BIOMARIN PHARMACEUTICAL INC
Form 10-K
February 27, 2009
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2008

Or

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

For the transition period from to .

Commission file number: 000-26727

BioMarin Pharmaceutical Inc.

(Exact name of registrant issuer as specified in its charter)

Delaware	**68-0397820**
(State of other jurisdiction of Incorporation or organization)	**(I.R.S. Employer Identification No.)**
105 Digital Drive,	
Novato, California	**94949**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number: (415) 506-6700

(Former name, former address and former fiscal year, if changed since last report)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $.001 par value	**The NASDAQ Global Select Market**
Preferred Share Purchase Rights	

Securities registered under Section 12(g) of the Act:

None

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

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

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

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

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

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

Indicate the number of shares outstanding of each of the issuer s classes of common stock, as of the latest practicable date: 99,945,778 shares common stock, par value $0.001, outstanding as of February 17, 2009. The aggregate market value of the voting and non-voting stock held by non-affiliates of the registrant as of June 30, 2008 was $2,875.1 million.

The documents incorporated by reference are as follows:

Portions of the Registrant s Proxy Statement for the Annual Meeting of Stockholders to be held May 12, 2009, are incorporated by reference into Part III.

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BIOMARIN PHARMACEUTICAL INC.

2008 FORM 10-K ANNUAL REPORT

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Part I.

FORWARD LOOKING STATEMENTS

This Form 10-K contains forward-looking statements as defined under securities laws. Many of these statements can be identified by the use of terminology such as believes, expects, anticipates, plans, may, will, projects, continues, estimates, potential, opportunity a These forward-looking statements may be found in *Risk Factors*, *Business*, and other sections of this Form 10-K. Our actual results or experience could differ significantly from the forward-looking statements. Factors that could cause or contribute to these differences include those discussed in *Risk Factors*, as well as those discussed elsewhere in this Form 10-K. You should carefully consider that information before you make an investment decision.

You should not place undue reliance on these statements, which speak only as of the date that they were made. These cautionary statements should be considered in connection with any written or oral forward-looking statements that we may issue in the future. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the filing of this Form 10-K to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the notes thereto appearing elsewhere in this annual report. In addition to the other information in this Form 10-K, investors should carefully consider the following discussion and the information under *Risk Factors* when evaluating us and our business.

Item 1. Business

Overview

BioMarin Pharmaceutical Inc. (BioMarin, the Company, we or our) develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. We select product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market or offer a significant benefit over existing products. Our product portfolio is comprised of three approved products and multiple investigational product candidates. Approved products include Naglazyme (galsulfase), Kuvan (sapropterin dihydrochloride) tablets and Aldurazyme (laronidase).

We are conducting clinical trials on several investigational product candidates for the treatment of genetic diseases including: PEG-PAL, an enzyme substitution therapy for the treatment of phenylketonurics that are not responsive to Kuvan. We expect to start clinical trials of GALNS, an enzyme replacement therapy for the treatment of Mucopolysaccharidosis Type IV or Morquio Syndrome Type A (MPS IV A), a lysosomal storage disease, in the first half of 2009. We are also developing 6R-BH4, the active ingredient in Kuvan, for the treatment of multiple cardiovascular indications, including sickle cell disease.

We are conducting preclinical development of several other enzyme product candidates for genetic and other diseases, including a small molecule for the treatment of Duchenne muscular dystrophy.

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A summary of our various commercial products and development programs, including key metrics as of December 31, 2008, is provided below:

Program	Indication	Orphan Drug Designation	Stage	2008 Total Net Product Revenues (in millions)	2008 Research & Development Expense (in millions)
Naglazyme	MPS VI	Yes	Approved	$ 132.7	$ 9.6
Aldurazyme (1)	MPS I	Yes	Approved	$ 72.5	$ 1.6
Kuvan	PKU	Yes	Approved	$ 46.7	$ 10.8
6R-BH4	Cardiovascular Indications	Not yet determined	Clinical	N/A	$ 14.7
PEG-PAL	PKU	Yes	Clinical	N/A	$ 11.0
GALNS for Morquio Syndrome Type A	MPS IVA	Not yet determined	Clinical First half of 2009	N/A	$ 12.6

(1) The Aldurazyme total product revenue noted above is the total product revenue recognized by us in accordance with the terms of our restructured agreement with Genzyme Corporation (Genzyme). See *Commercial Products Aldurazyme* below for further discussion.

Recent Developments

In February 2009, we announced the results from our Phase 2 multi-center, randomized, double-blind, placebo-controlled clinical study of 6R-BH4 in patients with symptomatic peripheral arterial disease (PAD). The Phase 2 multi-center, randomized, double-blind, placebo-controlled study enrolled 190 subjects and was conducted at 31 sites in the U.S. and Argentina. 161 patients completed the study. The primary objective of the study was to evaluate mean changes in peak walking time (PWT) from baseline to week 24. The secondary objective of the study was to evaluate the mean change in claudication onset time from baseline to week 24. The primary endpoint of the study, peak walking time (PWT), did not show a significant difference between 6R-BH4 and placebo, and the secondary endpoint, claudication onset time, also did not show a difference. 6R-BH4 was well tolerated in peripheral arterial disease patients and had a safety profile similar to previous studies. We are currently evaluating the impact of these results on our overall BH4 development program.

BioMarin/La Jolla Pharmaceutical Company Development and Commercialization Agreement for Riquent

On January 6, 2009, we announced that we entered into an agreement with La Jolla Pharmaceutical Company (La Jolla) to develop and commercialize Riquent®, La Jolla s investigational drug for lupus nephritis, in the U.S., Europe and all other territories of the world, excluding the Asia Pacific region. Riquent was being evaluated by La Jolla in an international double blind, placebo controlled randomized Phase 3 clinical study referred to as the Phase 3 ASPEN study, which was designed to demonstrate that Riquent treatment delays the time to renal flare and reduced proteinuria in patients with lupus renal disease. On February 12, 2009. The Independent Data Monitoring Board determined that the continuation of the trial was futile. Based on the results of the interim analysis, we and La Jolla have decided to stop the study, unblind the data and evaluate the clinical results, including secondary end points.

On January 19, 2009, we paid La Jolla a cash payment of $7.5 million and on January 20, 2009, we purchased 339,104 preferred shares of La Jolla s Series B Preferred Stock at a price per share of $22.12, for $7.5 million. The preferred shares are initially convertible at a rate of thirty shares of common stock for every one preferred share. This is equivalent to a common stock purchase price of $0.74, a 20% premium to the average closing price for La Jolla s common stock over the 20 trading days prior to January 4, 2009.

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Kuvan Marketing Approval in the European Union

On December 9, 2008, we announced that our partner Merck Serono, a division of Merck KGaA (Darmstadt, Germany), received marketing approval for Kuvan for the treatment of hyperphenylalaninemia (HPA) in phenylketonuria (PKU) or BH4 deficient patients from the European Commission, or the EC. In the fourth quarter of 2008, we earned a milestone payment from Merck Serono of $30.0 million, which was paid in January 2009, for this marketing approval and will receive royalties on net sales of Kuvan in the E.U.

Initiation of Clinical Assessment Program for Morquio A Syndrome

On November 3, 2008, we announced the initiation of the Morquio Clinical Assessment Program for patients with MPS IVA. We expect to initiate a Phase 1b clinical trial of the experimental enzyme replacement therapy in the first half of 2009.

Positive Phase 2a Clinical Study Results of 6R-BH4 in Patients in Sickle Cell Disease

On October 15, 2008, we announced results from our Phase 2a multi-center, open-label, dose-escalation clinical study of 6R-BH4 in patients with sickle cell disease designed to evaluate whether 6R-BH4 can improve the endothelial dysfunction observed in sickle cell disease patients. Oral administration of 6R-BH4 was associated with an improvement in endothelial dysfunction in sickle cell disease patients. We are currently in the process of determining whether we will proceed with additional clinical development of 6R-BH4 for sickle cell disease. We expect to make the decision in the second quarter of 2009.

Commercial Products

Naglazyme

Naglazyme is a recombinant form of N-acetylgalactosamine 4-sulfatase (arylsulfatase B) indicated for patients with mucopolysaccharidosis VI (MPS VI). MPS VI is a debilitating life-threatening genetic disease for which no other drug treatment currently exists and is caused by the deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B), an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs). Patients with MPS VI typically become progressively worse and experience multiple severe and debilitating symptoms resulting from the build-up of carbohydrate residues in all tissues in the body. These symptoms include: inhibited growth, spinal cord compression, enlarged liver and spleen, joint deformities and reduced range of motion, skeletal deformities, impaired cardiovascular function, upper airway obstruction, reduced pulmonary function, frequent ear and lung infections, impaired hearing and vision, sleep apnea, malaise and reduced endurance.

Naglazyme was granted marketing approval in the U.S. in May 2005 and in the E.U. in January 2006. Naglazyme has been granted orphan drug status in the U.S. and the E.U., which confers seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS VI, expiring in 2012 and 2016, respectively. However, different drugs can be approved for the same condition and even the same active ingredient can be approved for the same condition if the new product has a better safety or efficacy profile than Naglazyme. We

market Naglazyme in the U.S., E.U., Latin America and Turkey using our own sales force and commercial organization. Additionally, we use local distributors in several other countries to help us pursue registration and/or market Naglazyme on a named patient basis. Naglazyme net product sales for 2008 totaled $132.7 million, as compared to $86.2 million for 2007. Naglazyme net product sales for 2006 were $46.5 million.

Kuvan

Kuvan was granted marketing approval for the treatment of PKU in the U.S. in December 2007. We market Kuvan in the U.S. using our own sales force and commercial organization. Kuvan has been granted orphan drug status in the U.S., which confers seven years of market exclusivity in the U.S for the treatment of PKU, expiring

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in 2014. Kuvan net product sales for 2008 were $46.7 million. Kuvan net product sales for 2007 the approximate two-week period after approval and launch in December 2007 were $0.4 million.

Kuvan is a proprietary synthetic oral form of 6R-BH4, a naturally occurring enzyme co-factor for phenylalanine hydroxylase (PAH) indicated for patients with PKU. Kuvan is the first drug for the treatment of PKU, which is an inherited metabolic disease that affects at least 50,000 diagnosed patients under the age of 40 in the developed world. We believe that approximately 30-50% of those with PKU could benefit from treatment with Kuvan. PKU is caused by a deficiency of activity of an enzyme, PAH, which is required for the metabolism of phenylalanine (Phe). Phe is an essential amino acid found in all protein-containing foods. Without sufficient quantity or activity of PAH, Phe accumulates to abnormally high levels in the blood resulting in a variety of serious neurological complications, including severe mental retardation and brain damage, mental illness, seizures and other cognitive problems.

In the U.S. and most developed countries, PKU is diagnosed at birth through a blood test. To manage the disease and maintain non-toxic blood Phe levels, people with PKU must adhere to a highly-restrictive diet comprised of foods that are low in Phe and supplemented with medical foods. Compliance with this diet is difficult for patients and usually only occurs through middle childhood, a period critical to ensuring normal brain development. Recent data demonstrates that adolescent and adult PKU patients who no longer follow restricted diets suffer from a number of psychological and neurological symptoms. In October 2000, a Consensus Panel convened by the National Institutes of Health recommended that all people with PKU should adhere to this special diet throughout their lives. Kuvan is intended to provide PKU patients with a more convenient and effective way to manage their disease and maintain blood Phe levels at the recommended levels.

In July 2008, we announced that Asubio Pharma Co., Ltd. (a subsidiary of Daiichi Sankyo), received marketing approval from the Japanese Ministry of Health, Labour and Welfare for a label extension of Biopten (sapropterin dihydrochloride), which contains the same active ingredient as Kuvan in the U.S., for the treatment of patients with PKU. We received a milestone payment of $1.5 million for this marketing approval and will receive double-digit royalties on net sales of Biopten for the PKU indication in Japan under an exclusive license that we entered into with Asubio in September 2007 of data and intellectual property contained in the Kuvan new drug application.

In May 2005, we entered into an agreement with Merck Serono for the further development and commercialization of Kuvan and PEG-PAL for PKU and 6R-BH4, the active ingredient in Kuvan, for other diseases such as cardiovascular indications including those associated with endothelial dysfunction. Through the agreement, Merck Serono acquired exclusive rights to market these products in all territories outside the U.S. and Japan, and we retained exclusive rights to market these products in the U.S. On December 8, 2007, we announced that we re-acquired Canadian rights for BH4 from Merck Serono. We and Merck Serono have shared equally all development costs following successful completion of Phase 2 clinical trials for each product candidate in each indication. On December 9, 2008, we announced that Merck Serono had received marketing approval in the E.U. for Kuvan for the treatment of PKU. We earned a $30.0 million milestone payment from Merck Serono in the fourth quarter of 2008 as a result of the approval of Kuvan in the E.U. The commercial launch of Kuvan in the E.U. is expected in the first half of 2009. Over the next several years, we expect to receive from Merck Serono a net royalty of approximately 4% on net sales of Kuvan in the E.U. We recorded collaborative agreement revenue associated with Kuvan in the amounts of $38.9 million in 2008, $28.3 million in 2007 and $18.7 million in 2006.

Aldurazyme

Aldurazyme has been approved for marketing in the U.S., E.U. and other countries for patients with mucopolysaccharidosis I (MPS I). MPS I is a progressive and debilitating life-threatening genetic disease for which no other drug treatment currently exists, that is caused by the deficiency of alpha-L-iduronidase, a lysosomal enzyme normally required for the breakdown of GAGs. Patients with MPS I typically become

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progressively worse and experience multiple severe and debilitating symptoms resulting from the build-up of carbohydrate residues in all tissues in the body. These symptoms include: inhibited growth, delayed and regressed mental development (in the severe form), enlarged liver and spleen, joint deformities and reduced range of motion, impaired cardiovascular function, upper airway obstruction, reduced pulmonary function, frequent ear and lung infections, impaired hearing and vision, sleep apnea, malaise and reduced endurance.

