenue on a straight-line basis through October 2009, our remaining obligated performance period under the Strategic Alliance Agreement.

In June 2007, we entered into license and collaboration and co-promotion agreements with Bayer. The agreements provide Bayer with an exclusive license to develop and sell RECOTHROM outside of the United States and Bayer will also promote RECOTHROM in the United States for up to four years. We will record all United States product sales revenue and Bayer will be entitled to a commission on United States sales for five or six years, depending on how long they co-promote RECOTHROM in the United States. We received a $30.0 million upfront milestone payment in 2007, and $46.5 million in milestone payments in 2008, $20.0 million of which will be repaid to Bayer as United States sales bonuses under the co-promotion. We are entitled to various other milestones based on regulatory filings, regulatory approvals and annual sales thresholds achieved by Bayer outside of the United States. These milestone payments will be recorded as deferred revenue and recognized as revenue using the proportional performance model to the extent they are received during the remaining period in which we will fulfill our obligations under the agreements. We currently anticipate completing these obligations in 2013.

Collaborations and licenses revenue was $58.9 million for the year ended December 31, 2008, an increase of $26.7 million as compared to the same period in 2007. The increase primarily resulted from license fees of $21.0 million earned in October 2008 under our Ig fusion agreement with Bristol-Myers Squibb and an increase in the recognition of license fees related to our RECOTHROM agreements with Bayer. Partially offsetting this increase were milestones earned in 2007 under our IL-21 and IL-31 agreements with Novo Nordisk for which no comparable amounts were earned in 2008. Revenues from collaborations and licenses increased from $18.5 million in 2006 to $32.2 million in 2007. The increase was primarily attributable to recognition in 2007 of license fee revenue related to our RECOTHROM agreements with Bayer; milestone payment revenue from Novo Nordisk under our Factor XIII, IL-31 and IL-21 agreements; and milestone payment revenue from Merck Serono under our atacicept and FGF-18 agreements.

As of December 31, 2008, the deferred revenue related to the Merck Serono agreements and the Bayer agreement was $15.5 million and $52.3 million, respectively. We currently expect all of the remaining Merck Serono deferred revenue to be recognized in 2009.

In addition, in January 2009, we entered into a co-development/co-promotion and license agreement with Bristol-Myers Squibb for the type-3 interferon family, which includes our development candidate PEG-Interferon lambda. On February 26, 2009, the effective date, we became eligible to receive an initial license fee of $85.0 million within 10 days and will receive an additional license fee of $20.0 million in March 2009. Additionally, we expect to receive various milestone payments based on the achievement of certain objectives, including $95.0 million expected later in 2009 related to the initiation of Phase 2 clinical trials; profit sharing and

co-promotion rights in the U.S.; and may receive royalties on sales outside of the U.S. We are also eligible for sales bonuses based on world-wide sales of licensed products. We provide a license to related technology and are obligated to fund the first $100.0 million of costs for development in the U.S. and Europe, after which we will be responsible for 20% of such costs. We expect to record revenue related to the license fees and near-term milestone payments over an approximately three-year period, which corresponds to the period in which we will incur most of our costs and perform our obligations under the agreement.

Costs and expenses

Costs of product sales. Costs of product sales were $5.7 million in 2008, following approval of RECOTHROM January 2008. Prior to FDA approval of RECOTHROM, all third party manufacturing costs and an allocation of our labor and overhead associated with the manufacturing of RECOTHROM for commercial sale were expensed as research and development costs as incurred. Subsequent to approval, third party manufacturing costs and labor and overhead associated with the commercial manufacturing of RECOTHROM are recorded as inventory. Accordingly, our costs of product sales will be reduced during the time we are selling product manufactured prior to approval, which included 2008 and will include all of 2009. Costs of product sales include the inventory and distribution costs associated with RECOTHROM product revenue. Additionally, we recorded a $4.2 million charge to costs of product sales in 2008 for manufacturing costs incurred subsequent to FDA approval for product that is expected to become obsolete.

Research and development. Research and development expense has been our most significant expense to date, primarily consisting of salaries and benefit expenses, costs of consumables, contracted services and stock-based compensation. Our research and development activities have generally expanded from year-to-year, particularly related to our recently approved commercial product, RECOTHROM, and clinical stage product candidates, atacicept, IL-21 and PEG-IFN-λ. However, this trend was reversed in 2008 following the approval of RECOTHROM and a reduction in research and development headcount. In each of the past three years, research and development expense was partially offset by cost reimbursements from our collaborators for work we performed on various development programs. The breakdowns within major categories of research and development expense are shown in the following table (in thousands):

	2008	2007	2006
Salaries and benefits	$ 53,457	$ 57,731	$ 52,554
Consumables	10,907	11,658	11,093
Facility costs	8,886	8,934	8,090
Contracted services	47,391	55,668	43,552
Depreciation and amortization	4,902	5,421	5,370
Stock-based compensation	13,572	13,591	12,102
Subtotal	139,115	153,003	132,761
Cost reimbursement from collaborators	(12,437)	(10,663)	(4,311)
Net research and development expense	$126,678	$142,340	$128,450

Salaries and benefits and consumables generally track with changes in our employee base from year to year. The $4.3 million decrease in salaries and benefits in 2008 and the corresponding decrease in consumables was due to the February 2008 termination of 37 research and development employees and costs related to RECOTHROM manufacturing being included in inventory costs subsequent to the January 17, 2008 FDA approval of RECOTHROM instead of being recorded as research and development expense. The $5.2 million increase in salaries and benefits in 2007 was attributable to an increase in research and development headcount.

Contracted services include the cost of items such as contract research, contract manufacturing, clinical trials, non-clinical studies and payments to collaborators. These costs relate primarily to clinical development programs and can fluctuate substantially from period to period depending on the stage of our various programs.

Generally, these external costs increase as a program advances toward commercialization, but there can be periods between major clinical trials or manufacturing campaigns during which costs decline. Contracted services decreased by $8.3 million in 2008 due to reduced contract manufacturing costs, which decreased to $2.8 million in 2008 as compared to $22.7 million for the same period in 2007, reflecting the discontinued expensing of pre-approval manufacturing of rThrombin (RECOTHROM) bulk drug and finished product inventory after FDA approval in January 2008. This decrease was offset by other cost increases. Our clinical trial costs increased in 2008 as compared to 2007, primarily reflecting the costs incurred for the atacicept lupus nephritis clinical trial that began in late 2007. Payments to collaborators also increased for the same period primarily reflecting our portion of atacicept development costs under our collaboration with Merck Serono. In August 2008, we amended our collaboration with Merck Serono whereby Merck Serono will be responsible for all development costs associated with atacicept subsequent to August 2008. Contracted services increased by $12.1 million in 2007 due to increased contract manufacturing costs related to the manufacture of rThrombin bulk drug and finished product inventory and clinical trial material for IL-21 and atacicept. Our clinical trial costs slightly decreased in 2007, as compared to the same period in 2006, primarily reflecting the completion of rThrombin Phase 3 clinical trials prior to FDA submission in late 2006, partially offset by the increase in preparation costs associated with the atacicept lupus nephritis clinical trial.

To date, our business needs have not required us to fully allocate all research and development costs among our various programs. However, we track direct labor, contracted services and certain consumable costs by program, which we monitor to ensure appropriate utilization of our company resources. We also incur indirect costs that are not allocated to specific programs. These costs include indirect labor, certain consumable costs, facility costs and depreciation and amortization, all of which benefit all of our research and development programs. The following table presents our research and development costs allocated to clinical development, preclinical and research programs, together with the unallocated costs that benefit all programs for the periods presented (in thousands):

	2008	2007	2006	Inception To Date
Clinical development programs:				
Hemostasis	$ 18,708	$ 39,690	$ 41,938	$198,730
Autoimmunity and oncology	30,119	25,962	17,077	112,495
Antiviral	5,094	5,125	5,240	18,937
Preclinical and research programs	22,836	22,051	18,428	
Unallocated indirect costs	49,921	49,512	45,767	
Total	$126,678	$142,340	$128,450	

The following summarizes the reasons for fluctuations in research and development program costs for the three years presented in the table:

- Hemostasis clinical development program (Factor XIII and rThrombin) costs in 2006 reflected the conduct of process validation and manufacturing campaigns for rThrombin to support the filing of a license application with the FDA in late 2006. The 2007 costs included approximately $19.0 million of manufacturing costs incurred for rThrombin commercial product prior to FDA approval on January 17, 2008. Without these manufacturing-related costs, the program costs would have substantially declined, reflecting the lower level of development activities while awaiting FDA approval. The reduction in costs from 2007 to 2008 reflect the discontinued expensing of RECOTHROM manufacturing costs, which were included in inventory subsequent to FDA approval on January 17, 2008.
- Autoimmunity and oncology clinical development program (atacicept and IL-21) costs increased from 2006 to 2007 primarily due to an increase in our share of atacicept joint development costs paid to Merck Serono. Costs increased in 2008 as compared to 2007 primarily due to an increase in our share of costs related to the manufacturing of clinical material and clinical trial activity. Such increases were primarily related to evaluating atacicept for the treatment of lupus, rheumatoid arthritis and multiple

sclerosis. These costs are expected to decrease in the future due to the amended agreements with Merck Serono completed in August 2008 whereby Merck Serono is responsible for future development costs.

- Antiviral clinical development program costs have not changed significantly over the three years presented.
- Preclinical and research program costs were flat in 2008 as compared to 2007. The increase in costs from 2006 to 2007 reflected increased activity in new discovery programs.
- Unallocated indirect costs were consistent between 2008 and 2007. The increase in 2007 as compared to 2006 was primarily due to an increase in personnel-related costs.

Selling, general and administrative. Selling, general and administrative expense, which consists primarily of salaries and benefit expenses, professional fees and other corporate costs, increased 28% in 2008 as compared to 2007 and 41% in 2007 as compared to 2006. The increases were primarily due to the hiring of our sales force early in the third quarter of 2007 to support the launch and commercialization of RECOTHROM in 2008 and then the increased sales and marketing activities throughout all of 2008. An increase in legal costs also contributed to the 2007 increase.

Stock-based compensation. Effective January 1, 2006, we adopted Statement of Financial Accounting Standards No. 123(R) *Share-Based Payment*, which addresses the accounting for share-based payment transactions in which an enterprise receives employee services in exchange for (a) equity instruments of the enterprise or (b) liabilities that are based on the fair value of the enterprise's equity instruments or that may be settled by the issuance of such equity instruments. The Statement eliminated the election to account for share-based compensation transactions using APB 25 and generally requires that such transactions be accounted for using a fair-value-based method. We determine fair value using the Black-Scholes valuation method. The following amounts of stock-based compensation expense were recorded for the three years reported (in thousands):

	2008	2007	2006
Research and development expense	$13,572	$13,591	$12,102
Selling, general and administrative expense	7,700	7,286	6,813
Total	$21,272	$20,877	$18,915

Other Income (Expense)

Investment income. Investment income is generated primarily from investment of our cash reserves in investment grade, fixed-income securities. There are four primary factors affecting the amount of investment income that we report: the amount of cash reserves invested, the effective interest rate, the amount of realized gains or losses on investments held during the period and the amount of other-than-temporary impairment recorded in the period. The decrease in 2008 as compared to 2007 was primarily due to a lower average cash balance and effective interest rate, as well as realized losses on investments and an other-than-temporary loss on an investment security. The decrease in 2007 as compared to 2006 was primarily due to a lower average cash balance. The following table shows how each of these factors affected investment income for the three years reported (in thousands):

	2008	2007	2006
Weighted average amount of cash reserves	$119,939	$207,817	$308,912
Effective interest rate	3.72%	4.92%	4.55%
Investment income before gains (losses)	4,464	10,218	14,050
Net gain (loss) on investments	(231)	66	(148)
Other-than-temporary impairment loss	(400)	—	—
Investment income, as reported	$ 3,833	$ 10,284	$ 13,902

Interest expense. We have accounted for a sale-leaseback transaction completed in October 2002 as a financing transaction. Under this method of accounting, an amount equal to the net proceeds of the sale is considered a long-term interest bearing liability. Rent payments under the leases are considered to be payments toward the liability and are allocated to principal and interest. We recorded related interest expense of $7.7 million, $7.7 million and $7.6 million for the years ended December 31, 2008, 2007 and 2006, respectively. In addition, we recorded interest expense of $933,000 in 2008 related to the Deerfield financing arrangement, which represents amortization of the deferred financing costs, including the fair value of the warrants issued; 4.9% interest on the $25.0 million drawn in November 2008; and additional interest expense equal to 2% of RECOTHROM net sales in the U.S. beginning upon receipt of the $25.0 million draw.