Aldurazyme has been granted orphan drug status in the U.S. and the E.U., which gives Aldurazyme seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS I, expiring in 2010 and 2013, respectively. However, different drugs can be approved for the same condition and even the same active ingredient can be approved for the same condition if the new product has a better safety or efficacy profile than Aldurazyme. We developed Aldurazyme through a 50/50 joint venture with Genzyme Corporation. Prior to the restructuring of our collaboration with Genzyme in January 2008, as discussed below, we were responsible for product development, manufacturing and U.S. regulatory submissions while Genzyme was responsible for sales, marketing, distribution, obtaining reimbursement for Aldurazyme worldwide and international regulatory submissions.

On January 3, 2008, we announced the restructuring of our relationship with Genzyme, regarding the manufacturing, marketing and sale of Aldurazyme. Under the revised structure, the operational responsibilities for Genzyme and us did not significantly change; however, the restructured terms allows for each party to have control over its own operational responsibilities, without the need to obtain the approval of the other party. Further, each party will realize 100% of the benefit of their own increased operational efficiencies, thus creating incentives for each party to identify and implement cost saving measures. Under the previous 50/50 structure, each company shared 50% of the expense associated with the other s inefficiencies and only received 50% of the benefit of its own efficiencies. Specifically, we will be able to realize the full benefit of any manufacturing cost reductions and Genzyme will be able to realize the full benefit of any sales and marketing efficiencies. As part of this restructuring, we entered into a number of agreements (the Restructuring Agreements) with Genzyme and the joint venture limited liability company founded by Genzyme and BioMarin (the LLC). Effective January 1, 2008, we entered into a Manufacturing, Marketing and Sales Agreement with Genzyme and the LLC. Genzyme continues to globally distribute, market and sell Aldurazyme, and is required to purchase its requirements exclusively from us. We will continue to manufacture Aldurazyme. The parties are subject to a non-competition restriction preventing both parties from participating in certain activities related to Aldurazyme and other pharmaceutical compositions of alpha-L-iduronidase (Collaboration Products) for alpha-L-iduronidase deficiencies outside of the Restructuring Agreements.

Effective January 1, 2008, Genzyme, the LLC and we also amended and restated our Collaboration Agreement. The LLC no longer engages in commercial activities related to Aldurazyme and its sole activities are to (1) hold the intellectual property relating to Aldurazyme and other Collaboration Products and license all such intellectual property on a royalty-free basis to us and Genzyme to allow us to exercise our rights and perform our obligations under the agreements related to the restructuring and (2) engage in research and development activities that are mutually selected and funded by Genzyme and us. Genzyme and we license rights related to Aldurazyme to the LLC, and the LLC sublicenses these rights to Genzyme and us such that each may perform our obligations under the Restructuring Agreements.

Pursuant to a Members Agreement entered into by Genzyme, the LLC and us related to the restructuring, in February 2008 the LLC distributed cash and inventory to us and cash, accounts receivable and certain other assets and liabilities to Genzyme, such that the fair value of the net assets distributed to us and to Genzyme was equivalent to both parties according to the terms of the restructuring. The value of the assets, including cash and inventory, that we received was $43.5 million.

However, as part of the restructuring of our relationship with Genzyme, beginning in January 2008, Genzyme will record sales of Aldurazyme and is required to pay us, on a quarterly basis, a 39.5 to 50% royalty on worldwide net product sales. In addition, we recognize product transfer revenue when product is released to

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Genzyme and all of our obligations have been fulfilled. Genzyme s return rights for Aldurazyme are limited to defective product. The product transfer revenue represents the fixed amount per unit of Aldurazyme that Genzyme is required to pay us if the product is unsold by Genzyme. The amount of product transfer revenue will eventually be deducted from the calculated royalty rate when the product is sold by Genzyme.

Aldurazyme net product revenues of $72.5 million for 2008 include $60.1 million of royalty revenue on net Aldurazyme sales by Genzyme. Royalty revenue from Genzyme is based on 39.5% 42.0% of net Aldurazyme sales by Genzyme, which totaled $151.3 million for 2008. Incremental Aldurazyme net product transfer revenue of $12.4 million for 2008 reflects incremental shipments of Aldurazyme to Genzyme to meet future product demand. In January 2008, we transferred existing finished goods on-hand to Genzyme under the restructured terms of the BioMarin/Genzyme LLC agreements, resulting in the recognition of significant incremental product transfer revenue during 2008. In the future, to the extent that Genzyme Aldurazyme inventory quantities on hand remain consistent, we expect that our total Aldurazyme revenues will approximate the 39.5% to 50% royalties on net product sales by Genzyme.

Products in Clinical Development

PEG-PAL is an investigational enzyme substitution therapy. It is being developed as a subcutaneous injection and is intended for those patients with PKU that do not respond to Kuvan. In preclinical models, PEG-PAL produced a rapid, dose-dependent reduction in blood phenylalanine (Phe) levels, the same endpoint that was used in the Kuvan studies. In May 2008, we initiated a Phase 1 open-label, single-dose, dose-escalation clinical trial of PEG-PAL for PKU. The primary objective of the study is to assess the safety and tolerability of a single, subcutaneous injection of PEG-PAL in patients with PKU that do not respond to Kuvan. The secondary objectives of the study are to evaluate the pharmacokinetics of single, subcutaneous injections of PEG-PAL administered at escalating doses and to evaluate the effect of PEG-PAL on Phe concentrations in subjects with PKU. We expect clinical trial results in the first half of 2009, depending on trial enrollment rates.

During 2007 and the first part of 2008, we devoted significant resources to developing BH4 for the treatment of other indications, including indications associated with endothelial dysfunction. Endothelial dysfunction has been associated with many cardiovascular diseases, such as hypertension and peripheral arterial disease. Endothelial dysfunction is a condition characterized by the inability of the endothelium (the single cell layer lining of the blood vessels) to respond to physiological changes correctly. In preclinical and investigator-sponsored studies, administration of BH4 has improved vascular endothelial function in animal models and in patients with diabetes and other cardiovascular diseases. BH4 is a naturally occurring enzyme cofactor required for the production of nitric oxide, a molecule that is key to the regulation of dilation and constriction of blood vessels. Data from preclinical and clinical trials suggest that treatment with BH4 is generally safe and well tolerated.

In January 2007, we announced the initiation of a Phase 2 clinical trial of 6R-BH4 for peripheral arterial disease, which was a 24-week, multi-center, double-blind, placebo-controlled study. We released results from the Phase 2 clinical trial in February 2009. In May 2007, we announced the initiation of a Phase 2 clinical trial of 6R-BH4 for sickle cell disease, which is a 16-week, multi-center, open label, dose-escalation study. We announced results from this Phase 2 clinical trial in October 2008. We are currently in the process of determining whether we will proceed with additional clinical development of 6R-BH4 for other indications. We expect to make this decision in the second quarter of 2009.

We are also developing GALNS, an enzyme substitution therapy for the treatment of MPS IV A. On November 3, 2008, we announced the initiation of the Morquio Clinical Assessment Program for patients with MSP IVA Syndrome and expect to initiate a Phase 1b clinical trial of GALNS in the first half of 2009.

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Manufacturing

We manufacture Naglazyme and Aldurazyme, which are both recombinant enzymes, in our approved Good Manufacturing Practices (GMP) production facility located in Novato, California. Vialing and packaging are performed by contract manufacturers. We believe that we have ample operating capacity to support the commercial demand of both Naglazyme and Aldurazyme through at least the next five years.

Our facilities have been licensed by the U.S. Food and Drug Administration (FDA), or the EC and health agencies in other countries for the commercial production of Aldurazyme and Naglazyme. Our facilities and those of any third-party manufacturers will be subject to periodic inspections confirming compliance with applicable law. Our facilities must be GMP certified before we can manufacture our drugs for commercial sales.

Kuvan is manufactured on a contract basis. There are two approved manufacturers of the active pharmaceutical ingredient (API) for Kuvan. In general, we expect to continue to contract with outside service providers for certain manufacturing services, including final product vialing and packaging operations for our recombinant enzymes and API production and tableting for Kuvan. Third-party manufacturers facilities are subject to periodic inspections confirming compliance with applicable law and must be GMP certified. We believe that our current agreements with third party manufacturers provide for ample operating capacity to support the anticipated commercial demand for Kuvan. In certain instances, there is only one approved contract manufacturer for certain aspects of the manufacturing process. In such cases, we attempt to prevent disruption of supplies through supply agreements, maintaining safety stock and other appropriate strategies. Although we have never experienced a disruption in supply from our contract manufacturers, we cannot provide assurance that we will not experience a disruption in the future.

Raw Materials

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

sourcing strategies, especially for critical raw materials. Although to date we have not experienced any significant delays in obtaining any raw materials from our suppliers, we cannot provide assurance that we will not face shortages from one or more of them in the future.

Sales and Marketing

We have established a commercial organization to support our product lines directly in the U.S., Europe, Latin America and Turkey. For other selected markets, we have signed agreements with other companies to act as distributors of Naglazyme. Most of these agreements generally grant the distributor the right to market the product in the territory and the obligation to secure all necessary regulatory approvals for commercial or named patient sales. Additional markets are being assessed at this time and additional agreements may be signed in the future. We maintain a relatively small sales force in the U.S. that markets Naglazyme and Kuvan and in the E.U. that markets Naglazyme. We believe that the size of our sales force is appropriate to effectively reach our target audience in markets where Naglazyme and Kuvan are directly marketed. We utilize third-party logistics companies to store and distribute Naglazyme and Kuvan.

Pursuant to our prior joint venture agreement, Genzyme was responsible for sales, marketing, distribution, obtaining reimbursement worldwide and international regulatory submissions of Aldurazyme. Pursuant to the restructuring of our relationship with Genzyme, effective January 1, 2008, Genzyme has the exclusive right to distribute, market and sell Aldurazyme globally and is required to purchase its requirements exclusively from us. See *Commercial Products-Aldurazyme* for information regarding the restructuring of our relationship with Genzyme.

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Customers

Our Naglazyme and Kuvan customers include a limited number of specialty pharmacies and end-users, such as hospitals, which act as retailers. We also sell Naglazyme to our authorized European distributors and to certain larger pharmaceutical wholesalers, which act as intermediaries between us and end-users and generally do not stock quantities of Naglazyme. During 2008, 68% of our net Naglazyme and Kuvan product revenues were generated by six customers. Genzyme is our sole customer for Aldurazyme and is responsible for marketing and selling Aldurazyme to third parties.

Despite the significant concentration of customers, the demand for Naglazyme and Kuvan is driven primarily by patient therapy requirements and we are not dependent upon any individual distributor with respect to Naglazyme or Kuvan sales. Due to the pricing of Naglazyme and Kuvan and the limited number of patients, the specialty pharmacies and wholesalers generally carry a very limited inventory, resulting in sales of Naglazyme being closely tied to end-user demand. In the E.U., hospital customers are generally serviced by an authorized distributor, which is our primary customer in the E.U.

Competition

The biopharmaceutical industry is rapidly evolving and highly competitive. The following is a summary analysis of known competitive threats for each of our major product programs:

Naglazyme, Aldurazyme and GALNS for Morquio Syndrome Type A (MPS IV A)

We know of no active competitive program for enzyme replacement therapy for MPS VI, MPS I, or MPS IV A that has entered clinical trials. However, we know of one other company that has a preclinical competitive product for MPS IV A. It is our understanding that this company has suspended its development efforts for technical and financial reasons.

Bone marrow transplantation has been used to treat severely affected patients, generally under the age of two, with some success. Bone marrow transplantation is associated with high morbidity and mortality rates as well as with problems inherent in the procedure itself; including graft vs. host disease, graft rejection and donor availability, which limits its utility and application. There are other developing technologies that are potential competitive threats to enzyme replacement therapies. However, we know of no such technology that has entered clinical trials related to MPS VI, MPS I, or MPS IV A.

Kuvan and PEG-PAL

There are currently no other approved drugs for the treatment of PKU. PKU is commonly treated with a medical food diet that is highly-restrictive and unpalatable. We perceive medical foods as a complement to Kuvan and PEG-PAL and not a significant competitive threat. Dietary supplements of large neutral amino acids (LNAA) have also been used in the treatment of PKU. This treatment may be a competitive threat to Kuvan and PEG-PAL. However, because LNAA is a dietary supplement, the FDA has not evaluated any claims of efficacy of LNAA.

With respect to Kuvan, we are aware of one other company that produces forms of 6R-BH4 (or BH4) for sale outside of Japan, and that BH4 has been used in certain instances for the treatment of PKU. We do not believe, but cannot know for certain, that this company is currently actively developing BH4 in sponsored trials as a drug product to treat PKU in the U.S. or E.U. Although a significant amount of specialized knowledge and resources would be required to develop and commercially produce BH4 as a drug product to treat PKU in the

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U.S. and E.U., this company may build or acquire the capability to do so. Additionally, we are aware that another company is developing an oral enzyme therapy to treat PKU; however we understand that the therapy is in an early stage of preclinical development.

With respect to BH4 as a drug product to treat endothelial dysfunction, there is currently no comparable directly competing product on the market. However, there is a significant amount of competition for the treatment of hypertension, peripheral arterial disease and other conditions associated with endothelial dysfunction through other active ingredients, some of which are currently on the market or are in development. We believe that the BH4 mechanism of action is unique and has multiple levels of benefit, with a good safety profile. We are not currently aware of other companies that are actively developing or conducting clinical trials of BH4 for the treatment of hypertension, peripheral arterial disease and other conditions associated with endothelial dysfunction.