Gain on sale of fixed assets, net. In August of 2008, we sold undeveloped land near our corporate headquarters for $11.8 million and recognized a gain of $7.0 million.

Liquidity and Capital Resources

As of December 31, 2008, we had cash, cash equivalents and short-term investments of $89.9 million, which we intend to use to fund our operations and capital expenditures. These cash reserves are held in a variety of fixed-income securities, including corporate bonds, commercial paper and money market instruments that were investment grade at the time of purchase. Subsequent to purchase, some asset-backed securities (see Note 2 of our audited financial statements) have been downgraded by the major bond rating agencies. Together with the discretionary investment manager responsible for investing our portfolio, we monitor our investments closely and, based on market conditions and our expected working capital requirements, recorded other-than-temporary impairment loss of $400,000 on one security in the third quarter of 2008. We consider all other unrealized losses totaling $1.7 million to be temporary.

In June 2008, we completed a debt financing arrangement with Deerfield Management enabling us to draw up to $100.0 million in $25.0 million increments until January 2010. In November 2008, we received our first draw of $25.0 million. Interest accrues on amounts outstanding at a rate of 4.9% per annum, compounded quarterly, and will be due, along with outstanding principal, in June 2013. Each $25.0 million draw entitles the lender to a royalty equal to 2% of RECOTHROM net sales in the U.S. The cumulative royalty will not exceed $45.0 million over the five-year term of the arrangement assuming we draw the entire $100.0 million. In addition, we issued 1.5 million in six-year warrants upon receiving the initial draw in November 2008 and will issue an additional 1.0 million warrants upon receipt of each additional draw.

We expect to fund our future operations using our existing cash resources; revenues from RECOTHROM sales; and cash generated from existing and newly established collaborations and licenses. In particular, the co-development/co-promotion and license agreement with Bristol-Myers Squibb, executed in January 2009 (see Note 15 of our audited financial statements), will provide $105.0 million of committed funding in the first quarter of 2009 and $95.0 million of contingent funding expected to be received in the second half of 2009. We believe that, together, these existing and anticipated cash resources will be sufficient to fund our operations well beyond 2009. Furthermore, we intend to pursue additional cost saving measures and opportunities to raise additional funds through new licenses and/or collaboration transactions.

If the contingent funding under the Bristol-Myers Squibb agreement is not received as expected, we might need to access funding under the Deerfield Management financing arrangement. These funds are contractually committed; however, if for some reason such funds were not available when requested, our continued operations beyond 2009 would be dependent upon the completion of new licenses, collaborations or financing transactions. If these efforts were not successful, we could be required to significantly curtail our existing operations.

Cash flows from operating activities

The amount of cash used to fund our operating activities generally tracks our net losses, with the following exceptions:

- noncash items, such as depreciation and amortization of fixed assets, amortization of deferred debt issue costs, gain or loss on sale or disposal of assets and stock-based compensation, which do not result in uses of cash;
- net realized gains and losses and accretion and amortization of discounts and premiums on short-term investments, which are reflected as sources of cash from investing activities upon maturity or sale of the respective investments;
- changes in receivables, which generally represent temporary timing differences between the recognition of certain revenues and the subsequent receipt of cash payments;
- additions to RECOTHROM inventory subsequent to the January 17, 2008 approval date which reflect the use of cash but will not be expensed until the related product is sold;
- changes in deferred revenue, which reflect the difference in timing between the receipt of cash from option fees, license fees, other upfront payments and milestone payments, and the subsequent recognition of these amounts as revenue over the period we are contractually required to provide other rights or services that represent continuing obligations; and
- changes in other assets and liabilities, which generally represent temporary timing differences between the recognition of certain expenses and their payment.

Generally, with the exception of certain noncash items, changes in deferred revenue and RECOTHROM inventory increases, we do not expect these items to generate material year-to-year fluctuations in the relationship between our net loss and the amount of net cash used in operating activities. Substantial license or upfront fees may be received upon the date we enter into new licensing or collaborative agreements and be recorded as deferred revenue. For example, we have received milestone payments from Bayer related to the RECOTHROM collaboration totaling $76.5 million as of December 31, 2008, that have been recorded as deferred revenue and are being recognized as revenue through the first quarter of 2013. For the years ended December 31, 2008 and 2007, we recognized $18.0 million and $6.2 million, respectively, of previously deferred revenue relating to Bayer and other collaborations. The timing of additional deferred revenue transactions, including from the Bristol-Myers Squibb transaction in January 2009, is expected to be irregular and, accordingly, has the potential to create fluctuations in the relationship between our net loss and the amount of cash used in operating activities.

Cash flows from investing activities

Our most significant use of cash in investing activities is for capital expenditures. We expend a certain amount each year on routine items to maintain the effectiveness of our business, e.g., to adopt newly developed technologies, expand into new functional areas, adapt our facilities to changing needs or replace obsolete assets. In addition, we have used cash at various times to purchase land and expand facilities. In August 2008, we sold land that we purchased in 2001 and 2002 for $11.8 million. Cash flows from investing activities also reflect large amounts of cash used to purchase short-term investments and receipts from the sale and maturity of short-term investments. These amounts primarily relate to shifts between cash and cash equivalents and short-term investments. Because we manage our cash usage with respect to our total cash, cash equivalents and short-term investments, we do not consider movements in these investments to be important to an understanding of our liquidity and capital resources.

Cash flows from financing activities

In 2008, we received $25.0 million from our debt financing arrangement with Deerfield and had related financing costs of $1.2 million. We can borrow up to an additional $75.0 million through January 2010 and principle and accrued interest will be due in June 2013. In addition, we periodically receive proceeds from the exercise of employee stock options.

We expect to incur substantial additional losses in the coming years as we continue to build the market for RECOTHROM and advance our pipeline candidates, such as PEG-IFN-λ. We are optimistic regarding the long-term commercial prospects for RECOTHROM; however it might be quite some time, if ever, before our RECOTHROM revenues enable us to achieve positive operating cash flow. If at any time our prospects for funding our various initiatives decline, we may decide to look for ways to reduce our ongoing investment. For instance, we might consider discontinuing our funding under existing co-development arrangements, as we did with our atacicept collaboration with Merck Serono. Further, we may establish new co-development arrangements for other product candidates to provide additional funding sources, as we did in early 2009 with our PEG-IFN-λ collaboration with Bristol-Myers Squibb. Also, we may out-license products, product candidates or certain rights related to products or product candidates that we might otherwise choose to develop and commercialize internally. Additionally, we could consider delaying or discontinuing development of product candidates to reduce the level of our related expenditures.

In the first quarter of 2009, subject to the closing of our collaboration agreement with Bristol-Myers Squibb, we expect to receive $105.0 million. We expect to receive an additional $95.0 million under the collaboration based on clinical progress expected later in 2009. Until January 2010, we have the ability to draw $75.0 million of additional funding under our Deerfield Management funding arrangement, which is repayable in 2013. We expect these funds, together with our existing cash and investments, to cover our operating requirements for at least the next two years. However, we may also seek additional funding through public or private financings, including debt or equity financings. If any of these sources of funds are not available as we currently believe they will be, we may need additional funding sooner than we expect. Similarly, poor financial results, unanticipated expenses or unanticipated opportunities that require financial commitments could give rise to additional financing requirements. However, financing may be unavailable when we need it or may not be available on acceptable terms, especially if the difficult economic conditions continue. If we raise additional funds by issuing, equity or equity-based securities (including convertible debt), the percentage ownership of our existing shareholders would be reduced, and these securities could have rights superior to those of our common stock. If we are unable to raise additional funds when we need them, we could be required to delay, scale back or eliminate expenditures for some of our development programs, or grant rights to third parties to develop and market product candidates that we would prefer to develop and market internally, with license terms that are not favorable to us.

Contractual Obligations

At December 31, 2008 we were contractually obligated to make payments as follows (in thousands):

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	4-5 Years	More than 5 Years
Building lease obligations	$100,243	$ 8,152	$17,170	$18,393	$56,528
Operating leases	31,213	2,539	5,358	5,756	17,560
Development contracts	643	643	—	—	—
RECOTHROM manufacturing contracts	94,351	38,310	21,741	9,800	24,500
Total	$226,450	$49,644	$44,269	$33,949	$98,588

The building lease obligations resulted from our 2002 sale-leaseback financing transaction and run until May 2019. In addition, we entered into a noncancelable master lease agreement in March 2008 for office and

parking space in a building near our corporate headquarters, which extended the lease term for all related leased space to April 2019. We have certain renewal provisions at our option, which are not reflected in the above table, for the building leases and the operating leases. RECOTHROM manufacturing contracts include the manufacture of rThrombin bulk drug and RECOTHROM finished product for commercial sale.

Critical Accounting Estimates

Royalty revenue

We earn royalties on several products marketed by other companies. Royalties on these products are received within 60 days after the end of each calendar quarter. We accrue estimated royalties at the end of each quarter based on historical sales data and the patent life associated with the product. Adjustments are made in the following quarter reflecting the difference between our estimates and actual reported royalties. To date, these adjustments have not been significant.

License fees, milestone payments and upfront fees

We enter into various collaborative agreements that generate significant license, option or other upfront fees with subsequent milestone payments earned upon completion of development milestones. Where we have no continuing performance obligations under an arrangement, we recognize milestone payments as revenue upon receipt, as these payments represent the culmination of a separate earnings process. Where we have continuing performance obligations under an arrangement, revenue is recognized using one of two methods. Where we are able to estimate the total amount of services under the arrangement, revenue is recognized using a proportional performance model. Costs incurred to date compared to total expected costs are used to determine proportional performance, as this is considered to be representative of the delivery of outputs under the arrangement. Revenue recognized at any point in time is limited to cash received and amounts contractually due. Changes in estimates of total expected performance are accounted prospectively as a change in estimate. Where we cannot estimate the total amount of service that is to be provided, a time-based method is used to recognize revenue. Under the time-based method, revenue is recognized over the arrangement's estimated performance period, starting with the contract's commencement, but not before the removal of any contingencies for each milestone. Revenue recognition is determined based on the elapsed time compared to the total estimated performance period. Revenue recognized at any point in time is limited to the completed portion of the non-contingent payments received or due.

Product sales returns and allowances

We sell RECOTHROM to wholesalers, who in turn sell to hospitals. Sales of RECOTHROM are recognized as revenue when the product is received by the wholesaler and title and risk of loss have passed.

Product sales are recorded net of estimated cash discounts, wholesaler fees for service, chargebacks, (collectively "gross-to-net adjustments") and returns and are recognized as a reduction in product sales revenue. Gross-to-net adjustments are based on actual amounts allowed plus estimates of the amounts yet to be claimed on previously recorded sales. These estimates take into consideration the terms of our current contracts with group purchasing organizations and wholesalers, levels of wholesaler inventory, known sales trends, historical claims experience and forecasted customer buying patterns. Amounts accrued for gross-to-net adjustments are revised when trends or significant events indicate that an adjustment is appropriate. Accrued amounts are also adjusted to reflect actual results. To date, such adjustments have not been material to our results of operations or financial position.

Accruals for estimated sales returns are recorded in the same period that the related product sales are recorded and are also recognized as reductions in product sales revenue. Returns are estimated by comparing and analyzing inventory information provided by our wholesalers, shipping information and historical return data on

a production lot basis. To date, sales returns have been insignificant and the impact of any adjustments, have not been material to our results of operations or financial position.

Inventory obsolescence

We establish provisions for obsolete and excess inventory and include it as a component of costs of product sales. The bulk drug substance form of RECOTHROM has a shelf life of five years and once placed in the vial, has a shelf life of two years. The provision for obsolete and excess inventory is evaluated for adequacy at each quarter end based on estimated future product sales, production commitments, and existing inventory levels at all stages of manufacturing.

Investment impairment

We review our available-for-sale investment impairments in accordance with the provisions of FAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities*, and related guidance issued by the Financial Accounting Standards Board (FASB) and the SEC. We determine the impairment classification of any individual security as either temporary or other-than-temporary. The differentiating factors between temporary and other-than-temporary impairments are primarily the length of the time and the extent to which the fair value has been less than cost, the financial condition and near-term prospects of the issuer and the intent and our ability to retain our investment in the issuer for a period of time sufficient to allow for any anticipated recovery in fair value. We record other-than-temporary impairments in gain (loss) on investments, net in our consolidated statements of operations and we record temporary impairments within accumulated other comprehensive (loss) income in our consolidated balance sheets.