Patents and Proprietary Rights

Our success depends on an intellectual property portfolio that supports our future revenue streams and also erects barriers to our competitors. We are maintaining and building our patent portfolio through: filing new patent applications; prosecuting existing applications; licensing and acquiring new patents and patent applications; and enforcing our issued patents. Furthermore, we seek to protect our ownership of know-how, trade secrets and trademarks through an active program of legal mechanisms including assignments, confidentiality agreements, material transfer agreements, research collaborations and licenses.

The number of our issued patents now stands at approximately 252, including approximately 42 patents issued by the U.S. Patent and Trademark Office (USPTO). Furthermore, our portfolio of pending patent applications totals approximately 384 applications, including approximately 23 pending U.S. applications.

With respect to Naglazyme, we have five issued patents including a U.S. patent that covers our ultrapure *N*-acetylgalactosamine-4-sulfatase compositions of Naglazyme, methods of treating deficiencies of *N*-acetylgalactosamine-4-sulfatase, including MPS VI, and methods of producing and purifying such ultrapure *N*-acetylgalactosamine-4-sulfatase compositions. A second U.S. patent covers the use of any recombinant human *N*-acetylgalactosamine-4-sulfatase to treat MPS VI at approved doses.

With respect to Kuvan and BH4, we have or have licensed a number of patents and pending patent applications that relate generally to formulations and forms of our drug substance, and methods of use for various indications under development and the dose regimen. With respect to the pending patent applications, unless and until actually issued, the protective value of these applications is impossible to determine.

We have 19 issued patents, including six U.S. patents related to Aldurazyme. These patents cover our ultra-pure alpha-L-iduronidase composition of Aldurazyme, methods of treating deficiencies of alpha-L-iduronidase by administering pharmaceutical compositions comprising such ultra-pure alpha-L-iduronidase, a method of purifying such ultra-pure alpha-L-iduronidase and the use of compositions of ultra-pure biologically active fragments of alpha-L-iduronidase.

Three U.S. patents on alpha-L-iduronidase are owned by an affiliate of Women s and Children s Hospital Adelaide. We have examined such issued U.S. patents, the related U.S. and foreign applications and their file histories, the prior art and other information. Corresponding foreign applications were filed in Canada, Europe and Japan. The European application was rejected and abandoned and cannot be re-filed. After a failure to timely file a court challenge to the Japanese Board of Appeals decision upholding the final rejection of all claims in the corresponding

Japanese application, the Japanese application has also lapsed and cannot be re-filed. Claims in the related Canadian application have recently issued. We believe that such patents and patent applications may not survive a challenge to patent validity. However, the processes of patent law are uncertain and any patent proceeding is subject to multiple unanticipated outcomes. We believe that it is in the best interest of our joint

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venture with Genzyme to market Aldurazyme with commercial diligence, in order to provide MPS I patients with the benefits of Aldurazyme. We believe that these patents and patent applications do not affect our ability to market Aldurazyme in Europe. As described above, a European patent application with similar claims was rejected by the European Patent Office, abandoned by the applicants, and cannot be re-filed.

Government Regulation

We operate in a highly regulated industry, which is subject to significant federal, state, local and foreign regulation. Our present and future business has been, and will continue to be, subject to a variety of laws including, the Federal Food, Drug and Cosmetic Act or FDC Act, the Medicaid rebate program, the Veterans Health Care Act of 1992, and the Occupational Safety and Health Act, among others.

The FDC Act and other federal and state statutes and regulations govern the testing, manufacture, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products. As a result of these laws and regulations, product development and product approval processes are very expensive and time consuming.

FDA Approval Process

In the U.S., pharmaceutical products are subject to extensive regulation by the FDA. The FDC Act and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications or NDAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical product development in the U.S. typically involves preclinical laboratory and animal tests, the submission to the FDA of a notice of claimed investigational exemption or an investigational new drug application or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not commented on or questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations, good clinical practices or GCP, as well as under protocols detailing the objectives of the trial, the

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parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population, to determine the effectiveness of the drug for a particular indication or indications, dosage tolerance and optimum dosage, and identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product s pharmacology, chemistry, manufacture, and controls.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for non-priority drug products are reviewed within ten months. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with current good manufacturing practices or cGMPs, is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues an approval letter, an approvable letter or a not-approvable letter. Both approvable and not-approvable letters generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. It is not unusual, however, for the FDA to reject an application because it believes that the drug is not safe enough or effective enough or because it does not believe that the data submitted are reliable or conclusive.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling

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restrictions which can materially affect the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The Hatch-Waxman Act

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant s product or FDA approved method of using this product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. ANDA applicants are not required to conduct or submit results of pre-clinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA s Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product s listed patents or that such patents are invalid is called a Paragraph IV certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which the FDA cannot grant effective approval of an ANDA based on that listed drug.

Other Regulatory Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet.

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Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control as well as drug manufacture, packaging, and labeling procedures must continue to conform to current good manufacturing practices, or cGMPs, after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the agency inspects manufacturing facilities to access compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Pediatric Information

Under the Pediatric Research Equity Act of 2003, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan drug designation has been granted.

Fast Track Designation

The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a fast track drug concurrent with or after the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor s request.

In addition to other benefits such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track drug s NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA s time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority Review

Under the FDA policies, a drug candidate is eligible for priority review, or review within a six-month time frame from the time a complete NDA is accepted for filing, if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. A fast track designated drug candidate would ordinarily meet the FDA s criteria for priority review.

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Accelerated Approval

Under the FDA s accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the safety and efficacy data of an existing product, or published literature, in support of its application.

Section 505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon certain preclinical or clinical studies conducted for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) NDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Thus approval of a Section 505(b)(2) NDA can be delayed until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) NDA applicant.

Food and Drug Administration Amendments Act of 2007

On September 27, 2007, the Food and Drug Administration Amendments Act, or the FDAAA, was enacted into law, amending both the FDC Act and the Public Health Service Act. The FDAAA makes a number of substantive and incremental changes to the review and approval processes in ways that could make it more difficult or costly to obtain approval for new pharmaceutical products, or to produce, market and distribute existing pharmaceutical products. Most significantly, the law changes the FDA s handling of post market drug product safety issues by giving the FDA authority to require post approval studies or clinical trials, to request that safety information be provided in labeling, or to require an NDA applicant to submit and execute a Risk Evaluation and Mitigation Strategy, or REMS.

The FDAAA also reauthorized the authority of the FDA to collect user fees to fund the FDA s review activities and made certain changes to the user fee provisions to permit the use of user fee revenue to fund the FDA s drug safety activities and the review of Direct-to-Consumer, or DTC advertisements.

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The FDAAA also reauthorized and amended the PREA. The most significant changes to PREA are intended to improve FDA and applicant accountability for agreed upon pediatric assessments.

Orphan Drug Designation

Naglazyme, Aldurazyme and Kuvan have received orphan drug designations from the FDA. Orphan drug designation is granted by the FDA to drugs intended to treat a rare disease or condition, which for this program is defined as having a prevalence of less than 200,000 individuals in the U.S. Orphan drug designation must be requested before submitting a marketing application. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug.

Orphan drug designation does not shorten the regulatory review and approval process for an orphan drug, nor does it give that drug any advantage in the regulatory review and approval process. However, if an orphan drug later receives approval for the indication for which it has designation, the relevant regulatory authority may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years in the U.S. Although obtaining approval to market a product with orphan drug exclusivity may be advantageous, we cannot be certain:

that we will be the first to obtain approval for any drug for which we obtain orphan drug designation;

that orphan drug designation will result in any commercial advantage or reduce competition; or

that the limited exceptions to this exclusivity will not be invoked by the relevant regulatory authority.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Regulation in the European Union

Drugs are also subject to extensive regulation outside of the United States. In the E.U., for example, there is a centralized approval procedure that authorizes marketing of a product in all countries of the E.U. (which includes most major countries in Europe). If this procedure is not used, approval in one country of the E.U. can be used to obtain approval in another country of the E.U. under two simplified application processes, the mutual recognition procedure or the decentralized procedure, both of which rely on the principle of mutual recognition. After receiving regulatory approval through any of the European registration procedures, pricing and reimbursement approvals are also required in most

countries.

A similar system for orphan drug designation exists in the E.U. Naglazyme, Aldurazyme and Kuvan received orphan medicinal product designation by the European Committee for Orphan Medicinal Products. Orphan designation does not shorten the regulatory review and approval process for an orphan drug, nor does it give that drug any advantage in the regulatory review and approval process. However, if an orphan drug later receives approval for the indication for which it has designation, the relevant regulatory authority may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for 10 years in the E.U.

Employees

As of February 6, 2009, we had 649 full-time employees, 287 of whom are in operations, 181 of whom are in research and development, 101 of whom are in sales and marketing and 80 of whom are in administration.

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We consider our employee relations to be good. Our employees are not covered by a collective bargaining agreement. We have not experienced employment related work stoppages.

Research and Development

For information regarding research and development expenses incurred during 2006, 2007 and 2008 see Item 7, *Management Discussion and Analysis of Financial Condition and Results of Operations Research and Development* .

Geographic Area Financial Information

Our chief operating decision makers (i.e., chief executive officer, certain of his direct reports and our board of directors) review financial information on a consolidated basis, for the purposes of allocating resources and evaluating financial performance. There are no segment managers who are held accountable by the chief operating decision makers, or anyone else, for operations, operating results and planning for levels or components below the consolidated unit level. Accordingly, we consider ourselves to have a single reporting segment and operating unit structure.

Net product revenues by geography are based on patients locations for Naglazyme and Kuvan, and are based on Genzyme s U.S. location for Aldurazyme. The following table outlines revenues and long-lived assets by geographic area (in thousands):

	Year Ended December 31,		
	2006	2007	2008
Net product revenues:			
United States	$ 18,593	$ 18,072	$ 140,418
Europe	27,932	51,878	63,333
Latin America	496	6,409	25,250
Rest of the World	2,585	10,443	22,850
Total net product revenues	$ 49,606	$ 86,802	$ 251,851

	Year Ended December 31,	
	2007	2008
Long-lived assets:		
United States	$ 126,550	$ 167,644
International	890	1,355

Total long-lived assets	$ 127,440	$ 168,999

Other Information

We were incorporated in Delaware in October 1996 and began operations on March 21, 1997. Our principal executive offices are located at 105 Digital Drive, Novato, California 94949 and our telephone number is (415) 506-6700. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, proxy statements, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act are available free of charge at *www.bmrn.com* as soon as reasonably practicable after electronically filing such reports with the U.S. Securities and Exchange Commission (SEC). Such reports and other information may be obtained by visiting the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549 or by calling the SEC at 1-800-SEC-0330. Additionally, these reports are available at the SEC s website at *http://www.sec.gov*. Information contained in our website is not part of this or any other report that we file with or furnish to the SEC.

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Item 1A. Risk Factors

An investment in our securities involves a high degree of risk. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our securities to decline, and you may lose all or part of your investment.

If we continue to incur operating losses for a period longer than anticipated, we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

Since we began operations in March 1997, we have been engaged in very substantial research and development and have operated at a net loss until 2008. Although we were profitable during 2008, based on our current business plans, we expect to operate at an annual net loss for 2009 and possibly beyond. Our future profitability depends on our marketing and selling of Naglazyme and Kuvan, the successful commercialization of Aldurazyme by Genzyme, the receipt of regulatory approval of our product candidates, our ability to successfully manufacture and market any approved drugs, either by ourselves or jointly with others, and our spending on our development programs. The extent of our future losses and the timing of profitability are highly uncertain. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

If we fail to obtain the capital necessary to fund our operations, our financial results and financial condition will be adversely affected and we will have to delay or terminate some or all of our product development programs.

We may require additional financing to fund our future operations, including the commercialization of our approved drugs and drug product candidates currently under development, preclinical studies and clinical trials, and potential licenses and acquisitions. We may be unable to raise additional financing if needed due to a variety of factors, including our financial condition, the status of our product programs, and the general condition of the financial markets. If we fail to raise additional financing if we need such funds, we may have to delay or terminate some or all of our product development programs and our financial condition and operating results will be adversely affected.

We expect to continue to spend substantial amounts of capital for our operations for the foreseeable future. The amount of capital we will need depends on many factors, including:

- our ability to successfully market and sell Naglazyme;
- our ability to successfully market and sell Kuvan;
- Genzyme s ability to successfully commercialize Aldurazyme;
- the progress, timing and scope of our preclinical studies and clinical trials;

the time and cost necessary to obtain regulatory approvals and the costs of post-marketing studies which may be required by regulatory authorities;

the time and cost necessary to develop commercial manufacturing processes, including quality systems, and to build or acquire manufacturing capabilities;

the time and cost necessary to respond to technological and market developments;

any changes made to or new developments in our existing collaborative, licensing and other commercial relationships or any new collaborative, licensing and other commercial relationships that we may establish; and

whether our convertible debt is converted to common stock in the future.

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Moreover, our fixed expenses such as rent, license payments, interest expense and other contractual commitments are substantial and may increase in the future. These fixed expenses may increase because we may enter into:

- additional licenses and collaborative agreements;
- additional contracts for product manufacturing; and
- additional financing facilities.