Stock-based compensation

We have estimated the volatility of our common stock by blending historical volatility with the implied volatility of market traded options. Prior to 2008, we did not have historical trading information for our common stock for a long enough period to calculate historical volatility solely based on the trading of our common stock. Furthermore, the market for options on our common stock is illiquid and cannot be relied upon as a source of implied volatility. Accordingly, we augmented our own data with the historical volatility and implied volatility of market traded options of similar companies. The risk-free interest rate used in the option valuation model is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term of the options. We estimated the expected life of our stock options using the simplified method for determining the expected term as prescribed by the SEC's Staff Accounting Bulletin 107, *Share-based Payment* for the years 2007 and 2006. We used historical data to determine an estimate for the expected life of our stock options granted in 2008. We do not anticipate paying any cash dividends in the foreseeable future and therefore an expected dividend yield of zero is used in the option valuation model. Forfeitures are estimated at the time of grant and revised in subsequent periods if actual forfeitures differ from those estimates. Accordingly, stock-based compensation expense is recorded only for those awards that vest. All stock-based payment awards are amortized on a straight-line basis over the requisite service periods of the awards, which are generally the vesting periods.

Item 7A. Qualitative and Quantitative Disclosures About Market Risk

Until recently, our exposure to market risk has been primarily limited to interest income sensitivity, which is affected by changes in the general level of United States interest rates, particularly because the majority of our investments are in short-term debt securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. To minimize risk, we maintain our portfolio of cash, cash equivalents and short-term investments in a variety of interest-bearing instruments, which may include United States government and agency securities, high-grade United States corporate bonds, asset-backed securities, commercial paper and money market funds.

In 2008, due to deteriorating conditions in the debt markets, our exposure to market risk has increased and has impacted our investment portfolio. Overall liquidity for many debt issues has declined substantially, meaning that we may realize losses if we are required to liquidate securities upon short notice. Additionally, the credit quality of certain issues has declined substantially, causing ratings downgrades and in some cases uncertainty regarding the ability of issuers to repay principal amounts. Also, with respect to asset backed securities, overall economic conditions have generated concerns about the value of underlying assets held as collateral, and highlighted risks associated with insurance policies used to enhance the credit of the related debt issues. To date, we have not experienced defaults on any of our investment securities. We continue to monitor our investments closely and, based on market conditions, recorded an other-than-temporary impairment loss of $400,000 on one security in the third quarter of 2008. We have reviewed our investments as of December 31, 2008, and at this time do not believe that any additional other-than-temporary impairment loss is warranted.

We have no material foreign currency exposure, nor do we hold derivative financial instruments.

Item 8. Financial Statements and Supplementary Data

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors
and Shareholders of ZymoGenetics, Inc.:

In our opinion, the accompanying consolidated balance sheets and the related consolidated financial statements listed in the accompanying index present fairly, in all material respects, the financial position of ZymoGenetics, Inc. and its subsidiaries at December 31, 2008 and 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2008 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting section under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

PricewaterhouseCoopers LLP

Seattle, Washington

March 5, 2009

ZYMOGENETICS, INC.

CONSOLIDATED BALANCE SHEETS
(in thousands)

	December 31, 2008	December 31, 2007
Assets		
Current assets		
Cash and cash equivalents	$ 50,088	$ 29,237
Short-term investments	39,799	141,704
Receivables	11,249	7,237
Inventory	28,241	—
Prepaid expenses	3,579	4,604
Total current assets	132,956	182,782
Property and equipment, net	63,676	70,701
Deferred financing costs, net	6,726	—
Long-term investment	1,547	2,915
Other assets	5,141	6,683
Total assets	$ 210,046	$ 263,081
Liabilities and Shareholders' Equity		
Current liabilities		
Accounts payable	$ 8,834	$ 11,952
Accrued liabilities	13,099	22,955
Lease obligations	563	—
Deferred revenue	34,472	29,053
Total current liabilities	56,968	63,960
Lease obligations	67,366	67,044
Debt obligation	25,000	—
Deferred revenue	33,374	11,864
Other long-term liabilities	3,979	5,383
Commitments and contingencies		
Shareholders' equity		
Preferred stock, no par value, 30,000 shares authorized, no shares issued and outstanding	—	—
Common stock, no par value, 150,000 shares authorized, 68,736 and 68,528 issued and outstanding at December 31, 2008 and 2007, respectively	786,736	758,836
Non-voting common stock, no par value, 30,000 shares authorized, no shares issued and outstanding	—	—
Accumulated deficit	(762,203)	(645,962)
Accumulated other comprehensive (loss) income	(1,174)	1,956
Total shareholders' equity	23,359	114,830
Total liabilities and shareholders' equity	$ 210,046	$ 263,081

The accompanying notes are an integral part of these consolidated financial statements.

ZYMOGENETICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Year ended December 31,		
	2008	2007	2006
Revenues			
Product sales, net	$ 8,779	$ —	$ —
Royalties	6,290	6,259	6,851
Collaborations and licenses	58,920	32,218	18,529
Total revenues	73,989	38,477	25,380
Costs and expenses			
Costs of product sales	5,672	—	—
Research and development	126,678	142,340	128,450
Selling, general and administrative	60,238	46,890	33,224
Total costs and expenses	192,588	189,230	161,674
Loss from operations	(118,599)	(150,753)	(136,294)
Other income (expense)			
Investment income	3,833	10,284	13,902
Interest expense	(8,582)	(7,677)	(7,611)
Gain on sale of fixed assets, net	7,107	2	8
Other	—	—	(7)
Total other income	2,358	2,609	6,292
Net loss	$(116,241)	$(148,144)	$(130,002)
Basic and diluted net loss per share	$ (1.69)	$ (2.17)	$ (1.94)
Weighted-average number of shares used in computing net loss per share	68,696	68,156	66,917

The accompanying notes are an integral part of these consolidated financial statements.

ZYMOGENETICS, INC.

CONSOLIDATED STATEMENT OF CHANGES IN SHAREHOLDERS' EQUITY
(in thousands)

	Common stock		Accumulated deficit	Accumulated other comprehensive income (loss)	Total
	Shares	Amount			
Balance at January 1, 2006	65,935	$702,957	$(367,816)	$(1,478)	$ 333,663
Comprehensive loss:					
Net loss	—	—	(130,002)	—	(130,002)
Unrealized gain on short-term investment	—	—	—	853	853
Unrealized gain on long-term investments	—	—	—	1,213	1,213
Total comprehensive loss					(127,936)
Common stock issued in connection with stock option exercises	1,564	11,009	—	—	11,009
Stock-based compensation expense	—	18,948	—	—	18,948
Balance at December 31, 2006	67,499	732,914	(497,818)	588	235,684
Comprehensive loss:					
Net loss	—	—	(148,144)	—	(148,144)
Unrealized gain on short-term investment	—	—	—	667	667
Unrealized gain on long-term investments	—	—	—	701	701
Total comprehensive loss					(146,776)
Common stock issued in connection with stock option exercises	1,029	5,045	—	—	5,045
Stock-based compensation expense	—	20,877	—	—	20,877
Balance at December 31, 2007	68,528	$758,836	$(645,962)	$ 1,956	$ 114,830
Comprehensive loss:					
Net loss	—	—	(116,241)	—	(116,241)
Unrealized loss on short-term investment	—	—	—	(1,763)	(1,763)
Unrealized loss on long-term investments	—	—	—	(1,367)	(1,367)
Total comprehensive loss					(119,371)
Common stock issued in connection with stock option exercises	151	454	—	—	454
Common stock issued in connection with stock awards	57	746	—	—	746
Warrants issued in connection with financing arrangement	—	6,174	—	—	6,174
Stock-based compensation expense	—	20,526	—	—	20,526
Balance at December 31, 2008	68,736	$786,736	$(762,203)	$(1,174)	$ 23,359

The accompanying notes are an integral part of these consolidated financial statements.

ZYMOGENETICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2008	2007	2006
Operating activities			
Net loss	$(116,241)	$(148,144)	$(130,002)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	7,173	7,221	6,740
Amortization of debt issuance costs	673	—	—
Stock-based compensation	21,272	20,877	18,915
Inventory impairment	4,150	—	—
Net gain on disposition of property and equipment	(7,107)	(2)	(8)
Net realized loss (gain) on sale of short-term investments	231	(66)	148
Impairment loss on short-term investments	400	—	—
Net amortization (accretion) of premium (discount) on short-term investments	204	(769)	(654)
Changes in operating assets and liabilities			
Receivables	(4,012)	(1,980)	(154)
Inventory	(32,391)	—	—
Prepaid expenses	1,025	(879)	56
Other assets	1,542	(750)	(504)
Accounts payable	(3,118)	4,054	4,148
Accrued liabilities	(9,856)	8,833	2,211
Lease obligations	885	(43)	333
Deferred revenue	26,929	23,398	(15,479)
Other long-term liabilities	(1,404)	749	504
Net cash used in operating activities	(109,645)	(87,501)	(113,746)
Investing activities			
Purchases of property and equipment	(4,802)	(6,442)	(6,525)
Purchases of short-term investments	(63,397)	(171,094)	(238,562)
Proceeds from sale of property and equipment	11,761	3	—
Proceeds from sale and maturity of short-term investments	162,704	283,649	231,079
Net cash provided by (used in) investing activities	106,266	106,116	(14,008)
Financing activities			
Proceeds from debt financing	25,000	—	—
Proceeds from exercise of stock options	454	5,045	11,009
Debt financing costs	(1,224)	—	—
Net cash provided by financing activities	24,230	5,045	11,009
Net increase (decrease) in cash and cash equivalents	20,851	23,660	(116,745)
Cash and cash equivalents at beginning of period	29,237	5,577	122,322
Cash and cash equivalents at end of period	$ 50,088	$ 29,237	$ 5,577
Supplemental disclosures			
Cash paid for interest	$ 7,721	$ 7,677	$ 7,611
Warrants issued in connection with the Deerfield financing arrangement	$ 6,174	$ —	$ —

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and summary of significant accounting policies

Nature of operations

ZymoGenetics, Inc. (the Company) was incorporated in the state of Washington in June 1981 and operated independently until it was acquired in 1988 by Novo Nordisk North America, a wholly owned subsidiary of Novo Nordisk A/S (Novo Nordisk). In November 2000, the Company became independent from Novo Nordisk upon completion of a private placement of Series B mandatorily redeemable convertible preferred stock with an investor consortium. In February 2002, the Company completed an initial public offering of common stock; at which time all Series A and B mandatorily redeemable convertible preferred stock was converted to common stock. Through this and other subsequent stock offerings and stock option exercises, Novo Nordisk's ownership percentage has been reduced to approximately 30% at December 31, 2008.

The Company is focused on the discovery, development and commercialization of protein therapeutics for the treatment of significant human diseases. The Company has generated a pipeline of proprietary product candidates and intends to commercialize them through internal development, collaborations with biopharmaceutical partners or out-licensing of patents. The first of these products, RECOTHROM®, was approved by the U.S. Food and Drug Administration in January 2008.

The Company expects to fund its future operations using its existing cash resources; revenues from RECOTHROM sales; and cash generated from existing and newly established collaborations and licenses. In particular, the co-development/co-promotion and license agreement with Bristol-Myers Squibb, executed in January 2009 (see Note 15), will provide the Company with $105.0 million in March 2009 and $95.0 million of contingent funding is expected to be received in the second half of 2009. The Company believes that, together, these existing and anticipated cash resources will be sufficient to fund its operations well beyond 2009. In addition, the Company has $75.0 million contractually available under a financing arrangement with Deerfield Management that can be drawn at any time until January 2010 (see Note 8). Furthermore, the Company intends to pursue additional cost saving measures and opportunities to raise additional funds through new licenses and/or collaboration transactions.

If the funding under the Bristol-Myers Squibb agreement is not received as expected, the Company would need to access funding under the Deerfield Management financing arrangement. These funds are contractually committed; however, if for some reason such funds were not available when requested, the Company's continued operations in 2009 and beyond would be dependent upon the completion of new licenses, collaborations or financing transactions. If these efforts were not successful, the Company could be required to significantly curtail its existing operations.

Use of estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities; disclosure of contingent assets and liabilities at the date of the financial statements; and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and cash equivalents

The Company considers all highly liquid investments with a contractual maturity at date of purchase of three months or less to be cash and cash equivalents. The Company invests its cash and cash equivalents with major financial institutions, the amount of which generally exceeds federally insured limits. The Company has not experienced any losses on its cash and cash equivalents.