We believe that our cash, cash equivalents and short-term investment securities at December 31, 2008 will be sufficient to meet our operating and capital requirements for the foreseeable future based on our current long-term business plans. These estimates are based on assumptions and estimates, which may prove to be wrong. We may need to raise additional funds from equity or debt securities, loans or collaborative agreements if we are unable to satisfy our liquidity requirements. The sale of additional securities may result in additional dilution to our stockholders. Furthermore, additional financing may not be available in amounts or on terms satisfactory to us or at all. This could result in the delay, reduction or termination of our research, which could harm our business.

To obtain regulatory approval to market our products, preclinical studies and costly and lengthy preclinical and clinical trials are required and the results of the studies and trials are highly uncertain.

As part of the regulatory approval process, we must conduct, at our own expense, preclinical studies in the laboratory and clinical trials on humans for each product candidate. We expect the number of preclinical studies and clinical trials that the regulatory authorities will require will vary depending on the product candidate, the disease or condition the drug is being developed to address and regulations applicable to the particular drug. Generally, the number and size of clinical trials required for approval increases based on the expected patient population that may be treated with a drug. We may need to perform multiple preclinical studies using various doses and formulations before we can begin clinical trials, which could result in delays in our ability to market any of our product candidates. Furthermore, even if we obtain favorable results in preclinical studies, the results in humans may be significantly different. After we have conducted preclinical studies, we must demonstrate that our drug products are safe and efficacious for use in the targeted human patients in order to receive regulatory approval for commercial sale.

Adverse or inconclusive clinical results would stop us from filing for regulatory approval of our product candidates. Additional factors that can cause delay or termination of our clinical trials include:

- slow or insufficient patient enrollment;
- slow recruitment of, and completion of necessary institutional approvals at, clinical sites;
- longer treatment time required to demonstrate efficacy;
- lack of sufficient supplies of the product candidate;

adverse medical events or side effects in treated patients;

lack of effectiveness of the product candidate being tested; and

regulatory requests for additional clinical trials.

Typically, if a drug product is intended to treat a chronic disease, as is the case with some of our product candidates, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more.

If we fail to obtain or maintain orphan drug exclusivity for some of our products, our competitors may sell products to treat the same conditions and our revenues will be reduced.

As part of our business strategy, we intend to develop some drugs that may be eligible for FDA and E.U. orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is

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a drug intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S. The company that first obtains FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. Similar regulations are available in the E.U. with a 10-year period of market exclusivity.

Because the extent and scope of patent protection for some of our drug products is limited, orphan drug designation is especially important for our products that are eligible for orphan drug designation. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition and our revenues will be reduced.

Even though we have obtained orphan drug designation for certain of our products and product candidates and even if we obtain orphan drug designation for our future product candidates, due to the uncertainties associated with developing pharmaceutical products, we may not be the first to obtain marketing approval for any particular orphan indication. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

If we fail to maintain regulatory approval to commercially market and sell our drugs, or if approval is delayed, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.

We must obtain regulatory approval before marketing or selling our drug products in the U.S. and in foreign jurisdictions. In the U.S., we must obtain FDA approval for each drug that we intend to commercialize. The FDA approval process is typically lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. Naglazyme, Aldurazyme and Kuvan have received regulatory approval to be commercially marketed and sold in the U.S., E.U. and other countries. If we fail to obtain regulatory approval for our other product candidates, we will be unable to market and sell those drug products. Because of the risks and uncertainties in pharmaceutical development, our product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval.

From time to time during the regulatory approval process for our products and our product candidates, we engage in discussions with the FDA and foreign regulatory authorities regarding the regulatory requirements for our development programs. To the extent appropriate, we accommodate the requests of the regulatory authorities and, to date, we have generally been able to reach reasonable accommodations and resolutions regarding the underlying issues. However, we are often unable to determine the outcome of such deliberations until they are final. If we are unable to effectively and efficiently resolve and comply with the inquiries and requests of the FDA and foreign regulatory authorities, the approval of our product candidates may be delayed and their value may be reduced.

After any of our products receive regulatory approval, they remain subject to ongoing regulation, including, for example, changes to the product labeling, new or revised regulatory requirements for manufacturing practices and reporting adverse reactions and other information. If we do not comply with the applicable regulations, the range of possible sanctions includes issuance of adverse publicity, product recalls or seizures, fines, total or partial suspensions of production and/or distribution, suspension of marketing applications, enforcement actions, including injunctions and civil or criminal prosecution. The FDA and foreign regulatory agencies can withdraw a product s approval under some circumstances, such as the failure to comply with regulatory requirements or unexpected safety issues. Further, the government authorities may condition approval of

our product candidates

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on the completion of additional post-marketing clinical studies. These post-marketing studies may suggest that a product causes undesirable side effects or may present a risk to the patient. If data we collect from post-marketing studies suggest that one of our approved products may present a risk to safety, the government authorities could withdraw our product approval, suspend production or place other marketing restrictions on our products. If regulatory sanctions are applied or if regulatory approval is delayed or withdrawn, the value of our company and our operating results will be adversely affected. Additionally, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased.

If we fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.

Before we can begin commercial manufacture of our products, we, or our contract manufacturer, must obtain regulatory approval of our manufacturing facilities, processes and quality systems. In addition, pharmaceutical manufacturing facilities are continuously subject to inspection by the FDA, the State of California and foreign regulatory authorities, before and after product approval. Our manufacturing facilities have been inspected and licensed by the State of California for pharmaceutical manufacture and have been approved by the FDA, the EC and health agencies in other countries for the manufacture of Aldurazyme, and by the FDA and EC for the manufacture of Naglazyme. In addition, our third-party manufacturers facilities involved with the manufacture of Naglazyme, Kuvan and Aldurazyme have also been inspected and approved by various regulatory authorities.

Due to the complexity of the processes used to manufacture our products and product candidates, we may be unable to continue to pass or initially pass federal or international regulatory inspections in a cost effective manner. For the same reason, any potential third-party manufacturer of Naglazyme, Kuvan, and Aldurazyme or our product candidates may be unable to comply with GMP regulations in a cost effective manner.

If we, or third-party manufacturers with whom we contract, are unable to comply with manufacturing regulations, we may be subject to fines, unanticipated compliance expenses, recall or seizure of our products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

If we are unable to successfully develop manufacturing processes for our drug products to produce sufficient quantities at acceptable costs, we may be unable to meet demand for our products and lose potential revenue, have reduced margins or be forced to terminate a program.

Due to the complexity of manufacturing our products we may not be able to manufacture drug products successfully with a commercially viable process or at a scale large enough to support their respective commercial markets or at acceptable margins.

Improvements in manufacturing processes typically are very difficult to achieve and are often very expensive and may require extended periods of time to develop. If we contract for manufacturing services with an unproven process, our contractor is subject to the same uncertainties, high standards and regulatory controls, and may therefore experience difficulty if further process development is necessary.

Even a developed manufacturing process can encounter difficulties due to changing regulatory requirements, human error, mechanical breakdowns, malfunctions of internal information technology systems, and other events that cannot always be prevented or anticipated. Many of

the processes include biological systems, which add significant complexity, as compared to chemical synthesis. We expect that, from time to time, consistent with biotechnology industry expectations, certain production lots will fail to produce product that meets our quality control release acceptance criteria. To date, our historical failure rates for all of our product programs, including Naglazyme and Aldurazyme, have been within our expectations, which are based on industry norms.

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In order to produce product within our time and cost parameters, we must continue to produce product within our expected success rate and yield expectations. Because of the complexity of our manufacturing processes, it may be difficult or impossible for us to determine the cause of any particular lot failure and we must effectively take corrective action in response to any failure in a timely manner.

Although we have entered into contractual relationships with third-party manufacturers to produce the active ingredient in Kuvan, 6R-BH4, if those manufacturers are unwilling or unable to fulfill their contractual obligations, we may be unable to meet demand for that product or sell that product at all and we may lose potential revenue. We also rely on third parties for portions of the manufacture of Naglazyme and Aldurazyme. If those manufacturers are unwilling or unable to fulfill their contractual obligations, we may be unable to meet demand for these products or sell these products at all and we may lose potential revenue. Further, the availability of suitable contract manufacturing capacity at scheduled or optimum times is not certain.

In addition, our manufacturing processes subject us to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of hazardous materials and wastes resulting from their use. We may incur significant costs in complying with these laws and regulations.

If we are unable to effectively address manufacturing issues, we may be unable to meet demand for our products and lose potential revenue, have reduced margins, or be forced to terminate a program.

Our manufacturing facility for Naglazyme and Aldurazyme is located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facility and equipment, or that of our third-party manufacturers or single-source suppliers, which could materially impair our ability to manufacture Naglazyme and Aldurazyme or our third-party manufacturer s ability to manufacture Kuvan.

Our Galli Drive facility is our only manufacturing facility for Naglazyme and Aldurazyme. It is located in the San Francisco Bay Area near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We, and the third-party manufacturers with whom we contract and our single-source suppliers of raw materials, are also vulnerable to damage from other types of disasters, including fires, floods, power loss and similar events. If any disaster were to occur, or any terrorist or criminal activity caused significant damage to our facilities or the facilities of our third-party manufacturers and suppliers, our ability to manufacture Naglazyme and Aldurazyme, or to have Kuvan manufactured, could be seriously, or potentially completely impaired, and our Naglazyme, Kuvan, and Aldurazyme commercialization efforts, revenue from the sale of Naglazyme, Kuvan and Aldurazyme could be seriously impaired. The insurance we maintain and our risk mitigation plans, may not be adequate to cover our losses resulting from disasters or other business interruptions.

Supply interruptions may disrupt our inventory levels and the availability of our products and cause delays in obtaining regulatory approval for our product candidates, or harm our business by reducing our revenues.

Numerous factors could cause interruptions in the supply of our finished products, including:

- timing, scheduling and prioritization of production by our contract manufacturers or a breach of our agreements by our contract manufacturers;

labor interruptions;

changes in our sources for manufacturing;

the timing and delivery of shipments;

our failure to locate and obtain replacement manufacturers as needed on a timely basis; and

conditions affecting the cost and availability of raw materials.

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Any interruption in the supply of finished products could hinder our ability to distribute finished products to meet commercial demand.

With respect to our product candidates, production of product is necessary to perform clinical trials and successful registration batches are necessary to file for approval to commercially market and sell product candidates. Delays in obtaining clinical material or registration batches could delay regulatory approval for our product candidates.

Because the target patient populations for some of our products are small, we must achieve significant market share and obtain high per-patient prices for our products to achieve profitability.

Naglazyme, Aldurazyme and Kuvan all target diseases with small patient populations. As a result, our per-patient prices must be relatively high in order to recover our development and manufacturing costs and achieve profitability. For Naglazyme, we believe that we will need to market worldwide to achieve significant market penetration of the product. Due to the expected costs of treatment for our products for genetic diseases, we may be unable to maintain or obtain sufficient market share at a price high enough to justify our product development efforts and manufacturing expenses.

If we fail to obtain an adequate level of reimbursement for our drug products by third-party payers, the sales of our drugs would be adversely affected or there may be no commercially viable markets for our products.

The course of treatment for patients using Naglazyme, Kuvan and Aldurazyme is expensive. We expect patients to need treatment throughout their lifetimes. We expect that most families of patients will not be capable of paying for this treatment themselves. There will be no commercially viable market for Naglazyme, Kuvan or Aldurazyme without reimbursement from third-party payers. Additionally, even if there is a commercially viable market, if the level of reimbursement is below our expectations, our revenue and gross margins will be adversely affected.

Third-party payers, such as government or private health care insurers, carefully review and increasingly challenge the prices charged for drugs. Reimbursement rates from private companies vary depending on the third-party payer, the insurance plan and other factors. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis.

Reimbursement in the E.U. must be negotiated on a country-by-country basis and in many countries the product cannot be commercially launched until reimbursement is approved. The negotiation process in some countries can exceed 12 months.

For our future products, we will not know what the reimbursement rates will be until we are ready to market the product and we actually negotiate the rates. If we are unable to obtain sufficiently high reimbursement rates for our products, they may not be commercially viable or our future revenues and gross margins may be adversely affected.

A significant portion of our international sales are made based on special access programs, and changes to these programs could adversely affect our product sales and revenue in these countries.

We make a significant portion of our international sales of Naglazyme through special access or named patient programs, which do not require full product approval. The specifics of the programs vary from country to country. Generally, special approval must be obtained for each patient. The approval normally requires an application or a lawsuit accompanied by evidence of medical need. Generally, the approvals for each patient must be renewed from time to time.

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These programs are not well defined in some countries and are subject to changes in requirements and funding levels. Any change to these programs could adversely affect our ability to sell product in those countries and delay sales. If the programs are not funded by the respective government, there could be insufficient funds to pay for all patients.

Without the special access programs we would need to seek full product approval to commercially market and sell the products. This can be an expensive and time-consuming process. Because the number of patients is so small in some countries, it may not be economically feasible to seek and maintain a full product approval, and therefore the sales in such country would be permanently reduced or eliminated. For all of these reasons, if the special access programs that we are currently using are eliminated or restricted, our revenues could be adversely affected.

If we fail to compete successfully with respect to product sales, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product and our revenue could be adversely affected.

Our competitors may develop, manufacture and market products that are more effective or less expensive than ours. They may also obtain regulatory approvals for their products faster than we can obtain them (including those products with orphan drug designation) or commercialize their products before we do. If we do not compete successfully, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product.

In the future, government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenue and results of operations.

We expect that, in the future, reimbursement will be increasingly restricted both in the U.S. and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. Governmental and private third-party payers have proposed health care reforms and cost reductions. A number of federal and state proposals to control the cost of health care, including the cost of drug treatments, have been made in the U.S. In some foreign markets, the government controls the pricing, which can affect the profitability of drugs. Current government regulations and possible future legislation regarding health care may affect reimbursement for medical treatment by third-party payers, which may render our products not commercially viable or may adversely affect our future revenues and gross margins.