Short-term and long-term investments

Short-term investments

Short-term investments are classified as available-for-sale. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported as a separate component of shareholders' equity. Interest on securities classified as available-for-sale is included in investment income. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to expected maturity. For investments in asset-backed securities, amortization of premiums and accretion of discounts are recognized in interest income using the interest method, adjusted for anticipated prepayments, as applicable. Estimates of expected cash flows are updated periodically and changes are recognized in the calculated effective yield prospectively. Amortization of premiums and accretion of discounts are included in investment income. Realized gains and losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in investment income. The cost of securities sold is based on the specific identification method.

Long-term investments

Included in other assets is a long-term investment in common shares of BioMimetic Therapeutics, Inc., a company that licensed certain technologies from the Company and made certain payments in shares of common stock. These shares are publicly traded and are adjusted to fair value, with the unrealized gain reported as a separate component of shareholders' equity. As of December 31, 2008 and 2007, the unrealized gain on the investment was $547,000 and $1.9 million, respectively.

Fair value of financial instruments

The carrying values of cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate their respective fair values due to their relative short maturities. The carrying values of certain other assets and corresponding other long-term liabilities relate to the Company's deferred compensation plan and are adjusted to market value at the end of each quarterly reporting period.

Effective January 1, 2008, the Company adopted Financial Accounting Standards Board (FASB) Statement No. 157, *Fair Value Measurements* (FAS 157). FAS 157 establishes that fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date (exit price) and establishes a fair value hierarchy based on the inputs used to measure fair value. The three levels of the fair value hierarchy defined by FAS 157 are as follows:

- Level 1 – Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities (for example, exchange quoted prices);
- Level 2 – Observable inputs, other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not sufficiently active to qualify as Level 1, other observable inputs or inputs that can be corroborated by observable market data for substantially the full term of the assets or liabilities; and
- Level 3 – Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

As required by FAS 157, financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement requires judgment and may affect the valuation of fair value assets and liabilities and their placement within the fair value hierarchy levels.

FASB Statement No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities,* (FAS 159), became effective on January 1, 2008. FAS 159 permits an instrument by instrument irrevocable election to account for selected financial assets and financial liabilities at fair value. The Company has not elected to apply the fair value option to any eligible financial assets or financial liabilities in 2008.

Inventory

Inventory is stated at the lower of cost or market. Cost includes amounts related to materials, labor and overhead, and is determined on a specific identification basis in a manner which approximates the first-in, first-out (FIFO) method. Prior to FDA approval of RECOTHROM®, recombinant thrombin on January 17, 2008, all manufacturing related costs were expensed as research and development.

Property and equipment

Property and equipment are stated at cost. Additions, betterments and improvements are capitalized and depreciated. When assets are retired or otherwise disposed of, the cost of the assets and related depreciation is eliminated from the accounts and any resulting gain or loss is reflected in the consolidated statements of operations. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which include five years for furniture and lab equipment, ten years for pilot plant equipment and 40 years for buildings. Expenditures for repairs and maintenance are charged to expense as incurred.

Leasehold improvements are amortized ratably over their estimated useful lives or the remaining term of the lease, whichever is shorter. At December 31, 2008, the Company is amortizing its leasehold improvements over periods ranging from 10 to 17 years.

Impairment of long-lived assets

The Company assesses the impairment of long-lived assets whenever events or changes in business circumstances indicate that the carrying amounts of the assets may not be fully recoverable. Measurement of an impairment is required when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. The amount of a recognized impairment loss is the excess of an asset's carrying value over its fair value. The Company has not recognized any impairment losses of long-lived assets in 2008, 2007 or 2006.

Revenue recognition

The Company recognizes collaborative and license revenue in accordance with Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements*, as amended by Staff Accounting Bulletin No. 104, *Revenue Recognition*, and Emerging Issues Task Force Issue No. 00-21, *Revenue Agreements with Multiple Deliverables*. Revenue is recognized only when evidence of an agreement exists, terms are fixed and determinable, delivery has occurred and collection is probable.

Product sales

Sales of RECOTHROM are recognized as revenue when the product is shipped and title and risk of loss have passed. Product sales are recorded net of provisions for estimated discounts, rebates, chargebacks and returns.

Royalties

The Company earns royalties on certain products marketed by other companies. Royalties on these products are received within 60 days after the end of each calendar quarter. The Company accrues estimated royalties at

the end of each quarter based on historical sales data and the patent life associated with the product. Adjustments are made in the following quarter reflecting the differences between the Company's estimates and actual reported royalties and, to date, adjustments have not been significant.

Collaborations and licenses

The Company enters into various collaborative agreements that generate significant upfront fees with subsequent milestone payments earned upon completion of development milestones. Where the Company has no continuing performance obligations under an arrangement, the Company recognizes milestone payments as revenue upon achievement of the milestone event, as this represents the culmination of a separate earnings process. Where the Company has continuing performance obligations under an arrangement, revenue is recognized using one of two methods. Where the Company is able to estimate the total amount of services under the arrangement, revenue is recognized using a proportional performance model. Costs incurred to date compared to total expected costs are used to determine proportional performance, as this is considered to be representative of the delivery of outputs under the arrangement. Revenue recognized at any point in time is limited to cash received and amounts contractually due. Changes in estimates of total expected performance are accounted for prospectively as a change in estimate. Where the Company cannot estimate the total amount of service that is to be provided, a time-based method is used to recognize revenue. Under the time-based method, revenue is recognized over the arrangement's estimated performance period, starting with the contract's commencement, but not before the removal of any contingencies for each milestone. Revenue recognition is determined based on the elapsed time compared to the total estimated performance period, and at any point in time is limited to the non-contingent payments received or due.

Deferred revenue arises from payments received in advance of the culmination of the earnings process. Deferred revenue expected to be recognized within the next twelve months is classified as a current liability. Deferred revenue will be recognized as revenue in future periods when the applicable revenue recognition criteria have been met.

Cost of product sales

Prior to FDA approval, all third party manufacturing costs and an allocation of Company labor and overhead associated with the manufacturing of RECOTHROM for commercial sale were expensed as research and development costs as incurred. Subsequent to RECOTHROM approval, these costs are recorded as inventory. Costs of product sales includes the inventory and distribution costs associated with RECOTHROM product sales and costs incurred subsequent to FDA approval for product that is not expected to be sold.

Research and development costs

Research and development costs, consisting of salaries and benefits, costs of consumables, facility costs, contracted services and stock-based compensation, are expensed as incurred. Costs to acquire technologies that are utilized in research and development and that have no future use are expensed when incurred. Reimbursement for shared research and development expenses received from collaboration partners are recorded as reductions to research and development expenses.

Patent costs

Costs relating to filing, pursuing and defending patent applications are expensed to selling, general and administrative costs as incurred.

Income taxes

The Company records a provision for income taxes in accordance with Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes*, which requires the liability method of accounting for income taxes. Deferred tax assets or liabilities are recorded for all temporary differences between financial and tax reporting. Deferred tax expense or benefit results from the net change during the period of the deferred tax assets and liabilities. A valuation allowance is recorded when it is more likely than not that the deferred tax asset will not be realized.

Stock-based compensation

Effective January 1, 2006, the Company adopted Statement of Financial Accounting Standards No. 123(R), *Share-Based Payment*, (FAS 123(R)), that addresses the accounting for share-based payment transactions in which an enterprise receives employee services in exchange for (a) equity instruments of the enterprise or (b) liabilities that are based on the fair value of the enterprise's equity instruments or that may be settled by the issuance of such equity instruments. Fair value is determined using the Black-Scholes valuation method.

The Company uses the straight-line method of allocating the fair value of compensation expense over the requisite service period of the related award under FAS 123(R). As required by FAS 123(R), the Company estimates expected forfeitures and recognizes only the compensation cost for those stock options expected to vest.

The Company recorded the following amounts of stock-based compensation expense for the years ended December 31 (in thousands):

	2008	2007	2006
Research and development expense	$13,572	$13,591	$12,102
Selling, general and administrative expense	7,700	7,286	6,813
Total	$21,272	$20,877	$18,915

Comprehensive income or loss

Comprehensive income or loss is the change in shareholders' equity resulting from net income or loss and unrealized gains and losses on short-term and long-term investments. Amounts are reclassified from other comprehensive income into results of operations to the extent unrealized gains and losses become realized.

Segments

Statement of Financial Accounting Standards No. 131, *Disclosures about Segments of an Enterprise and Related Information*, establishes standards for the way public business enterprises report information about operating segments in annual financial statements and requires that those enterprises report selected information about operating segments in interim financial reports. The Company manages and evaluates its operations in one reportable segment.

Guarantees

In the normal course of business, the Company indemnifies other parties, including healthcare providers, wholesalers, collaboration partners, lessors and parties to other transactions with the Company, with respect to

certain matters. The Company has agreed to hold the parties harmless against losses arising from a breach of representations and covenants, or out of intellectual property infringement or other claims made against these parties. These agreements may limit the time within which an indemnification claim can be made and the amount of the claim. It is not possible to determine the maximum potential obligation under these indemnification agreements since any claim would be based on the facts and circumstances of the claim and the particular provisions of each agreement.

Concentration of Risks

The Company's cash and cash equivalents are invested with financial institutions in deposits that generally may exceed federally insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents. Management believes that the institutions are financially sound and, accordingly, that minimal credit risk exists.

The Company is subject to credit risk from its accounts receivable related to product sales, and periodically assesses the financial strength of its customers and establishes allowances for anticipated losses, when necessary. Three wholesalers accounted for approximately 91% of U.S. sales in 2008. The Company believes that if these wholesalers ceased distributing RECOTHROM, other wholesalers already distributing RECOTHROM would absorb the incremental sales volume with minimal interruption to the Company's business or the Company would sell directly to hospitals.

The Company is dependent on a single contract manufacturer for each step of its manufacturing process, and some of the key components in the Company's products come from single or limited sources of supply.

Loss per share

Basic and diluted net loss per share have been computed based on net loss and the weighted-average number of common shares outstanding during the applicable period. The Company has excluded options to purchase common stock, restricted stock units and warrants to purchase common stock, as such potential shares are antidilutive for all periods presented.

The following table presents the calculation of basic and diluted net loss per share for years ended December 31 (in thousands, except per share data):

	2008	2007	2006
Net loss	$(116,241)	$(148,144)	$(130,002)
Weighted-average shares used in computing basic and diluted net loss per share	68,696	68,156	66,917
Basic and diluted net loss per share	$ (1.69)	$ (2.17)	$ (1.94)
Securities not included in net loss per share calculation:			
Options to purchase common stock	14,385	12,702	11,982
Restricted stock units	583	—	—
Warrants to purchase common stock	1,500	—	—

Recent accounting pronouncements

In November 2007, the EITF reached a final consensus on EITF Issue No. 07-1, *Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property* (EITF 07-1). EITF 07-1 will require the Company to disclose the nature and purpose of its collaborative arrangements in its annual financial statements, its rights and obligations under the collaborative arrangements, the stage of the underlying endeavors' life cycle, the Company's accounting policies for the arrangements and the income statement classification and amount of significant financial statement amounts related to the collaborative arrangements. EITF 07-1 will be effective for the Company's 2009 financial statements and will require retrospective application as a change in accounting principle to all prior periods for all collaborative arrangements existing on January 1, 2009. The Company has determined that the implementation of EITF 07-01 will result in increased revenues and operating costs but will have no impact on results of operations, cash flows or financial condition.

In February 2008, the FASB issued FASB Statement No. 157-2, *Effective Date of FASB Statement No. 157*, which delays the effective date of FAS 157 for all non-financial assets and non-financial liabilities, except those that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually), until fiscal years beginning after November 15, 2008, and interim periods within those fiscal years. These non-financial items include assets and liabilities such as reporting units measured at fair value in a goodwill impairment test and non-financial assets acquired and liabilities assumed in a business combination. Effective January 1, 2008, the Company adopted FAS 157 for financial assets and liabilities recognized at fair value on a recurring basis. The partial adoption of FAS 157 for financial assets and liabilities did not have a material impact on the Company's results of operations, cash flows or financial condition. See Note 2 for information and related disclosures regarding fair value measurements. The Company does not expect the adoption of FAS 157 as it pertains to non-financial assets and liabilities to have a material impact on its results of operations, cash flows or financial condition.

2. Short-term investments

Short-term investments consisted of the following (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
December 31, 2008				
Type of security:				
Corporate debt securities	$ 7,749	$ 4	$ (123)	$ 7,630
Asset-backed securities	24,804	—	(1,760)	23,044
U.S. government and agency securities	8,967	158	—	9,125
	$ 41,520	$162	$(1,883)	$ 39,799
Contractual maturity date:				
Less than one year	$ 16,765			$ 16,805
Due in 1-5 years	13,724			13,195
Due in 5-10 years	—			—
Due in 10 years or more	11,031			9,799
	$ 41,520			$ 39,799
December 31, 2007				
Type of security:				
Corporate debt securities	$ 34,582	$ 80	$ (207)	$ 34,455
Asset-backed securities	77,114	221	(277)	77,058
U.S. government and agency securities	29,966	225	—	30,191
	$141,662	$526	$ (484)	$141,704
Contractual maturity date:				
Less than one year	$ 27,620			$ 27,499
Due in 1-5 years	96,323			96,600
Due in 5-10 years	4,255			4,294
Due in 10 years or more	13,464			13,311
	$141,662			$141,704

As of December 31, 2008, the weighted average expected maturity dates for all securities did not exceed three years.

In assessing potential impairment of its short-term investments, the Company evaluates the impact of interest rates, quality of assets underlying asset backed securities, changes in credit quality, the length of time and extent to which the market value has been less than cost and the Company's intent and ability to retain the security to allow for an anticipated recovery in fair value. In 2008, the Company recorded an other-than-temporary impairment loss of $400,000 on one of its asset-backed security investments.

The Company's management has concluded that besides the $400,000 of other-than-temporary impairment recorded in 2008, the unrealized losses are temporary and the Company has the ability and intent to hold the investments until all of the cost of the investments is recovered. For the years ended December 31, 2008 and 2007, the weighted average expected maturity dates for all securities did not exceed three years.

At December 31, 2008, the aggregate estimated fair value of the investments with unrealized losses was as follows (in thousands):

	Fair Value	Unrealized Loss
Corporate debt securities	$ 6,399	$ (123)
Asset-backed securities	23,044	(1,760)
U.S. government and agency securities	—	—
	$29,443	$(1,883)

Unrealized loss positions for which other-than-temporary impairments have not been recognized at December 31, 2008, are summarized as follows (in thousands):

	Fair Value	Unrealized Loss
Less than one year	$ 6,449	$ (123)
Greater than one year	22,994	(1,760)
	$29,443	$(1,883)

Realized gains were $521,000, $379,000 and $115,000 for the years ended December 31, 2008, 2007 and 2006, respectively. Realized losses were $752,000, $313,000 and $263,000 for the years ended December 31, 2008, 2007 and 2006, respectively. Reclassification adjustments reflected in other comprehensive income for net realized losses were $209,000, $159,000 and $146,000 for the years ended December 31, 2008, 2007 and 2006, respectively. The Company recorded an other-than-temporary impairment of $400,000 in 2008.

Fair value measurements

The Company's short-term and long-term investments accounted for at fair value as of December 31, 2008 are summarized below (in thousands):

	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$30,057	$ —	$—	$30,057
Short-term investments:				
Corporate debt securities	$ —	$ 6,876	$—	$ 6,876
Asset-backed securities	—	23,797	—	23,797
U.S. government and agency securities	6,047	3,079	—	9,126
	$ 6,047	$33,752	$—	$39,799
Long-term investment:				
BMTI common stock	$ 1,547	$ —	$—	$ 1,547

3. Inventory

Inventory balances reflect the cost of post-approval manufacturing activities for RECOTHROM. The manufacturing of RECOTHROM requires multiple steps which are performed by a series of single source third party contractors based upon the Company's specifications. As protection against product shortages, the

Company maintains safety stocks of inventory at each stage in the manufacturing process. The Company reduces inventory to its estimated net realizable value by reserving for excess and obsolete inventories based on forecasted demand. Inventories have been reduced by $4.2 million during 2008 for such reserves.

Inventory consisted of the following at December 31, 2008 (in thousands):

Raw materials	$ 1,664
Work in process	25,751
Finished goods	826
Total	$28,241

4. Property and equipment

Property and equipment consisted of the following at December 31 (in thousands):

	2008	2007
Land and buildings	$ 71,055	$ 75,435
Leasehold improvements	3,005	2,885
Furniture and equipment	55,351	53,515
	129,411	131,835
Less: Accumulated depreciation and amortization	(65,735)	(61,134)
	$ 63,676	$ 70,701

Land and buildings include assets deemed owned in connection with the sale and leaseback financing transaction described in Note 7.

5. Sale of land

In August 2008, the Company sold land located near its corporate headquarters for $11.8 million and recognized a gain of $7.1 million. The gain is included in other income (expense) on the consolidated statement of operations as gain on sale of fixed assets, net.

6. Accrued liabilities

Accrued liabilities consisted of the following at December 31 (in thousands):

	2008	2007
Incentive compensation	$ 4,315	$ 5,586
Vacation pay	4,043	3,914
Contract services	1,567	12,653
Sales discounts and allowances	1,436	—
Other	1,738	802
	$13,099	$22,955

7. Lease obligation

In October 2002, the Company completed a sale and leaseback transaction involving its headquarter buildings located in Seattle, Washington. The three buildings were sold for a total sale price of $52.3 million. Net proceeds from the transaction amounted to $50.5 million. Simultaneously, the Company agreed to lease the buildings from the purchaser for a period of 15 years, subject to four five-year renewal options. The initial rental payment of $5.1 million per year increases by 3.5% each year during the term. Rent for the renewal terms under these lease agreements will be the greater of fair market value or 90% of the rent for the last year prior to renewal. The Company has provided the lessor a security deposit in the form of pledged securities equal to two months base rent or $1.4 million.

The Company has accounted for the transaction as a financing due to a technical provision within the leases related to condemnation, which could, under remote circumstances, result in continuing ownership involvement by the Company in the three buildings. Under this method of accounting, the net proceeds of the sale are considered to be a long-term interest bearing liability. Rent payments under the leases are considered to be payments toward the liability and are allocated to principal and interest. The Company initially recorded a liability of $50.5 million with an effective annual interest rate of approximately 11%.

In 2003, the Company exercised its option to expand one of the leased buildings and, effective May 2004, the Company assumed occupancy of the new space. The Company incurred total project costs of approximately $21.0 million excluding equipment and received an advance from the landlord of $14.9 million. The advance from the landlord of $14.9 million was included as an addition to the long-term lease obligation with an annual effective interest rate of approximately 12%. At the end of the lease term, the remaining balance of the liability will approximate the net book value of the buildings leased. Upon the completion of the expansion project, the lease terms for all three buildings were reset to 15 years from the date of occupancy of the expansion space.

The Company is required to develop certain space within the expanded facility by June 2011. If this requirement is not satisfied, the Company must post a $1.0 million letter of credit (LOC) made available to the landlord until the lease specifications have been met. If the Company does not develop the space within specification by the end of the 15-year lease term, the landlord will have the right to draw down the full amount of the LOC in satisfaction of this obligation.

The following table presents the Company's scheduled payments under the lease obligation. In addition, the Company has certain renewal provisions at its option, which are not reflected in the table.

Year ending December 31,	
2009	$ 8,152
2010	8,437
2011	8,733
2012	9,038
2013	9,355
Thereafter	56,528
	$100,243

8. Debt financing

In June 2008, the Company entered into a financing arrangement with Deerfield Management (Deerfield), whereby the Company can borrow up to $100.0 million in four draws of $25.0 million each until January 2010.

Interest will accrue on amounts outstanding at a rate of 4.9% per annum, compounded quarterly, and will be due, along with outstanding principal, in June 2013. Each $25.0 million draw entitles Deerfield to a royalty equal to 2% of RECOTHROM net sales in the U.S. The cumulative royalty will not exceed $45.0 million assuming the Company draws the entire $100.0 million. The cumulative limit on royalties will be lower if the Company borrows less than $100.0 million. In addition, the Company agreed to issue Deerfield warrants to purchase 1.5 million shares of common stock at $10.34 per share at the earlier of the first draw or January 2010, and warrants to purchase 1.0 million shares each upon the second, third and fourth draws exercisable at a 25% premium to the average sale price of the Company's common stock for the 15 trading days prior to the draw. All warrants will have a six-year term and the Company is obligated to register with the SEC the common stock issuable under the warrants. The Company can repay borrowed amounts in whole or in part at any time, without penalty, and all associated interest and royalty obligations will cease.

In November 2008, the Company borrowed the first $25.0 million under the Deerfield financing arrangement and issued the related 1.5 million warrants. The Company has calculated the fair value of the initial 1.5 million warrants to be $6.2 million using the Black Scholes option pricing model with the following assumptions: expected volatility of 55.2%; expected dividend yield of 0.0%; risk free rate of 3.5%; and a contractual life of six years. The amount was recorded as deferred financing costs and warrants, a component of common stock.

Deferred financing costs, consisting of a $1.0 million loan issuance fee paid to Deerfield, $299,000 of other costs associated with the transaction, and the $6.2 million fair value of the initial 1.5 million warrants, will be amortized to interest expense through June 2013.

9. Related party transactions

Novo Nordisk owned approximately 30% and 31% of the Company's outstanding common stock at December 31, 2008 and 2007, respectively. The following table summarizes revenue earned from Novo Nordisk for the periods presented (in thousands):

	2008	2007	2006
Royalties	$ 290	$ 1,261	$ 2,614
Collaborations and licenses			
Option and license agreement			
Option fees	—	—	6,472
IL-20	2,000	1,000	2,000
IL-21	—	3,500	—
IL-31	—	1,000	—
Other	30	1,183	104
Factor XIII	5,000	6,820	3,750
Total	$7,320	$14,764	$14,940

Royalties

The Company earned royalties on two products marketed and sold by Novo Nordisk, recombinant insulin and recombinant glucagon. These royalties ceased in 2008 due to patent expiration.

Collaborations and Licenses

Option and license agreement

In 2000, Novo Nordisk entered into an option and license agreement which, including extensions, expired in November 2006. Under the terms of the agreement, Novo Nordisk made annual payments to the Company and was responsible for all development activities. Novo Nordisk is also obligated to make payments upon the achievement of predefined development milestones and to pay royalties on sales of resulting products. During the term of the agreement, Novo Nordisk licensed seven proteins, of which four have been subsequently terminated. In 2006, the Company recognized $6.5 million related to this agreement.

IL-20

Pursuant to the option and license agreement and subsequent supplemental agreements and amendments, Novo Nordisk licensed the world-wide rights to IL-20. Milestone payments of $2.0 million, $1.0 million and $2.0 million were earned and recognized as revenue for the years 2008, 2007 and 2006, respectively as the Company has no continuing performance obligations.

IL-21

Under the option and license agreement, Novo Nordisk has licensed the rights to IL-21 in territories outside of North America. No material payments were received or revenue recognized in 2008 and 2006 related to development milestones or royalties under this license. In 2007, the Company received a milestone payment of $3.5 million and recognized the payment as revenue as the Company had no other significant rights or obligations under this agreement.

In January 2007, the parties entered into a manufacturing agreement whereby Novo Nordisk agreed to supply IL-21 clinical materials to the Company. The Company can terminate the manufacturing agreement at any time. During 2007, the Company incurred costs of $760,000 for the supply of clinical materials.

In January 2009, Novo Nordisk and the Company restructured their relationship as it relates to IL-21. As a result of the restructuring, the Company has world-wide development and commercialization rights to the IL-21 protein and will be obligated to pay Novo Nordisk milestone payments based on approval of any IL-21 protein derived products and pay royalties on any sales and third party license fees above a certain threshold. In addition, the IL-21 manufacturing agreement was terminated. Novo Nordisk maintained the rights to develop other embodiments of IL-21, including antibodies to IL-21, outside of North America and will be obligated to pay the Company milestones and royalties on any products developed.

Other

During 2008, 2007 and 2006 the Company had various additional license agreements in place with Novo Nordisk pursuant to the option and licensing agreement. Under these agreements, the Company had no continuing performance obligations and recognized revenue when contractually due.