In the U.S., we expect branded pharmaceutical products to be subject to increasing pricing pressures. Implementation of the Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA), which provides an out-patient prescription drug benefit under the Medicare program, became effective on January 1, 2006. While it is difficult to predict the final business impact of this legislation, there is additional risk associated with increased pricing pressures. While the MMA prohibits the Secretary of Health and Human Services (HHS) from directly negotiating prescription drug prices with manufacturers, we expect continued challenges to that prohibition over the next several years. Also, the MMA retains the authority of the HHS to prohibit the importation of prescription drugs, but we expect Congress to consider several measures that could remove that authority and allow for importation of products into the U.S. regardless of their safety or cost. If adopted, such legislation would likely have a negative effect on our U.S. sales.

As a result of the passage of the MMA, aged and disabled patients jointly eligible for Medicare and Medicaid receive certain prescription drug benefits through Medicare, instead of Medicaid, as of January 1, 2006. This may relieve some state budget pressures but is unlikely to result in reduced pricing pressures. Additionally, in the U.S., we are required to provide rebates to state governments on their purchases of certain of our products under state Medicaid programs. Many states have begun to implement supplemental rebates and restricted formularies in their Medicaid programs, and these programs are expected to continue in the post-MMA environment. Other cost containment measures have been

adopted or proposed by federal, state, and local

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government entities that provide or pay for health care. In most international markets, we operate in an environment of government-mandated cost containment programs, which may include price controls, reference pricing, discounts and rebates, restrictions on physician prescription levels, restrictions on reimbursement, compulsory licenses, health economic assessments, and generic substitution. Several states are also attempting to extend discounted Medicaid prices to non-Medicaid patients. Additionally, notwithstanding the federal law prohibiting pharmaceutical importation, several states have implemented importation schemes for their citizens, usually involving a website that links patients to selected Canadian pharmacies. At least one state has such a program for its state employees. In the absence of federal action to curtail state activities, we expect other states to launch importation efforts. As a result, we expect pressures on pharmaceutical pricing to continue.

International operations are also generally subject to extensive price and market regulations, and there are many proposals for additional cost-containment measures, including proposals that would directly or indirectly impose additional price controls or reduce the value of our intellectual property portfolio. As part of these cost containment measures, some countries have imposed or threatened to impose revenue caps limiting the annual volume of sales of Naglazyme. To the extent that these caps are significantly below actual demand, our future revenues and gross margins may be adversely affected.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenue and results of operations.

If we are found in violation of federal or state fraud and abuse laws, we may be required to pay a penalty or be suspended from participation in federal or state health care programs, which may adversely affect our business, financial condition and results of operation.

We are subject to various federal and state health care fraud and abuse laws, including antikickback laws, false claims laws and laws related to ensuring compliance. The federal health care program antikickback statute makes it illegal for any person, including a pharmaceutical company, to knowingly and willfully offer, solicit, pay or receive any remuneration, directly or indirectly, in exchange for or to induce the referral of business, including the purchase, order or prescription of a particular drug, for which payment may be made under federal health care programs, such as Medicare and Medicaid. Under federal government regulations, certain arrangements (safe harbors) are deemed not to violate the federal antikickback statute. We seek to comply with these safe harbors. False claims laws prohibit anyone from knowingly and willfully presenting or causing to be presented for payment to third party payers (including government payers) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services that were not provided as claimed, or claims for medically unnecessary items or services. Other cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products has resulted in the submission of false claims to government health care programs. Under the Health Insurance Portability and Accountability Act of 1996, we also are prohibited from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payers, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and/or exclusion or suspension from federal and state health care programs such as Medicare and Medicaid.

Many states have adopted laws similar to the federal antikickback statute, some of which apply to referral of patients for health care services reimbursed by any source, not just governmental payers. In addition, California passed a law that requires pharmaceutical companies to comply with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and the PhRMA Code on Interactions with Healthcare Professionals.

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Neither the government nor the courts have provided definitive guidance on the application of these laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. While we believe we have structured our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, we are required to pay a penalty or are suspended or excluded from participation in federal or state health care programs, our business, financial condition and results of operation may be adversely affected.

We conduct a significant amount of our sales and operations outside of the United States, which subjects us to additional business risks that could adversely affect our revenue and results of operations.

A significant portion of the sales of Aldurazyme and Naglazyme are generated from countries other than the United States. Additionally, we have operations in several European countries, Brazil and Turkey. We expect that we will continue to expand our foreign operations in the future. International operations inherently subject us to a number of risks and uncertainties, including:

- changes in foreign regulatory requirements;
- fluctuations in foreign currency exchange rates;
- political and economic instability;
- diminished protection of intellectual property in some countries outside of the United States;
- trade protection measures and import or export licensing requirements;
- difficulty in staffing and managing foreign operations;
- differing labor regulations and business practices; and
- potentially negative consequences from changes in tax laws or if foreign jurisdictions successfully challenge our interpretation of local taxation.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations.

As we expand our existing international operations, we may encounter new risks. For example, as we focus on building our international sales and distribution networks in new geographic regions, we must continue to develop relationships with qualified local distributors and trading companies. If we are not successful in developing these relationships, we may not be able to grow sales in these geographic regions. These or other similar risks could adversely affect our revenue and profitability.

If we are unable to protect our proprietary technology, we may not be able to compete as effectively.

Where appropriate, we seek patent protection for certain aspects of our technology. Patent protection may not be available for some of the products we are developing. If we must spend significant time and money protecting our patents, designing around patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed.

The patent positions of biopharmaceutical products are complex and uncertain. The scope and extent of patent protection for some of our products and product candidates are particularly uncertain because key information on some of our product candidates has existed in the public domain for many years. The composition and genetic sequences of animal and/or human versions of Naglazyme, Aldurazyme, and many of our product candidates have been published and are believed to be in the public domain. The chemical structure of BH4 has also been published. Publication of this information may prevent us from obtaining composition-of-matter patents, which are generally believed to offer the strongest patent protection.

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For enzymes or compounds with no prospect of broad composition-of-matter patents, other forms of patent protection or orphan drug status may provide us with a competitive advantage. As a result of these uncertainties, investors should not rely solely on patents as a means of protecting our products or product candidates, including Naglazyme, Kuvan, Aldurazyme or PEG-PAL.

We own or license patents and patent applications related to Naglazyme, Kuvan, Aldurazyme and certain of our product candidates. However, these patents and patent applications do not ensure the protection of our intellectual property for a number of reasons, including the following:

- We do not know whether our patent applications will result in issued patents. For example, we may not have developed a method for treating a disease before others developed similar methods.

- Competitors may interfere with our patent process in a variety of ways. Competitors may claim that they invented the claimed invention prior to us. Competitors may also claim that we are infringing on their patents and therefore cannot practice our technology as claimed under our patent. Competitors may also contest our patents by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our issued patents are not valid for a number of reasons. If a court agrees, we would lose that patent. We have no meaningful experience with competitors interfering with our patents or patent applications.

- Enforcing patents is expensive and may absorb significant time of our management. Management would spend less time and resources on developing products, which could increase our operating expenses and delay product programs.

- Receipt of a patent may not provide much practical protection. If we receive a patent with a narrow scope, then it will be easier for competitors to design products that do not infringe on our patent.

In addition, competitors also seek patent protection for their technology. Due to the number of patents in our field of technology, we cannot be certain that we do not infringe on those patents or that we will not infringe on patents granted in the future. If a patent holder believes our product infringes on their patent, the patent holder may sue us even if we have received patent protection for our technology. If someone else claims we infringe on their technology, we would face a number of issues, including the following:

- Defending a lawsuit takes significant time and can be very expensive.

- If the court decides that our product infringes on the competitor s patent, we may have to pay substantial damages for past infringement.

- The court may prohibit us from selling or licensing the product unless the patent holder licenses the patent to us. The patent holder is not required to grant us a license. If a license is available, we may have to pay substantial royalties or grant cross licenses to our patents.

- Redesigning our product so it does not infringe may not be possible or could require substantial funds and time.

It is also unclear whether our trade secrets are adequately protected. While we use reasonable efforts to protect our trade secrets, our employees or consultants may unintentionally or willfully disclose our information to competitors. Enforcing a claim that someone else illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts

outside the U.S. are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how.

We may also support and collaborate in research conducted by government organizations, hospitals, universities or other educational institutions. These research partners may be unwilling to grant us any exclusive rights to technology or products derived from these collaborations prior to entering into the relationship.

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If we do not obtain required licenses or rights, we could encounter delays in our product development efforts while we attempt to design around other patents or even be prohibited from developing, manufacturing or selling products requiring these licenses. There is also a risk that disputes may arise as to the rights to technology or products developed in collaboration with other parties.

The U.S. Patent and Trademark Office (USPTO) has issued three patents to a third-party that relate to alpha-L-iduronidase and a related patent has issued in Canada. If we are not able to successfully challenge these patents or a related patent in Japan, if it issues, we may be prevented from producing Aldurazyme in countries with issued patents unless and until we obtain a license.

The USPTO has issued three patents to Women s and Children s Hospital Adelaide that cover composition-of-matter, isolated genomic nucleotide sequences, vectors including the sequences, host cells containing the vectors, and method of use claims for human, recombinant alpha-L-iduronidase. Aldurazyme is based on human, recombinant alpha-L-iduronidase. A corresponding patent application was filed by a third party in the European Patent Office claiming composition-of-matter for human, recombinant alpha-L-iduronidase, and it was rejected over prior art and withdrawn and cannot be re-filed. The corresponding Japanese application was finally rejected by the Japanese Board of Appeals and the application, also lapsed after failure to timely file a court challenge, and cannot be re-filed. We do not know whether the Japanese application will issue or the scope of the claims that would issue. A corresponding Canadian patent recently issued and covers enzyme, pharmaceutical composition, nucleic acid encoding the enzyme, host and cell vector. We believe that these patents, and the Japanese patent application, if issued, are invalid or not infringed on a number of grounds. In addition, under U.S. law, issued patents are entitled to a presumption of validity, and a challenge to the U.S. patents may be unsuccessful. Even if we are successful, challenging the patents may be expensive, require our management to devote significant time to this effort and may adversely impact commercialization of Aldurazyme in the U.S. and Canada (or in Japan, should a patent issue arise in that country.)

If our Manufacturing, Marketing and Sales Agreement with Genzyme were terminated, we could be barred from commercializing Aldurazyme or our ability to successfully commercialize Aldurazyme would be delayed or diminished.

Either party may terminate the Manufacturing, Marketing and Sales Agreement (MMS Agreement) between Genzyme and us related to Aldurazyme for specified reasons, including if the other party is in material breach of the agreement, has experienced a change of control, or has declared bankruptcy and also is in breach of the agreement. Although we are not currently in breach of this agreement and we believe that Genzyme is not currently in breach of this agreement, there is a risk that either party could breach the agreement in the future. Either party may also terminate the agreement upon one year prior written notice for any reason.

If the MMS Agreement is terminated for breach, the breaching party will transfer its interest in the LLC to the non-breaching party, and the non-breaching party will pay a specified buyout amount for the breaching party s interest in Aldurazyme and in the LLC. If we are the breaching party, we would lose our rights to Aldurazyme and the related intellectual property and regulatory approvals. If the MMS Agreement is terminated without cause, the non-terminating party would have the option, exercisable for one year, to buy out the terminating party s interest in Aldurazyme and in the LLC at a specified buyout amount. If such option is not exercised, all rights to Aldurazyme will be sold and the LLC will be dissolved. In the event of termination of the buy out option without exercise by the non-terminating party as described above, all right and title to Aldurazyme is to be sold to the highest bidder, with the proceeds to be split between Genzyme and us in accordance with our percentage interest in the LLC.

If the MMS Agreement is terminated by either party because the other party declared bankruptcy, the terminating party would be obligated to buy out the other party and would obtain all rights to Aldurazyme exclusively. If the MMS Agreement is terminated by a party because the other party experienced a change of control, the terminating party shall notify the other party, the offeree, of its intent to buy out the offeree s interest in Aldurazyme and the LLC for a stated amount set by the terminating party at its discretion. The offeree must

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then either accept this offer or agree to buy the terminating party s interest in Aldurazyme and the LLC on those same terms. The party who buys out the other party would then have exclusive rights to Aldurazyme. The Amended and Restated Collaboration Agreement between us and Genzyme will automatically terminate upon the effective date of the termination of the MMS Agreement and may not be terminated independently from the MMS Agreement.

If we were obligated, or given the option, to buy out Genzyme s interest in Aldurazyme and the LLC, and gain exclusive rights to Aldurazyme, we may not have sufficient funds to do so and we may not be able to obtain the financing to do so. If we fail to buy out Genzyme s interest we may be held in breach of the agreement and may lose any claim to the rights to Aldurazyme and the related intellectual property and regulatory approvals. We would then effectively be prohibited from developing and commercializing Aldurazyme.

Our strategic alliance with Merck Serono may be terminated at any time by Merck Serono, and if it is terminated, our expenses could increase and our operating performance could be adversely affected.

Merck Serono may terminate the agreement forming our strategic alliance with them at any time by giving 90 days prior written notice if such termination occurs prior to the commercialization of any of the products licensed under our agreement, or by giving 180 days prior written notice if such termination occurs after the commercialization of such a product. Either Merck Serono or we may terminate our strategic alliance under certain circumstances, including if the other party is in material breach of the agreement and does not remedy the breach within a specified period of time, or has suffered certain financial difficulties, including filing for bankruptcy or making an assignment for the benefit of creditors. Although we are not currently in breach of the agreement and we believe that Merck Serono is not currently in breach of the agreement, there is a risk that either party could breach the agreement in the future. Upon a termination of the agreement by Merck Serono by giving notice or by us for a material breach by Merck Serono, all rights licensed to us under the agreement become irrevocable and fully-paid except in those countries where restricted by applicable law or for all intellectual property that Merck Serono does not own.