Factor XIII

In 2004, the Company entered into a license agreement with Novo Nordisk, with respect to recombinant Factor XIII. The license agreement provides that Novo Nordisk will develop and commercialize recombinant Factor XIII on a worldwide basis. The Company received $15.0 million upon signing of the agreement plus potential milestones and royalties. The initial $15.0 million payment was recognized over twenty months (the

period under which the Company had continuing obligations under the license agreement) beginning in 2004, with the Company recognizing related revenue of $3.8 million in 2006. The Company was scheduled to receive milestone payments in 2006 totaling $6.8 million upon the passage of time or the completion of certain defined events performed by Novo Nordisk. In 2006, Novo Nordisk asserted that, under the terms of the license agreement, the milestone dates should be extended due to circumstances beyond its control. The Company disagreed with Novo Nordisk's assertion but did not record the disputed revenue in 2006 as an agreement had not been reached. In December 2007, the Company and Novo Nordisk reached agreement on the dispute and the Company received $6.8 million and recorded the amount as revenue as all revenue recognition criteria had been met. In 2008, the Company received $5.0 million of milestone payments related to Novo Nordisk's achievement of certain manufacturing objectives. The entire amount was recognized as revenue since the Company does not have any significant remaining performance obligations.

Amounts receivable from Novo Nordisk were approximately $40,000 and $100,000 at December 31, 2008 and 2007, respectively.

10. Collaboration and License Agreements

Merck Serono

In August 2001, the Company entered into a Collaborative Development and Marketing Agreement with Merck Serono S.A (Merck Serono) for atacicept whereby the companies shared research and development expenses. In September 2004, the Company entered into a Strategic Alliance Agreement with Merck Serono, providing for a strategic research, development and commercialization alliance that expires in October 2009. Additionally, in a series of related transactions, the Company entered into four other product-related agreements pursuant to which it received upfront fees and potential milestones and royalties.

Effective August 28, 2008, the Company and Merck Serono modified these agreements as follows:

- the Collaborative Development and Marketing Agreement for atacicept was amended and converted to an exclusive world-wide license whereby the Company's responsibility for funding development costs ended and Merck Serono will pay the Company milestone fees and royalties on worldwide net sales.
- the Strategic Alliance Agreement was amended, eliminating the future co-development of product candidates jointly researched and establishing a mechanism by which each company would have alternating options to obtain exclusive rights to such product candidates.
- the existing co-development and co-commercialization agreements were amended, providing Merck Serono with an exclusive license and all rights to IL-17RC and the Company with an exclusive license and all rights to IL-31 in exchange for future milestones and royalties to the other party.

The Company will continue to be responsible for certain transitional activities related to atacicept through June 2009 and its related expenses will be reimbursed by Merck Serono. The Company has certain other remaining performance obligations under the Strategic Alliance Agreement through October 2009.

As part of the modifications discussed above, the Company will no longer have to pay $9.8 million of development costs that were previously required to be reimbursed to Merck Serono. The development costs had been previously expensed as research and development costs in the period June 1, 2008 to August 28, 2008. The forgiveness of these expenses was determined to be consideration for the licenses granted to Merck Serono and therefore we have considered the $9.8 million to be incremental revenue which is being deferred and recognized as license fee revenue on a straight-line basis through October 2009, our remaining obligated performance period under the Strategic Alliance Agreement. In total, the Company has deferred revenue under the Merck Serono

agreements of $15.5 million as of December 31, 2008, which will be ratably recognized through October 2009. The Company has recorded revenue of $11.3 million, $11.0 million and $5.7 million in 2008, 2007 and 2006 under these agreements.

Bayer Schering Pharma A.G.

In June 2007, the Company entered into a license and collaboration agreement and a co-promotion agreement with Bayer Schering Pharma A.G (Bayer). The agreements provide Bayer with an exclusive license to develop and sell rThrombin outside the United States and to co-promote rThrombin in the United States for three or four years. The Company will record all United States sales and Bayer will be entitled to commissions on United States sales for five or six years, depending on the period Bayer co-promotes in the United States.

The Company received a $30.0 million upfront milestone payment in 2007, a $40.0 million milestone payment in February 2008 based upon the January 17, 2008 FDA approval of rThrombin, $20.0 million of which is expected to be repaid to Bayer as United States sales bonuses under the co-promotion. In addition, the Company received milestone payments of $5.0 million for Bayer's filing of a marketing authorization application in Europe and $1.5 million for Bayer's filing of a new drug submission in Canada in 2008. The Company may also receive additional payments based on further regulatory filings, approvals and annual sales thresholds achieved by Bayer outside of the United States.

The Company has a number of obligations under the license and collaboration agreement and the co-promotion agreement; these include the grant of various licenses, the supply of bulk drug product, participation on a United States co-promotion committee, research and development support prior to regulatory approval, formation and maintenance of a United States sales force and supply of finished drug product. All of the substantive obligations under the agreements are expected to be delivered from the execution date of the agreement until the first quarter of 2013 commencing with the grant of various licenses, with the exception of bulk drug supply which the Company is obligated to supply over the entire term of the license and collaboration agreement.

The Company has evaluated the agreement under the provisions of EITF 00-21 and has determined that there are two separate units of accounting. The first unit of accounting consists of the grant of various licenses, participation on the United States co-promotion committee, research and development support prior to regulatory approval, formation and maintenance of a United States sales force and supply of finished drug product until the first quarter of 2013. The second unit of accounting consists of supplying bulk drug product over the term of the agreement. The Company believes the combined obligations in the first unit of accounting have value to Bayer on a standalone basis. Regarding the second unit of accounting, the Company also believes it has objective and reliable evidence of the fair value of the bulk drug product to be supplied over the term of the license and collaboration agreement based on the purchase price paid to the third party supplier of the bulk drug product. There are no general rights of return under the agreements.

The first unit of accounting is to be provided until the first quarter of 2013. Thereafter, the only undelivered element is to provide bulk drug product for the remaining term of the license and collaboration agreement. The Company uses the residual method to allocate its arrangement consideration between the two units of accounting. The Company recognizes revenue attributable to the first unit of accounting using a proportional performance model. The Company has the ability to estimate the proportional progress based on the costs expected to be incurred under the agreement. The Company has determined based upon the nature and timing of its obligations that cost inputs are the best measure of performance under the arrangements. The Company will recognize revenue attributable to the supply of bulk drug product as the bulk drug is delivered to the customer provided all other revenue recognition criteria are met.

During 2008 and 2007, the Company recognized $18.0 million and $6.2 million, respectively, of revenue for services performed under the agreements, which is included in license fee and milestone payments. Deferred revenue at December 31, 2008 related to the collaboration was $52.3 million.

Bristol-Myers Squibb

In October 2008, the Company entered into a binding, nonexclusive, worldwide license with Bristol-Myers Squibb Company (BMS) to the Company's patents related to immunoglobulin fusion proteins and has agreed to terminate the related patent infringement lawsuit filed in August 2006 against BMS. In return, BMS paid the Company a one-time license payment of $21.0 million. The Company has no future performance obligations under this arrangement and, accordingly, recorded the entire amount as license fee revenue in 2008.

University of Washington

In December 2008, the Company entered into a settlement agreement with University of Washington (UW) related to a Factor XIII license agreement. The Company agreed to pay UW a total of $1.25 million in satisfaction of all past and future obligations under the agreement. A payment of $500,000 was made in December 2008. The Company recognized the entire $1.25 million as research and development expense in 2008. The outstanding balance of $750,000 is included in accrued liabilities.

11. Retirement plans

Defined contribution

The Company maintains a 401(k) retirement plan covering substantially all of its employees. The plan provides for matching and discretionary contributions by the Company. Such contributions were approximately $2.6 million, $2.3 million and $2.3 million for the years ended December 31, 2008, 2007 and 2006, respectively.

Deferred compensation plan

The Company has a Deferred Compensation Plan (DCP) for key employees. Eligible plan participants are designated by the Company's Board of Directors. The DCP allows participants to defer up to 50% of their annual compensation and up to 100% of any bonus. At December 31, 2008 and 2007, approximately $3.8 million and $5.4 million, respectively, was deferred under the DCP and was recorded both as a long-term asset and a long-term liability.

12. Income taxes

At December 31, 2008, the Company had net operating loss carryforwards of $584.6 million, research and development tax credit carryforwards of $34.8 million, a rehabilitation tax credit carryforward of $1.5 million and alternative minimum tax credit carryforwards of $1.2 million. The carryforwards are available to offset future tax liabilities. The net operating loss carryforwards will begin to expire from 2021 – 2028, the research and development tax credits expire from 2009 – 2028 and the rehabilitation tax credit will expire in 2009. The alternative minimum tax credit will carry forward indefinitely. Utilization of the net operating loss and tax credit carryforwards may be subject to annual limitations under ownership change limitations established by the Internal Revenue Code Section 382. The annual limitations may result in the expiration of net operating loss and tax credit carryforwards before they can be utilized.

Deferred tax assets and liabilities arise from temporary differences between financial and tax reporting. The Company has provided a valuation allowance at December 31, 2008 and 2007 to offset the excess of deferred tax assets over the deferred tax liabilities, due to the uncertainty of realizing the benefits of the net deferred tax asset.

Deferred tax assets and liabilities were as follows as of December 31 (in thousands):

	2008	2007
Deferred tax assets:		
Net operating loss carryforwards	$ 204,612	$ 181,695
Research and development tax credit carryforwards	34,839	32,575
Alternative minimum tax credit carryforwards	1,242	1,242
Rehabilitation tax credit carryforward	1,507	1,507
Intellectual property purchased from Novo Nordisk	1,255	2,499
Deferred gain on sale of assets	8,861	7,367
Deferred revenue	22,832	12,361
Stock option compensation	7,332	4,399
Other	6,412	4,641
	288,892	248,286
Deferred tax liabilities:		
Deferred revenue	(4,193)	(3,076)
	284,699	245,210
Less: Valuation allowance	(284,699)	(245,210)
Net deferred tax asset	$ —	$ —

The valuation allowance increased by $39.5 million, $51.2 million and $49.5 million in 2008, 2007 and 2006 respectively, to fully reserve the net deferred tax assets.

In October 2000, the Company entered into a tax sharing agreement with Novo Nordisk. The agreement states that all research and development tax credit carryforwards generated by the Company prior to November 9, 2000 used by the Company to generate a tax benefit in future periods shall be reimbursed to Novo Nordisk. The total amount paid shall not exceed $12.0 million.

Realization of the deferred tax asset associated with intellectual property purchased from Novo Nordisk will be reflected as increases in shareholders' equity and will not be reflected as tax benefits in the consolidated statements of operations.

The reconciliation between the Company's effective tax rate and the income tax rate is as follows for the years ended December 31:

	2008	2007	2006
Federal income tax rate	(35)%	(35)%	(35)%
Research and development tax credits	(3)	(3)	(3)
Valuation allowance	38	35	38
Other	—	3	—
Effective tax rate	0 %	0 %	0%

The Company adopted the provisions of FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes*, on January 1, 2007.

The Company files its income tax return in the U.S. federal jurisdiction. The Company is no longer subject to U.S. federal tax examinations by tax authorities for years before 2004. However, the Internal Revenue Service (IRS) could adjust certain unused tax attributes carried forward from tax years prior to 2004. The Company believes that if subjected to an IRS income tax audit, any assessments would be immaterial to its financial statements. The Company files state tax returns in states where it has tax obligations.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

Balance at January 1, 2007	$ —
Additions based on tax positions related to the current year	854
Additions for tax positions of prior years	516
Reductions for tax positions of prior years	—
Settlements/Statute of Limitation Lapse	—
Balance at January 1, 2008	1,370
Additions based on tax positions related to the current year	—
Additions for tax positions of prior years	—
Reductions for tax positions of prior years	(1,370)
Settlements/Statute of Limitation Lapse	—
Balance at December 31, 2008	$ —

When and if applicable, the Company will classify income tax-related interest and penalties as income tax expense in its consolidated statements of operations.

13. Commitments and Contingencies

Operating lease commitments

Historically, the Company had various operating lease agreements for office and parking space in a building near its corporate headquarters in Seattle, Washington. In March 2008, the Company entered into a noncancelable master lease agreement which extended the lease term for all leased space to April 2019. There are certain renewal provisions at the Company's option, which are not reflected in the following operating lease commitment table. Total annual payments under the lease averages approximately $2.9 million per year over the term.

Gross rental expense for the years ended December 31, 2008, 2007 and 2006 was $1.9 million, $2.0 million and $1.5 million, respectively.

The following table presents the Company's commitments for future minimum rental payments under the noncancelable master operating lease (in thousands):

Year ending December 31,	
2009	$ 2,539
2010	2,631
2011	2,727
2012	2,826
2013	2,930
Thereafter	17,560
	$31,213

The master lease agreement provides for scheduled rent increases over its term. The Company is recognizing rent expense on a straight-line basis over the related lease term.