Upon a termination of the agreement by Merck Serono for a material breach by us or based on our financial difficulty, or upon the expiration of the royalty term of the products licensed under the agreement, all rights licensed to Merck Serono under the agreement become irrevocable and fully-paid upon the payment of amounts due by Merck Serono to us which accrued prior to the expiration of the royalty term, except in those countries where restricted by applicable law or for all intellectual property that we do not own and for which we do not have a royalty-free license. Upon a termination of the agreement for a material breach by us or for our financial difficulty, all rights and licenses granted by Merck Serono to us under or pursuant to the agreement will automatically terminate. Under the terms of our agreement with Merck Serono, Merck Serono is responsible to pay for a portion of the development costs of products developed pursuant to such agreement. However, at any time upon 90 days notice, Merck Serono can opt out of this responsibility. If Merck Serono opts out, or if the agreement is terminated by either Merck Serono or us, and we continue the development of products related to that agreement, we would be responsible for 100% of future development costs, our expenses could increase and our operating performance could be adversely affected.

If we fail to compete successfully with respect to acquisitions, joint venture or other collaboration opportunities, we may be limited in our ability to develop new products and to continue to expand our product pipeline.

Our competitors compete with us to attract organizations for acquisitions, joint ventures, licensing arrangements or other collaborations. To date, several of our product programs have been acquired through acquisitions, such as PEG-PAL, and several of our product programs have been developed through licensing or collaborative arrangements, such as Naglazyme, Aldurazyme and Kuvan. These collaborations include licensing proprietary technology from, and other relationships with, academic research institutions. Our future success will depend, in part, on our ability to identify additional opportunities and to successfully enter into partnering or acquisition agreements for those opportunities. If our competitors successfully enter into partnering arrangements

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or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Since each of these opportunities is unique, we may not be able to find a substitute. Several pharmaceutical and biotechnology companies have already established themselves in the field of genetic diseases. These companies, including Genzyme, have already begun many drug development programs, some of which may target diseases that we are also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

Universities and public and private research institutions also compete with us. While these organizations primarily have educational or basic research objectives, they may develop proprietary technology and acquire patents that we may need for the development of our product candidates. We will attempt to license this proprietary technology, if available. These licenses may not be available to us on acceptable terms, if at all. If we are unable to compete successfully with respect to acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to develop new products and to continue to expand our product pipeline.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

We depend upon our key personnel and our ability to attract and retain employees.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. The loss of the services of any member of our senior management or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. In particular, the loss of one or more of our senior executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. While certain of our senior executive officers are parties to employment agreements with us, these agreements do not guarantee that they will remain employed with us in the future. In addition, in many cases, these agreements do not restrict our senior executive officers ability to compete with us after their employment is terminated. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

Our success depends on our ability to manage our growth.

Our product candidates are intended for patient populations that are significantly larger than any of MPS I, MPS VI or PKU. In order to continue development and marketing of these products, if approved, we will need to significantly expand our operations. To manage expansion

effectively, we need to continue to develop and improve our research and development capabilities, manufacturing and quality capacities, sales and marketing capabilities and financial and administrative systems. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties.

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Changes in methods of treatment of disease could reduce demand for our products and adversely affect revenues.

Even if our drug products are approved, if doctors elect a course of treatment which does not include our drug products, this decision would reduce demand for our drug products and adversely affect revenues. For example, if gene therapy becomes widely used as a treatment of genetic diseases, the use of enzyme replacement therapy, such as Naglazyme and Aldurazyme in MPS diseases could be greatly reduced. Changes in treatment method can be caused by the introduction of other companies products or the development of new technologies or surgical procedures which may not directly compete with ours, but which have the effect of changing how doctors decide to treat a disease.

If product liability lawsuits are successfully brought against us, we may incur substantial liabilities.

We are exposed to the potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceuticals. We maintain insurance against product liability lawsuits for commercial sale of our products and for the clinical trials of our product candidates. Pharmaceutical companies must balance the cost of insurance with the level of coverage based on estimates of potential liability. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with the commercial use of Orapred, our clinical trials and commercial use of Naglazyme, Kuvan and Aldurazyme, or our clinical trials for BH4 or PEG-PAL, for which our insurance coverage may not be adequate.

The product liability insurance we will need to obtain in connection with the commercial sales of our product candidates if and when they receive regulatory approval may be unavailable in meaningful amounts or at a reasonable cost. In addition, while we continue to take what we believe are appropriate precautions, we may be unable to avoid significant liability if any product liability lawsuit is brought against us. If we are the subject of a successful product liability claim that exceeds the limits of any insurance coverage we obtain, we may incur substantial charges that would adversely affect our earnings and require the commitment of capital resources that might otherwise be available for the development and commercialization of our product programs.

Our business is affected by macroeconomic conditions.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and foreign currency exchange rates and overall economic conditions and uncertainties, including those resulting from the current and future conditions in the global financial markets. For instance, if inflation or other factors were to significantly increase our business costs, it may not be feasible to pass through price increases on to our customers due to the process by which health care providers are reimbursed for our products by the government. Interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the value of our investments and our ability to liquidate our investments in order to fund our operations. We purchase or enter into a variety of transactions, including investments in commercial paper, the extension of credit to corporations, institutions and governments and enter into hedging contracts. If any of the issuers or counter parties to these instruments were to default on their obligations, it could materially reduce the value of the transaction and adversely affect our cash flows.

Interest rates and the ability to access credit markets could also adversely affect the ability of our customers/distributors to purchase, pay for and effectively distribute our products. Similarly, these macroeconomic factors could affect the ability of our contract manufacturers, sole-source or single-source suppliers to remain in business or otherwise manufacture or supply product. Failure by any of them to remain a going concern could affect our ability to manufacture products.

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Our stock price may be volatile, and an investment in our stock could suffer a decline in value.

Our valuation and stock price since the beginning of trading after our initial public offering have had no meaningful relationship to current or historical earnings, asset values, book value or many other criteria based on conventional measures of stock value. The market price of our common stock will fluctuate due to factors including:

- product sales and profitability of Naglazyme, Aldurazyme and Kuvan;
- manufacture, supply or distribution of Naglazyme, Aldurazyme or Kuvan;
- progress of our product candidates through the regulatory process;
- results of clinical trials, announcements of technological innovations or new products by us or our competitors;
- government regulatory action affecting our product candidates or our competitors drug products in both the U.S. and foreign countries;
- developments or disputes concerning patent or proprietary rights;
- general market conditions and fluctuations for the emerging growth and pharmaceutical market sectors;
- economic conditions in the U.S. or abroad;
- broad market fluctuations in the U.S. or in the E.U.;
- actual or anticipated fluctuations in our operating results; and
- changes in company assessments or financial estimates by securities analysts.

In addition, the value of our common stock may fluctuate because it is listed on the Nasdaq Global Select Market. Listing on the exchange may increase stock price volatility due to:

- trading in different time zones;
- different ability to buy or sell our stock;

different market conditions in different capital markets; and

different trading volume.

In the past, following periods of large price declines in the public market price of a company s securities, securities class action litigation has often been initiated against that company. Litigation of this type could result in substantial costs and diversion of management s attention and resources, which would hurt our business. Any adverse determination in litigation could also subject us to significant liabilities. In addition, the current decline in the financial markets and related factors beyond our control, including the credit and mortgage crisis in the U.S. and worldwide, may cause our stock price to decline rapidly and unexpectedly.

Anti-takeover provisions in our charter documents, our stockholders rights plan and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of our company more difficult, even if a change in control would be beneficial to the stockholders. Our anti-takeover provisions include provisions in our certificate of incorporation providing that stockholders meetings may only be called by the board of directors and provisions in our bylaws providing that the stockholders may not take action by written consent and requiring that stockholders that desire to nominate any person for election to the board of directors or to make any proposal with respect to business to be conducted at a meeting of our stockholders be submitted in appropriate form to our Secretary within a specified period of time in advance of any such meeting. Additionally, our board of directors has the authority to issue an additional 249,886 shares of preferred stock and to determine

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the terms of those shares of stock without any further action by our stockholders. The rights of holders of our common stock are subject to the rights of the holders of any preferred stock that may be issued. The issuance of preferred stock could make it more difficult for a third-party to acquire a majority of our outstanding voting stock. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future.

In 2002, our board of directors authorized a stockholder rights plan and related dividend of one preferred share purchase right for each share of our common stock outstanding at that time. In connection with an increase in our authorized common stock, our board approved an amendment to this plan in June 2003. Our board of directors approved an additional amendment to the stockholder rights plan in February 2009. As long as these rights are attached to our common stock, we will issue one right with each new share of common stock so that all shares of our common stock will have attached rights. When exercisable, each right will entitle the registered holder to purchase from us one two-hundredth of a share of our Series B Junior Participating Preferred Stock at a price of $35.00 per 1/200 of a Preferred Share, subject to adjustment.

The rights are designed to assure that all of our stockholders receive fair and equal treatment in the event of any proposed takeover of us and to guard against partial tender offers, open market accumulations and other abusive tactics to gain control of us without paying all stockholders a control premium. The rights will cause substantial dilution to a person or group that acquires 15% or more of our stock on terms not approved by our board of directors. However, the rights may have the effect of making an acquisition of us, which may be beneficial to our stockholders, more difficult, and the existence of such rights may prevent or reduce the likelihood of a third-party making an offer for an acquisition of us.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

The following table contains information about our current significant owned and leased properties:

Location	Approximate Square Feet	Use	Lease Expiration Date
Several locations in Novato, California	163,000	Corporate headquarters, office and laboratory	2009-2019
Galli Drive facility, Novato, California	70,000	Clinical and commercial manufacturing and laboratory	NA: owned property
Bel Marin Keys facility, Novato, California	85,400	Technical operations, finance, administration, and laboratory	NA: owned property
Sierra Point Parkway facility, Brisbane, California	20,000	Biostatistics and office	2011

Our administrative office space and plans to develop additional space are expected to be adequate for the foreseeable future. In addition to the above, we also maintain small offices in London, England, Sao Paulo, Brazil, and Turkey. During 2009 and beyond, we plan to expand the capacity of our production facilities in order to meet future market demands and product development requirements. We believe that, to the extent required,

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we will be able to lease or buy additional facilities at commercially reasonable rates. We plan to use contract manufacturing when appropriate to provide product for both clinical and commercial requirements until such time as we believe it prudent to develop additional in-house clinical and/or commercial manufacturing capacity.

Item 3. Legal Proceedings

We have no material legal proceedings pending.

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

No matters were submitted to a vote of our security holders during the quarter ended December 31, 2008.

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Part II

Item 5. Market for Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is listed under the symbol BMRN on the Nasdaq Global Select Market. The following table sets forth the range of high and low quarterly closing sales prices for our common stock for the periods noted, as reported by Nasdaq.

		Prices	
Year	Period	High	Low
2007	First Quarter	$ 20.53	$ 15.53
2007	Second Quarter	$ 19.00	$ 15.95
2007	Third Quarter	$ 25.00	$ 17.63
2007	Fourth Quarter	$ 37.17	$ 24.81
2008	First Quarter	$ 40.39	$ 31.90
2008	Second Quarter	$ 39.72	$ 28.92
2008	Third Quarter	$ 32.55	$ 25.60
2008	Fourth Quarter	$ 26.29	$ 13.59

On February 17, 2009, the last reported sale price on the Nasdaq Global Select Market for our common stock was $18.11. We have never paid any cash dividends on our common stock and we do not anticipate paying cash dividends in the foreseeable future.

Equity Compensation Plans

We incorporate information regarding the securities authorized for issuance under our equity compensation plans into this section by reference from the section captioned Equity Compensation Plans in the proxy statement for our 2009 annual meeting of stockholders.

Issuer Purchase of Equity Securities

We did not make any purchases of our common stock during the year ended December 31, 2008.

Holders

As of February 17, 2009, there were 70 holders of record of 99,945,778 outstanding shares of our common stock. Additionally, on such date, options to acquire 12,223,016 shares of our common stock were outstanding.

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Performance Graph

The following is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933 or the Securities Exchange Act of 1934, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing.

The following graph shows the value of an investment of $100 on December 31, 2003 in BioMarin common stock, the Nasdaq Composite Index (U.S.) and the Nasdaq Biotechnology Index. All values assume reinvestment of the pretax value of dividends paid by companies included in these indices and are calculated as of December 31 of each year. Our common stock is traded on the Nasdaq Global Select Market and is a component of both the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The comparisons shown in the graph are based upon historical data and we caution that the stock price performance shown in the graph is not indicative of, nor intended to forecast, the potential future performance of our stock.

	12/31/03	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08
BioMarin Pharmaceutical Inc.	100.00	82.35	138.92	211.21	456.19	229.38
NASDAQ Composite	100.00	110.06	112.92	126.61	138.33	80.65
NASDAQ Biotechnology	100.00	112.17	130.53	130.05	132.24	122.10

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Item 6. Selected Consolidated Financial Data

The selected consolidated financial data set forth below contains only a portion of our financial statement information and should be read in conjunction with the consolidated financial statements and related notes and *Management s Discussion and Analysis of Financial Condition and Results of Operations* included in this annual report.