Purchase commitments

The Company maintains, with its contract manufacturers, rolling firm orders and annual minimum purchase commitments for RECOTHROM. These orders may be rescheduled or cancelled by the Company under limited conditions and, even then, with certain restrictions and penalties up to the full cost of the product.

The following table presents the Company's noncancelable annual purchase commitments to its contract manufacturers (in thousands):

Year ending December 31,	
2009	$38,310
2010	10,122
2011	11,619
2012	4,900
2013	4,900
Thereafter	24,500
	$94,351

Other commitments

Certain key employees have employment agreements with the Company which provide for salary, health insurance and certain additional severance benefits.

14. Stock incentive plans

In March 2000, the Company adopted the 2000 Stock Incentive Plan (the 2000 Plan). Upon completion of the Company's initial public offering in February 2002, the 2000 Plan was suspended and the 2001 Stock Incentive Plan (the 2001 Plan) became effective. Both Plans provide for the issuance of incentive stock options, nonqualified stock options, restricted stock and restricted stock units to employees, directors, consultants and other independent contractors who provide services to the Company. The Company's Board of Directors is responsible for administration of the Plans and determines the term of each option, exercise price and the vesting

terms. The 2001 Plan provides for an annual increase in authorized shares effective the first day of each year equal to the least of (i) 2,700,000 shares; (ii) 5% of the outstanding common stock as of the end of the Company's preceding fiscal year; and (iii) a lesser amount as determined by the Board of Directors. Any shares from the 2000 Plan that are not actually issued shall continue to be available for issuance under the 2001 Plan. The Company has reserved a total of 25,138,650 shares of common stock for issuance under the Plans, of which 4,184,592 are available for future grant at December 31, 2008. Options granted to employees under the Plans generally vest over a four-year period and expire ten years from the date of grant. Options to purchase 939,085 shares have been granted to board members as of December 31, 2008, of which 144,000 options were immediately exercisable, 543,085 options vest over approximately one year and 252,000 vest over four years.

Stock options

A summary of stock option activity under the Plans is presented below (shares and aggregate intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Balance, January 1, 2006	11,470	$10.88		
Granted	2,639	19.58		
Exercised	(1,564)	7.05		
Forfeited	(502)	17.94		
Expired	(61)	20.07		
Balance, December 31, 2006	11,982	$12.95	6.6	$52,611
Granted	2,724	15.06		
Exercised	(1,029)	4.92		
Forfeited	(562)	17.91		
Expired	(413)	18.27		
Balance, December 31, 2007	12,702	$13.66	6.6	$25,295
Granted	2,631	8.18		
Exercised	(151)	3.62		
Forfeited	(437)	15.92		
Expired	(360)	15.36		
Balance, December 31, 2008	14,385	$12.65	6.3	$ 345
Exercisable, December 31, 2008	9,656	$12.97	5.1	$ 345

As of December 31, 2008, there was $25.0 million of total unrecognized compensation costs related to stock options. These costs are expected to be recognized over a weighted average period of 2.3 years.

Estimated fair values of stock options granted have been determined using the Black-Scholes option pricing model with the following assumptions:

	2008	2007	2006
Expected stock price volatility	54%	53%	56%
Risk-free interest rate	2.88%	4.57%	4.55%
Expected life of options	5.8 years	6.1 years	6.1 years
Expected dividend yield	0%	0%	0%

The Company has estimated the volatility of its common stock by blending historical volatility with the implied volatility of market traded options. Prior to 2008, the Company did not have historical trading information for its common stock for a long enough period to calculate historical volatility solely based on the trading of its common stock. Furthermore, the market for options on the Company's common stock is illiquid and cannot be relied upon as a source of implied volatility. Accordingly, the Company has augmented its own data with the historical volatility and implied volatility of market traded options of similar companies. The risk-free interest rate used in the option valuation model is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term of the options. The Company has estimated the expected life of its stock options using the simplified method for determining the expected term as prescribed by the SEC's Staff Accounting Bulletin 107, *Share-based Payment* for the years 2007 and 2006. The Company used historical data to determine an estimate for the expected life of its stock options granted in 2008. The Company does not anticipate paying any cash dividends in the foreseeable future and therefore an expected dividend yield of zero is used in the option valuation model. Forfeitures are estimated at the time of grant and revised in subsequent periods if actual forfeitures differ from those estimates. Accordingly, stock-based compensation expense is recorded only for those awards that vest. All stock-based payment awards are amortized on a straight-line basis over the requisite service periods of the awards, which are generally the vesting periods.

A summary of stock option values under the Plans is presented below (in thousands, except per stock option share data):

	2008	2007	2006
Weighted average grant date fair value per stock option share granted	$ 4.29	$ 8.49	$ 11.37
Total intrinsic value of stock options exercised	$ 926	$10,213	$19,765
Total fair value of stock options vested	$21,161	$21,681	$18,402

Stock awards

In January 2008, the Company issued a total of 57,200 unrestricted shares of common stock to employees of the Company in recognition of FDA approval of RECOTHROM. The share price used to determine compensation was $13.05, based on the closing price on the date the compensation committee of the Company's board of directors approved the distribution. Additionally, the compensation amount was increased to include payroll taxes paid on behalf of the employees. The entire $1.1 million of costs related to the issuance were expensed in January 2008.

Restricted stock units

In February 2008, the Company granted 620,500 restricted stock units to non-officer employees under the Company's 2001 Plan. These shares vest over a three-year period with one-third vesting on each anniversary of the grant date. The grant date fair value for the restricted stock unit awards was the closing market price of the Company's common stock on the date of grant, which was $9.26 per share. As of December 31, 2008, total unrecognized compensation costs related to unvested restricted stock units was $3.9 million, which is being expensed on a straight-line basis through February 2011.

A summary of restricted stock unit activity is presented below (number of restricted stock units in thousands):

	Number of Restricted Stock Units	Weighted Average Grant-Date Fair Value Per Share
Outstanding at December 31, 2007	—	$ —
Granted	621	$9.26
Forfeited	(38)	$9.26
Vested	—	$ —
Outstanding at December 31, 2008	583	$9.26

15. Subsequent event

In January 2009, the Company entered into a co-development/co-promotion and license agreement with Bristol-Myers Squibb for the type-3 interferon family, which includes the Company's development candidate PEG-IFN-λ. The Company will receive an initial license fee of $85.0 million and an additional license fee of $20.0 million in March 2009; various milestone payments based on the achievement of certain objectives, including $95.0 million expected later in 2009 related to the initiation of Phase 2 clinical trials; profit sharing and co-promotion rights for the Company in the U.S.; and royalties on sales outside of the United States The Company is also eligible for sales bonuses based on world-wide sales of licensed products. The Company provides a license to related technology and is obligated to fund the first $100.0 million of costs for development in the U.S. and Europe, after which it will be responsible for 20% of such costs.

16. Quarterly financial results (unaudited)

The following table contains selected statements of operations information, which is unaudited and should be read in conjunction with the Company's financial statements and related notes included elsewhere in this report. The Company believes that the following unaudited information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period. Operating results for each quarter of 2008 and 2007 are summarized as follows (in thousands):

	March 31	June 30	September 30	December 31
2008				
Revenue	$ 13,512	$ 12,582	$ 11,876	$ 36,019
Net loss	$(40,896)	$(37,380)	$(28,790)	$ (9,176)
Basic and diluted net loss per common share	$ (0.60)	$ (0.54)	$ (0.42)	$ (0.13)
2007				
Revenue	$ 5,182	$ 4,237	$ 8,533	$ 20,525
Net loss	$(33,309)	$(37,255)	$(39,013)	$(38,567)
Basic and diluted net loss per common share	$ (0.49)	$ (0.55)	$ (0.57)	$ (0.56)

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

The Company maintains disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) that are designed to ensure that required information is recorded, processed, summarized and reported within the required timeframe, as specified in the rules set forth by the Securities and Exchange Commission. Our disclosure controls and procedures are also designed to ensure that information required to be disclosed is accumulated and communicated to management, including the Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding required disclosures.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2008 and, based on this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2008.

Management's Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Management conducted an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2008. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control — Integrated Framework*. Based on the results of this assessment and on those criteria, management concluded that our internal control over financial reporting was effective as of December 31, 2008.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2008 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Changes in Internal Control over Financial Reporting

During the fourth fiscal quarter, there were no changes to our internal control over financial reporting that materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

(a) The information required by this item with respect to our directors is incorporated by reference to the sections captioned "Proposal I: Election of Directors" and "Report of the Audit Committee" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009. We expect to file the proxy statement within 120 days of December 31, 2008, our fiscal year end.

(b) The information required by this item with respect to our executive officers is incorporated by reference to the section captioned "Executive Officers" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009.

(c) The information required by this item with respect to our corporate governance is incorporated by reference to the sections captioned "Corporate Governance," "Report of the Audit Committee" and "Section 16(a) Beneficial Ownership Reporting Compliance" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009. We have adopted a Code of Ethics applicable to our chief executive officer, chief financial officer and others responsible for our corporate financial reporting. A copy of the Code of Ethics is available on our website at www.zymogenetics.com.

Item 11. Executive Compensation

The information required by this item with respect to executive compensation is incorporated by reference to the sections captioned "Executive Compensation" and "Corporate Governance" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters

The information required by this item with respect to beneficial ownership is incorporated by reference to the section captioned "Security Ownership of Certain Beneficial Owners and Management" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009.

Equity Compensation Plan Information

The following table provides information regarding our equity compensation plans at December 31, 2008.

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))[1]
	(a)	(b)	(c)
Equity compensation plans approved by security holders	14,385,162	$12.65	4,184,592
Equity compensation plans not approved by security holders	—	—	—
Total	14,385,162	$12.65	4,184,592

(1) Does not include an increase of 2,700,000 shares, effective January 1, 2009, pursuant to a provision of the 2001 Plan that provides for an annual increase effective the first day of each year equal to the least of (i) 2,700,000 shares; (ii) 5% of the outstanding common stock as of the end of the Company's preceding fiscal year; and (iii) a lesser amount as determined by the Board of Directors.

Item 13. Certain Relationships and Related Transactions, and Director Independence

(a) The information required by this item with respect to certain relationships and related transactions is incorporated by reference to the section captioned "Certain Transactions" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009.

(b) The information required by this item with respect to director independence is incorporated by reference to the section captioned "Corporate Governance" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to the section captioned "Independent Registered Public Accounting Firm" in the proxy statement for our annual meeting of shareholders to be held on June 10, 2009.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this Form 10-K:

1. *Financial Statements.* The following financial statements are contained in Item 8 of this Annual Report on Form 10-K:

2. *Financial Statement Schedules*

All financial statement schedules have been omitted because the required information is either included in the financial statements or the notes thereto or is not applicable.