We derived the consolidated statement of operations data for the years ended December 31, 2004, 2005, 2006, 2007, and 2008 and consolidated balance sheet data as of December 31, 2004, 2005, 2006, 2007, and 2008 from audited financial statements. Historical results are not necessarily indicative of results that we may experience in the future.

	Year ended December 31, (in thousands, except for per share data)				
	2004	2005	2006	2007	2008
Consolidated statements of operations data:					
Revenues:					
Net product revenues	$ 18,641	$ 13,039	$ 49,606	$ 86,802	$ 251,851
Collaborative agreement revenues		12,630	18,740	28,264	38,907
Royalty and license revenues			15,863	6,515	5,735
Total revenues	18,641	25,669	84,209	121,581	296,493
Operating expenses:					
Cost of sales	3,953	2,629	8,740	18,359	52,509
Research and development	49,784	56,391	66,735	78,600	93,291
Selling, general and administrative	37,606	41,556	48,507	77,539	106,566
Amortization of acquired intangible assets	3,987	1,144	3,651	4,371	4,371
Acquired in-process research and development	31,453				
Impairment of acquired intangible assets	68,251				
Total operating expenses	195,034	101,720	127,633	178,869	256,737
Income (loss) from operations	(176,393)	(76,051)	(43,424)	(57,288)	39,756
Equity in the income (loss) of BioMarin/Genzyme LLC	(2,972)	11,838	19,274	30,525	(2,270)
Interest income	2,466	1,861	12,417	25,932	16,388
Interest expense	(10,544)	(11,918)	(13,411)	(14,243)	(16,394)
Debt conversion expense			(3,315)		
Impairment loss on investment					(4,056)
Net income (loss) before income taxes	(187,443)	(74,270)	(28,459)	(15,074)	33,424
Provision for income taxes			74	729	2,593
Net income (loss)	$ (187,443)	$ (74,270)	$ (28,533)	$ (15,803)	$ 30,831
Net income (loss) per share, basic	$ (2.91)	$ (1.08)	$ (0.34)	$ (0.16)	$ 0.31

Net income (loss) per share, diluted	$ (2.91)	$ (1.08)	$ (0.34)	$ (0.16)	$ 0.29
Weighted average common shares outstanding, basic	64,354	68,830	84,582	95,878	98,975
Weighted average common shares outstanding, diluted	64,354	68,830	84,582	95,878	103,572

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	December 31, (in thousands)				
	2004	2005	2006	2007	2008
Consolidated balance sheet data:					
Cash, cash equivalents and short-term investments	$ 48,815	$ 47,792	$ 288,847	$ 585,594	$ 559,792
Total current assets	85,159	68,941	334,224	644,297	737,696
Total assets	232,966	195,303	463,436	815,279	906,695
Long-term liabilities, net of current portion	230,890	232,398	299,589	566,010	499,939
Total stockholders equity (deficit)	(67,978)	(77,462)	117,802	187,726	276,675

You should read the following tables presenting our unaudited quarterly results of operations in conjunction with the consolidated financial statements and related notes contained elsewhere in this Annual Report on Form 10-K. We have prepared this unaudited information on the same basis as our audited consolidated financial statements. Our quarterly operating results have fluctuated in the past and may continue to do so in the future as a result of a number of factors, including, but not limited to, the timing and nature of research and development activities.

	Quarter Ended			
	March 31	June 30	September 30	December 31
	(In thousands, except per share data, unaudited)			
2008:				
Total revenue	$ 60,396	$ 64,174	$ 72,646	$ 99,277
Net income	1,686	3,810	829	24,506
Net income per share, basic	0.02	0.04	0.01	0.25
Net income per share, diluted	0.02	0.04	0.01	0.21
2007:				
Total revenue	$ 22,838	$ 28,884	$ 25,006	$ 44,853
Net income (loss)	(9,293)	(3,864)	(5,216)	2,570
Net income (loss) per share, basic	(0.10)	(0.04)	(0.05)	0.03
Net income (loss) income per share, diluted	(0.10)	(0.04)	(0.05)	0.03

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

This Form 10-K contains forward-looking statements as defined under securities laws. Many of these statements can be identified by the use of terminology such as believes, expects, anticipates, plans, may, will, projects, continues, estimates, potential, opportunity a These forward-looking statements may be found in Overview, and other sections of this Form 10-K. Our actual results or experience could differ significantly from the forward-looking statements. Factors that could cause or contribute to these differences include those discussed in *Risk Factors* in this Form 10-K. You should carefully consider that information before you make an investment decision.

You should not place undue reliance on these statements, which speak only as of the date that they were made. These cautionary statements should be considered in connection with any written or oral forward-looking statements that we may issue in the future. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the filing of this Form 10-K to reflect later events or circumstances, or to reflect the occurrence of unanticipated events.

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and notes to those statements included elsewhere in this Annual Report on Form 10-K.

Overview

We develop and commercialize innovative biopharmaceuticals for serious diseases and medical conditions. We select product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market. Our product portfolio is comprised of three approved products and multiple investigational product candidates. Approved products include Naglazyme, Aldurazyme, and Kuvan.

Naglazyme received marketing approval in the U.S. in May 2005, in the E.U. in January 2006, and subsequently in other countries. Naglazyme net product revenues for 2007 totaled $86.2 million and increased to $132.7 million for 2008.

Aldurazyme has been approved for marketing in the U.S., E.U., and in other countries. Prior to 2008, we developed and commercialized Aldurazyme through a joint venture with Genzyme. Effective January 2008, we restructured our relationship with Genzyme whereby Genzyme sells Aldurazyme to third parties and we recognize royalty revenue on net sales by Genzyme. We recognize a portion of the royalty as product transfer revenue when product is released to Genzyme and all obligations related to the transfer have been fulfilled. The product transfer revenue represents the fixed amount per unit of Aldurazyme that Genzyme is required to pay us if the product is unsold by Genzyme. The amount of product transfer revenue will eventually be deducted from the calculated royalties earned when the product is sold by Genzyme. Our Aldurazyme net product revenue for 2008 totaled $72.5 million.

Kuvan was granted marketing approval in the U.S. in December 2007 and in the E.U. in December 2008. Kuvan net product revenues for 2007 and 2008 totaled $0.4 million and $46.7 million, respectively.

We are developing PEG-PAL, an experimental enzyme substitution therapy for the treatment of PKU, for patients that are not responsive to Kuvan. In May 2008, we initiated a Phase 1 clinical trial of PEG-PAL in PKU patients. We expect to complete this 35 patient, open label study in the first half of 2009. The primary objective of this study is to assess the safety and tolerability of single subcutaneous injections of PEG-PAL in subjects with PKU. In 2007 and early 2008 we devoted substantial resources to the development of 6R-BH4, the active ingredient in Kuvan, for the treatment of certain cardiovascular indications including peripheral arterial disease and sickle cell disease. We released data from several 6R-BH4 trials in early February 2009. We expect to start

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clinical trails of GALNS, an enzyme replacement therapy for the treatment of MPS IVA, in the first half of 2009. We are conducting preclinical development of several other enzyme product candidates for genetic and other diseases, and a small molecule for the treatment of Duchenne muscular dystrophy.

Key components of our results of operations for the years ended December 31, 2006, 2007 and 2008, include the following:

	2006	2007	2008
Total net product revenues	$ 49,606	$ 86,802	$ 251,851
Collaborative agreement revenues	18,740	28,264	38,907
Cost of sales	8,740	18,359	52,509
Research and development expense	66,735	78,600	93,291
Selling, general and administrative expense	48,507	77,539	106,566
Net income (loss)	(28,533)	(15,803)	30,831
Stock-based compensation expense	9,590	18,283	25,250

See *Results of Operations* for discussion of the detailed components and analysis of the amounts above. Our cash, cash equivalents, and short-term investments totaled $559.8 million as of December 31, 2008 compared to $585.6 million as of December 31, 2007.

Critical Accounting Policies and Estimates

In preparing our consolidated financial statements, we make assumptions, judgments and estimates that can have a significant impact on our net income (loss), as well as on the value of certain assets and liabilities on our consolidated balance sheets. We base our assumptions, judgments and estimates on historical experience and various other factors that we believe to be reasonable under the circumstances. Actual results could differ materially from these estimates under different assumptions or conditions. On a regular basis, we evaluate our assumptions, judgments and estimates and make changes accordingly. Unless otherwise noted below, there have not been any recent changes to our assumptions, judgments or estimates included in our critical accounting policies. We believe that the assumptions, judgments and estimates involved in the accounting for the impairment of long-lived assets, revenue recognition and related reserves, income taxes, inventory, research and development and stock option plans have the greatest potential impact on our consolidated financial statements, so we consider these to be our critical accounting policies. Historically, our assumptions, judgments and estimates relative to our critical accounting policies have not differed materially from actual results. For further information on our critical and other accounting policies, see Note 2 to the accompanying consolidated financial statements.

Impairment of Long-Lived Assets

Our long-lived assets include our investment in BioMarin/Genzyme LLC, equity investment in Summit Corporation plc (Summit), property, plant and equipment, intangible assets and goodwill and, as of January 2009, an equity investment in La Jolla. We regularly review long-lived assets for impairment. The recoverability of goodwill and our equity investments in Summit and La Jolla are measured by available external market data, including quoted prices on public stock exchanges, and other relevant information. If the carrying amount of the asset is not recoverable, an impairment loss is recorded for the amount that the carrying value of the asset exceeds its fair value. No significant impairments were recognized for the years ended December 31, 2006 and 2007.

The recoverability of long-lived assets, other than goodwill and our equity investments in Summit and La Jolla, are measured by comparing the asset s carrying amount to the expected undiscounted future cash flows that the asset is expected to generate.

We currently operate in one business segment, the biopharmaceutical development and commercialization segment. When reviewing goodwill for impairment, we assess whether goodwill should be allocated to operating

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levels lower than our single operating segment for which discrete financial information is available and reviewed for decision-making purposes. These lower levels are referred to as reporting units. Currently, we have identified only one reporting unit as per Statement Financial Accounting Standard No. (SFAS) 142, *Goodwill and Other Intangible Assets*. The amount of our goodwill originated from the acquisition of the Orapred business in 2004. The Orapred business was eliminated as a reporting unit following the sublicense of North American rights for Orapred, which was previously our only separate reporting unit. Immediately prior to the sublicense, which was considered a triggering event, we performed an impairment test at the Orapred reporting unit level and determined that there was no impairment at March 2006. We perform an annual impairment test in the fourth quarter of each fiscal year by assessing the fair value and recoverability of our goodwill by comparing the carrying value of the reporting unit to its fair value as determined by available market value unless facts and circumstances warrant a review of goodwill for impairment before that time. No triggering events occurred during 2008 that required an impairment test.

Determining whether an impairment has occurred typically requires various estimates and assumptions, including determining which cash flows are directly related to the potentially impaired asset, the useful life over which cash flows will occur, their amount, and the asset s residual value, if any. In turn, measurement of an impairment loss requires a determination of fair value, which is based on the best information available. We use internal cash flow estimates, quoted market prices when available and independent appraisals as appropriate to determine fair value. We derive the required cash flow estimates from our historical experience and our internal business plans and apply an appropriate discount rate.

As a result of the restructuring of our joint venture with Genzyme, we have realized most of our investment in the joint venture through the distribution of cash and inventory in February 2008. We expect that our remaining ongoing investment in the joint venture will include our investment in the joint venture s cash on hand to fund certain research and development activities related to Aldurazyme and intellectual property management.

In 2008, we recorded an other-than-temporary impairment charge of $4.1 million for the decline in the value of our equity investment in Summit. The determination that the decline was other-than-temporary is, in part, subjective and influenced by several factors including, the length of time and the extent to which the market value of the shares had been less than the value at the time of purchase, Summit s financial condition and near-term prospects, including any events which may influence their operations, and our intent and ability to hold the investment for a period of time sufficient to allow for the anticipated recovery in market value. Based on the current market conditions, the low volume of trading in Summit securities and their current financial condition, we determined that our investment in Summit was other-than-temporarily impaired as of year end and adjusted the amount of our investment to the stock s market price on December 31, 2008.

The recoverability of the carrying value of buildings, leasehold improvements for our facilities and equipment will depend on the successful execution of our business initiatives and our ability to earn sufficient returns on our approved products and product candidates. Based on management s current estimates, we expect to recover the carrying value of such assets.

Revenue Recognition

We recognize revenue in accordance with the provisions of Securities and Exchange Commission Staff Accounting Bulletin No. 104 (SAB 104) *Revenue Recognition*, and Emerging Issues Task Force (EITF) Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*. Our revenues consist of net product revenues from Naglazyme and Orapred during 2006, Naglazyme and Kuvan product sales during 2007 and 2008, Aldurazyme product transfer and royalty revenues starting January 1, 2008, revenues from our collaborative agreement with Merck Serono and other license and royalty revenues. Milestone payments are recognized in full when the related milestone performance goal is achieved and we have no future performance obligations related to the payment.

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Naglazyme and Kuvan product revenues We recognize revenue from Naglazyme and Kuvan product sales when persuasive evidence of an arrangement exists, the product has been delivered to the customer, title and risk of loss have passed to the customer, the price to the buyer is fixed or determinable and collection from the customer is reasonably assured. Our product sales transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents. Amounts collected from customers and remitted to governmental authorities, which are primarily comprised of value-added taxes (VAT) in foreign jurisdictions, are presented on a net basis in our income statement, in that taxes billed to customers are not included as a component of net product sales, as per EITF Issue No. 06-3, *How Taxes Collected from Customers and Remitted to Governmental Authorities Should Be Presented in the Income Statement* .