3. *Exhibits*

Exhibit No.	Description	
3.1	Amended and Restated Articles of Incorporation of ZymoGenetics, Inc.	(A)
3.2	Articles of Amendment of ZymoGenetics, Inc.	(C)
3.3	Amended and Restated Bylaws.	(M)
9.1	Agreement and Waiver of Co-Sale Rights, dated July 16, 2001, by and among ZymoGenetics, Inc., the holders of Series B Preferred Stock listed on the signature pages thereto and Serono B.V.	(A)
9.2	Share Transfer and Voting Agreement, dated January 2, 2001, by and between Warburg, Pincus Equity Partners, L.P. and Mount Everest Advisors, L.L.C. and acknowledged by ZymoGenetics, Inc.	(A)
10.1†	Amended and Restated Employment Agreement, dated February 3, 2005, between ZymoGenetics, Inc. and Bruce L.A. Carter, Ph.D.	(H)
10.2†	Form of Employment Agreement for Executive Officers.	(P)
10.3†	Amended and Restated 2000 Stock Incentive Plan.	(A)
10.4†	2001 Stock Incentive Plan.	(A)
10.5†	Amended and Restated Stock Option Grant Program for Nonemployee Directors under the ZymoGenetics 2001 Stock Incentive Plan.	(J)
10.6†	2001 Stock Incentive Plan, Form of Stock Option Grant Notice.	(L)
10.7†	Deferred Compensation Plan for Key Employees.	(A)

Exhibit No.	Description	
10.8	First Amendment to ZymoGenetics Deferred Compensation Plan for Key Employees.	(O)
10.9	Second Amendment to ZymoGenetics Deferred Compensation Plan for Key Employees.	(O)
10.10	Third Amendment to ZymoGenetics Deferred Compensation Plan for Key Employees.	(O)
10.11*	License Agreement, dated January 18, 1994, including Amendment No. 1, dated January 1, 1997, and Amendment No. 2, dated June 5, 2000, between and among ZymoGenetics, Inc., Novo Nordisk A/S, Johnson & Johnson and Chiron Corporation.	(A)
10.12*	Royalty Agreement pertaining to the January 18, 1994 Agreement Relating to Platelet Derived Growth Factor, dated January 1, 2000, between ZymoGenetics, Inc. and Novo Nordisk.	(A)
10.13*	License Agreement, dated December 31, 1998, as amended on February 4, 1999 and October 23, 2000, between ZymoGenetics, Inc. and St. Jude Children's Research Hospital.	(A)
10.14*	Option and License Agreement, effective November 10, 2000, as amended effective as of June 16, 2000 and October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(A)
10.15*	Collaborative Development and Marketing Agreement, effective August 30, 2001 by and between ZymoGenetics, Inc. and Ares Trading S.A.	(A)
10.16*	First Amended and Restated Development and Marketing Agreement, dated August 28, 2008, between ZymoGenetics, Inc. and Ares Trading S.A.	(Q)
10.17*	Exclusive Patent License Agreement, effective December 18, 2002, between ZymoGenetics, Inc. and Aventis Behring GmbH.	(D)
10.18	Shareholders' Agreement by and among ZymoGenetics, Inc., Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc. and the investors listed on Schedule A thereto, effective as of November 10, 2000.	(A)
10.19	First Amendment to Shareholders' Agreement by and among ZymoGenetics, Inc., Novo Nordisk A/S, Novo Nordisk Pharmaceuticals, Inc. and the investors listed on Schedule A thereto, dated as of February 4, 2002.	(B)
10.20	Investors' Rights Agreement by and among ZymoGenetics, Inc., Novo Nordisk Pharmaceuticals, Inc. and the persons listed on Schedule A thereto, effective as of November 10, 2000.	(A)
10.21	Tax Sharing Agreement, effective October 20, 2000, between ZymoGenetics, Inc. and Novo Nordisk of North America, Inc.	(A)
10.22	Lease Agreement, dated October 4, 2002, between ZymoGenetics, Inc. and ARE-1201/1208 Eastlake Avenue, LLC.	(D)
10.23	Amendment No. 2 to Lease Agreement, dated July 19, 2004, between ZymoGenetics, Inc. and ARE-1201/1208 Eastlake Avenue, LLC.	(F)
10.24	Lease Agreement, dated October 4, 2002, between ZymoGenetics, Inc. and ARE-1208 Eastlake Avenue, LLC.	(D)
10.25	Amendment No. 2 to Lease Agreement, dated June 14, 2004, between ZymoGenetics, Inc. and ARE-/1208 Eastlake Avenue, LLC.	(F)
10.26	Restated Office Lease Agreement, dated March 1, 2008, between ZymoGenetics, Inc. and 1144 Eastlake LLC.	(O)
10.27*	Development and Supply Agreement, dated October 1, 2003, between ZymoGenetics, Inc. and Abbott Laboratories.	(E)
10.28*	Strategic Alliance Agreement, dated October 12, 2004, between ZymoGenetics, Inc. and Serono S.A.	(G)

Exhibit No.	Description	
10.29*	First Amended and Restated Strategic Alliance Agreement, dated August 28, 2008, between ZymoGenetics, Inc. and Serono Technologies S.A.	(Q)
10.30*	License Agreement for Recombinant Factor XIII, dated October 4, 2004, among ZymoGenetics, Inc., Novo Nordisk A/S and Novo Nordisk Health Care AG.	(G)
10.31*	Amendment No. 1 to License Agreement for Recombinant Factor XIII, dated December 7, 2007, among ZymoGenetics, Inc., Novo Nordisk A/S and Novo Nordisk Health Care AG.	(N)
10.32*	Collaborative Data Sharing and License Agreement dated August 11, 2005, between ZymoGenetics, Inc. and Novo Nordisk A/S.	(I)
10.33*	Manufacturing Service Agreement relating to rhThrombin between Patheon Italia S.p.A. and ZymoGenetics, Inc., executed January 19, 2007.	(K)
10.34	Amendment No. 1 to Manufacturing Service Agreement relating to rhThrombin between Patheon Italia S.p.A. and ZymoGenetics, Inc., executed December 3, 2007	(N)
10.35*	U. S. Co-Promotion Agreement by and between ZymoGenetics, Inc. and Bayer HealthCare, LLC, executed June 18, 2007.	(L)
10.36*	License and Collaboration Agreement by and between ZymoGenetics, Inc. and Bayer Schering Pharma AG, executed June 18, 2007.	(L)
10.37*	Facility Agreement dated June 26, 2008 among ZymoGenetics, Inc., Deerfield Private Design Fund, L.P. and Deerfield Private Design International, L.P. (Facility Agreement)	(P)
10.38*	Promissory Note dated June 26, 2008, with issuer ZymoGenetics, Inc. and holder Deerfield Private Design International, L.P.	(P)
10.39*	Promissory Note dated June 26, 2008, with issuer ZymoGenetics, Inc. and holder Deerfield Private Design Fund, L.P.	(P)
10.40*	Royalty Agreement dated June 26, 2008 among ZymoGenetics, Inc., Deerfield Private Design Fund, L.P. and Deerfield Private Design International, L.P.	(P)
10.41	Registration Rights Agreement dated June 26, 2008 among ZymoGenetics, Inc., Deerfield Private Design Fund, L.P. and Deerfield Private Design International, L.P.	(P)
10.42*	Form of Warrant to Purchase Common Stock of ZymoGenetics, Inc. relating to the Facility Agreement.	(P)
10.43*	Release and License Agreement, dated October 22, 2008, by and between ZymoGenetics and Bristol-Myers Squibb Company	
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.	
31.1	Certifications of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	
31.2	Certifications of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	
32.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	

† Management contract or compensatory plan or arrangement.

* Portions of these exhibits have been omitted based on a grant of confidential treatment from the Securities and Exchange Commission. The omitted portions of these exhibits have been filed separately with the SEC.

(A) Incorporated by reference to ZymoGenetics, Inc. Registration Statement on Form S-1 (No. 333-69190) filed on September 10, 2001, as amended.

(B) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended March 31, 2002.
(C) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended June 30, 2002.
(D) Incorporated by reference to ZymoGenetics, Inc. Annual Report on Form 10-K for the year ended December 31, 2002.
(E) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended September 30, 2003.
(F) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended June 30, 2004.
(G) Incorporated by reference to ZymoGenetics, Inc. Annual Report on Form 10-K for the year ended December 31, 2004.
(H) Incorporated by reference to ZymoGenetics, Inc. Current Report on Form 8-K dated as of February 3, 2005.
(I) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended September 30, 2005.
(J) Incorporated by reference to ZymoGenetics, Inc. Annual Report on Form 10-K for the year ended December 31, 2006.
(K) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended March 31, 2007.
(L) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended June 30, 2007.
(M) Incorporated by reference to ZymoGenetics, Inc. Current Report on Form 8-K dated as of November 15, 2007.
(N) Incorporated by reference to ZymoGenetics, Inc. Annual Report on Form 10-K for the year ended December 31, 2007.
(O) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended March 31, 2008.
(P) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended June 30, 2008.
(Q) Incorporated by reference to ZymoGenetics, Inc. Quarterly Report on Form 10-Q for the quarter ended September 30, 2008.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Company has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

ZYMOGENETICS, INC.

Date: March 5, 2009

By: /s/ DOUGLAS E. WILLIAMS, PH.D.
Douglas E. Williams, Ph.D.
Chief Executive Officer

Each person whose individual signature appears below hereby authorizes and appoints Douglas E. Williams, Ph.D. and James A. Johnson, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file, any and all amendments to this Report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Company and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ DOUGLAS E. WILLIAMS, PH.D. **Douglas E. Williams, Ph.D.**	Chief Executive Officer and Director (Principal Executive Officer)	March 5, 2009
/s/ JAMES A. JOHNSON **James A. Johnson**	Executive Vice President, Chief Financial Officer and Treasurer (Principal Accounting and Financial Officer)	March 5, 2009
/s/ BRUCE L.A. CARTER, PH.D. **Bruce L.A. Carter, Ph.D.**	Chairman of the Board of Directors	March 5, 2009
/s/ JAMES A. HARPER **James A. Harper**	Director	March 5, 2009
/s/ JUDITH A. HEMBERGER, PH.D. **Judith A. Hemberger, Ph.D.**	Director	March 5, 2009
/s/ DAVID I. HIRSH, PH.D. **David I. Hirsh, Ph.D.**	Director	March 5, 2009
/s/ JONATHAN S. LEFF **Jonathan S. Leff**	Director	March 5, 2009
/s/ DAVID H. MACCALLUM **David H. MacCallum**	Director	March 5, 2009
/s/ KURT ANKER NIELSEN **Kurt Anker Nielsen**	Director	March 5, 2009
/s/ EDWARD E. PENHOET, PH.D. **Edward E. Penhoet, Ph.D.**	Director	March 5, 2009
/s/ LARS REBIEN SØRENSEN **Lars Rebien Sørensen**	Director	March 5, 2009

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Company Info

BOARD OF DIRECTORS
Bruce L.A. Carter, Ph.D.
Chairman of the Board
ZymoGenetics, Inc.

James A. Harper
Former Group Vice President
Global Marketing and Sales
Eli Lilly and Company

Judith A. Hemberger, Ph.D.
Venture Partner
Nomura Phase4 Ventures
Former Executive Vice President
Chief Operating Officer
Pharmion Corporation

David I. Hirsh, Ph.D
Executive Vice President of Research
Columbia University

Jonathan S. Leff
Managing Director
Warburg Pincus LLC

David H. MacCallum
Managing Director
Outer Islands Capital

Kurt Anker Nielsen
Former Co-Chief Executive Officer
Novo A/S

Edward E. Penhoet, Ph.D.
Director
Alta Partners

Lars Rebien Sørensen
President and Chief Executive Officer
Novo Nordisk A/S

Douglas E. Williams, Ph.D.
Chief Executive Officer
ZymoGenetics, Inc.

EXECUTIVE OFFICERS
Heather L. Franklin
Senior Vice President
Business Development

Darren R. Hamby
Senior Vice President
Human Resources

James A. Johnson
Executive Vice President
Chief Financial Officer, Treasurer

Nicole Onetto, M.D.
Senior Vice President
Development
Chief Medical Officer

Suzanne M. Shema, J.D.
Senior Vice President
General Counsel, Secretary

Douglas E. Williams, Ph.D.
Chief Executive Officer

Stephen W. Zaruby
President

COMPANY HEADQUARTERS
ZymoGenetics, Inc.
1201 Eastlake Avenue E.
Seattle, Washington 98102
Telephone (206) 442-6600

WEBSITE
zymogenetics.com

TRANSFER AGENT AND REGISTRAR
BNY Mellon Shareowner Services
480 Washington Blvd
Jersey City, New Jersey 07310
877-261-9288
bnymellon.com/shareowner

GENERAL COUNSEL
Perkins Coie LLP
Seattle, Washington

INDEPENDENT ACCOUNTANTS
PricewaterhouseCoopers LLP
Seattle, Washington

STOCK LISTING
ZymoGenetics common stock is traded on The NASDAQ Stock Market under the symbol ZGEN.

ANNUAL MEETING
The annual meeting of shareholders will be held at 8:00 a.m. on Wednesday, June 10, 2009 at the Company headquarters.

SHAREHOLDER INQUIRIES
Information about the Company can be found on the Internet at *zymogenetics.com*. Inquiries regarding the Company and its activities may be directed to the Corporate Communications Department at the Company headquarters. Communications concerning stock and transfer requirements, lost certificates and changes of address should be directed to the Transfer Agent.

FORWARD-LOOKING STATEMENTS This annual report contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on the current intent and expectations of the management of ZymoGenetics. These statements are not guarantees of future performance and involve risks and uncertainties that are difficult to predict. ZymoGenetics actual results and the timing and outcome of events may differ materially from those expressed in or implied by the forward-looking statements because of risks associated with our unproven product sales and marketing abilities, discovery strategy, preclinical and clinical development, strategic partnering, regulatory oversight, intellectual property claims and litigation and other risks detailed in the company's public filings with the Securities and Exchange Commission, including the company's Annual Report on Form 10-K for the year ended December 31, 2008. Except as required by law, ZymoGenetics undertakes no obligation to update any forward-looking or other statements in this annual report, whether as a result of new information, future events or otherwise.