In the U.S., Naglazyme and Kuvan are generally sold to specialty pharmacies or end-users, such as hospitals, which act as retailers. In the other countries, Naglazyme is generally sold to our authorized distributors and also to hospitals, which act as end-users. Because of the pricing of our products, the limited number of patients and the customers limited return rights, Naglazyme customers and retailers generally carry a limited inventory. We also sell our products to certain larger pharmaceutical wholesalers, which, with respect to Naglazyme and Kuvan, act as intermediaries between us and end-users and generally do not stock quantities of Naglazyme and Kuvan. Accordingly, we expect that sales related to our products will be closely tied to end-user demand. In the future we expect to receive a net royalty of approximately 4% on net sales of Kuvan in the E.U., which will be recorded as a component of Kuvan net product revenues.

We record reserves for rebates payable under Medicaid and other government programs as a reduction of revenue at the time product sales are recorded. Our reserve calculations require estimates, including estimates of sales mix, to determine which sales will be subject to rebates and the amount of such rebates. We update our estimates and assumptions each period, and record any necessary adjustments to our reserves. To the extent actual rebates differ from our estimates, additional reserves may be required or reserves may need to be reversed. We have not experienced significant adjustments historically and our estimates have been generally accurate to date.

We record allowances for product returns, if appropriate, as a reduction of revenue at the time product sales are recorded. Several factors are considered in determining whether an allowance for product returns is required, including market exclusivity of the product based on its orphan drug status, the patient population, the customers return rights which are limited to defective product or product that does not meet applicable regulatory specification at the time of delivery and our historical experience of returns for Naglazyme, which is a similar product to Kuvan. Based on these factors, management has concluded that Naglazyme and Kuvan product returns will be minimal. In the future, if any of these factors and/or the history of product returns changes, an allowance for product returns may be required.

Our historical experience with rebates and returns specific to Naglazyme, which was approved for commercial sale in the U.S. during the second quarter of 2005, serves as a reasonable basis for our estimates of rebates and returns for both Naglazyme and Kuvan. Management uses, to the extent available, current estimated sales mix of which sales will be eligible for rebates, estimated rebate rates for state Medicaid programs and other government programs, as well as experience obtained through the commercialization of Aldurazyme by our joint venture with Genzyme, which is a similar product to Naglazyme and Kuvan. Certain of our customers receive distributor fees based on sales volume. In accordance with EITF Issue No. 01-09, *Accounting for Consideration given by a Vendor to a Customer (including a Reseller of a Vendor s Products),* these fees are presumed to be a reduction of the selling price of Naglazyme and, therefore, are presented as a reduction of revenue on our consolidated statements of operations. We were able to leverage our experience with Naglazyme to determine our estimates for Kuvan, while also considering factors unique to the Kuvan product. The nature and amount of our current estimates of the applicable revenue dilution item that are currently applied to aggregate world-wide gross sales of Naglazyme and Kuvan to derive net sales are described in the table below.

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Revenue Dilution Item	Percentage of Gross Sales	Description
Rebates	2-4%	Rebates payable to state Medicaid, other government programs and certain managed care providers
Distributor fees	3-5%	Fees paid to authorized distributors
Cash Discounts	1-2%	Discounts offered to customers for prompt payment of accounts receivable
Total	6-11%	

We maintain a policy to record allowances for doubtful accounts for estimated losses resulting from the inability of Naglazyme and Kuvan customers to make required payments. As of December 31, 2008, we had not experienced any bad debts and our allowance for doubtful accounts was insignificant. However, since we cannot predict changes in the financial stability of our customers, we cannot guarantee that allowances will not be required in the future. If we begin to experience credit losses, our operating expenses would increase.

Aldurazyme product revenues We began recognizing revenue related to Aldurazyme in the first quarter of 2008 effective with the restructuring of our joint venture with Genzyme (see Note 5 to the accompanying consolidated financial statements for further information). According to the terms of the joint venture restructuring, we receive a 39.5% to 50% royalty on worldwide net Aldurazyme sales by Genzyme depending on sales volume, which is included in net product revenues in the consolidated statements of operations. We recognize a portion of this amount as product transfer revenue when product is released to Genzyme as all of our obligations have been fulfilled at this point and title to, and risk of loss for, the product has transferred to Genzyme. Genzyme s return rights for Aldurazyme are limited to defective product. The product transfer revenue represents the fixed amount per unit of Aldurazyme that Genzyme is required to pay us if the product is unsold by Genzyme. The amount of product transfer revenue will eventually be deducted from the calculated royalty amount earned when the product is sold by Genzyme. We record the Aldurazyme royalty revenue based on net sales information provided by Genzyme and recognize product transfer revenue based on the fulfillment of Genzyme purchase orders in accordance with SAB 104 and the terms of the related agreements with Genzyme. In periods where BioMarin shipments of Aldurazyme to Genzyme exceed quantities sold to third parties by Genzyme, we will report incremental product transfer revenue. In periods where Genzyme sales to third parties exceed quantities released by BioMarin to Genzyme, we will report net product revenue representing the royalty from Genzyme related to current period sales by Genzyme less the previously recognized product transfer revenue related to the net decrease in Aldurazyme quantities at Genzyme.

We rely on Genzyme s revenue recognition policies and procedures with respect to net product revenue reporting and our recording of Aldurazyme royalty revenue. Our experience with the commercial aspects of Aldurazyme through BioMarin/Genzyme LLC and our relationship with Genzyme provide a reasonable basis to place such reliance on Genzyme and to make our own internal judgments and estimates regarding Aldurazyme revenue recognition. Genzyme s historical judgments and estimates have been accurate and have not changed significantly over time.

We understand that Genzyme recognizes revenue from Aldurazyme product sales when persuasive evidence of an arrangement exists, the product has been delivered to the customer, title and risk of loss have passed to the customer, the price to the buyer is fixed or determinable and collection from the customer is reasonably assured. The timing of product shipment and receipts can have a significant impact on the amount of Aldurazyme royalty revenue that we recognize in a particular period. Also, Aldurazyme is sold in part through distributors. Inventory in the distribution channel consists of inventory held by distributors, and inventory held by retailers, such as pharmacies and hospitals. Aldurazyme royalty revenue in a particular period can be impacted by increases or decreases in distributor inventories. If distributor inventories increased to excessive levels, we could experience reduced royalty revenue in subsequent periods. To determine the amount of Aldurazyme inventory in the U.S.

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distribution channel, we understand that Genzyme receives data on sales and inventory levels directly from its primary distributors for the product.

Collaborative agreement revenues Collaborative agreement revenues from Merck Serono include both license revenue and contract research revenue. Nonrefundable up-front license fees where we have continuing involvement through research and development collaboration are initially deferred and recognized as license revenue over the estimated period for which we continue to have a performance obligation. License revenue for 2008 includes amortization of $5.2 million related to the $25.0 million up-front license fee received from Merck Serono recognized as revenue during the year and the $30.0 million milestone payment related to the EMEA approval of Kuvan. In December 2008, we fulfilled all performance obligations related to the $25.0 million up-front license fee received from Merck Serono, which was consistent with the previously estimated time period. License revenue for 2007 includes amortization of $6.9 million related to the $25.0 million up-front license fee received from Merck Serono recognized as revenue during the development period and the $15.0 million milestone payment related to the EMEA acceptance of the Kuvan filing. Milestone payments related to our collaborative agreements are recognized in full when the related milestone performance goal is achieved and we have no further performance obligations related to that payment.

Our estimates of the period over which we have an ongoing performance obligation are based on the contractual terms of the underlying arrangement, the level of effort required for us to fulfill our obligation and the anticipated timing of the fulfillment of our obligation. Accordingly, we previously deferred the up-front license fee received from Merck Serono and recognized it as revenue on a straight-line basis over approximately 3.4 years, which represented our estimate of the time from inception of the agreement until European regulatory approval of Kuvan for the treatment of PKU, at which point our performance obligations to Merck Serono for developing Kuvan for the treatment of PKU ended. There is no cost of sales associated with the amortization of the up-front license fee received from Merck Serono.

Nonrefundable reimbursements received for shared development costs are recognized as revenue in the period in which the related expenses are incurred. Contract research revenue included in collaborative agreement revenues represented Merck Serono s share of Kuvan development costs under the agreement, which are recorded as research and development expenses.

Royalty and license revenues We recognize royalty revenue and royalty receivables in the periods these royalties are earned, in advance of collection. Royalty revenue and receivables are based upon communication with the sublicensee. Due to the significant role we play in the operations of Aldurazyme, primarily the manufacturing and regulatory activities, as well as the rights and responsibilities to deliver the product to Genzyme, we elected not to classify the Aldurazyme royalty as other royalty revenues.

The timing of customer purchases and the resulting product shipments by our sublicensees have a significant impact on the amount of royalty revenue that we recognize in a particular period. The majority of Orapred sales are made to wholesalers, which, in turn, resell the product to retail outlets. Inventory in the distribution channel consists of inventory held by wholesalers, who are the principal customers for Orapred, and inventory held by retailers. Royalty revenues from Orapred sales in a particular period will be impacted by increases or decreases in wholesaler inventory levels. If wholesaler inventories continue to substantially exceed the retail demand, we could experience reduced royalty revenue in subsequent periods.

We deferred the up-front license fee of $2.5 million received from a third party for the North American Orapred rights, and recognized it as revenue on a straight-line basis over a period of approximately 5 months, which represented the estimated time from inception of the agreement until commercial launch of Orapred ODT, at which point our performance obligations ended. Our estimate of the Orapred ODT commercial launch period was based on several underlying assumptions about uncertain events, including actions by U.S. regulatory authorities and successful commercialization efforts by the third party. There are no cost of sales associated with the royalties and license revenues recorded during the period and we do not expect to incur related cost of sales in future periods. The commercial launch of Orapred ODT by our sublicensee occurred in August 2006.

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Milestone payments are recognized in full when the related milestone performance goal is achieved and we have no future performance obligations related to that payment. As a result of the FDA approval for the marketing application for Orapred ODT in June 2006, we received a milestone payment of $7.5 million, which was recorded as revenue during 2006. As a result of the commercial launch of Orapred ODT, we also recognized $4.0 million in milestone revenue during the third quarter of 2006. We also received a milestone payment of $4.0 million in June 2007 for the one-year anniversary of FDA approval of Orapred ODT. Although the receipt of the $4.0 million payment was based solely on the passage of time from FDA approval, we did not recognize the payment during the twelve-month period following approval because the fee was not considered to be fixed or determinable until the due and payable date. In making this determination, management considered the extended one-year payment term and the related uncertain future product sales and our lack of experience with the third party.

Inventory

We value inventories at the lower of cost or net realizable value. We determine the cost of inventory using the average cost method. We analyze our inventory levels quarterly and write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory quantities in excess of expected requirements. Expired inventory is disposed of and the related costs are written off to cost of sales. The determination of whether or not inventory costs will be realizable requires estimates by our management. A critical estimate in this determination is the estimate of the future expected inventory requirements, whereby we compare our internal sales forecasts to inventory on hand. Actual results may differ from those estimates and inventory write-offs may be required in the future.

Regulatory approval in the U.S. for Naglazyme was received in May 2005 and regulatory approval in the U.S. for Kuvan was received in December 2007, and costs related to the manufacturing of those products prior to these dates were expensed as research and development expenses. We consider regulatory approval of product candidates to be uncertain, and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained, as such, the related manufacturing costs for Naglazyme and Kuvan, prior to regulatory approval, were not capitalized as inventory. When regulatory approval was obtained in May 2005 for Naglazyme and in December 2007 for Kuvan, we began capitalizing inventory at the lower of cost or net realizable value for the respective products.

Stock-based compensation of $1.7 million was capitalized into inventory for the year ended December 31, 2007. Stock-based compensation of $4.6 million was capitalized into inventory in the year end December 31, 2008.

Research and Development

Research and development expenses include expenses associated with contract research and development provided by third parties, product manufacturing prior to regulatory approval, clinical and regulatory costs, and internal research and development costs. In instances where we enter into agreements with third parties for research and development activities, costs are expensed upon the earlier of when non-refundable amounts are due or as services are performed unless there is an alternative future use of the funds in other research and development projects. Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables.

A critical accounting assumption by our management is that we believe that regulatory approval of our product candidates is uncertain, and we do not assume that product manufactured prior to regulatory approval will be sold commercially. As a result, inventory costs for product candidates are expensed as research and development expenses until regulatory approval in a major market is obtained, at which time inventory is capitalized at the lower of cost or fair value. Historically, there have been no changes to this assumption.

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Stock Option Plans

We account for stock-based compensation in accordance with SFAS No. 123R, *Share-Based Payment*. Under the fair value recognition provisions of this statement, share-based compensation cost is measured at the grant date based on the value of the award and is recognized as expense over the vesting period. Determining the fair value of share-based awards at the grant date requires judgment, including estimating our stock price volatility and employee stock option exercise behaviors. If actual results differ significantly from these estimates, stock-based compensation expense and our results of operations could be materially impacted.

Our expected volatility is based upon proportionate weightings of the historical volatility of our stock and the implied volatility of traded options on our stock. The expected life of options is based on contractual life and observed historical exercise patterns, which can vary over time.

As stock-based compensation expense recognized in the consolidated statements of operations is based on awards ultimately expected to vest, the amount of expense has been reduced for estimated forfeitures. SFAS No. 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Forfeitures are estimated based on historical experience.

If factors change and we employ different assumptions in the application of SFAS No. 123R, the compensation expense that we record in future periods may differ significantly from what we have recorded in the current period.

Income taxes

We record a valuation allowance to reduce our deferred tax assets to the amount that is more likely than not to be realized. We have recorded a full valuation allowance against our net deferred tax assets, the principal amount of which is the tax effect of net operating loss carryforwards and tax credits of approximately $232 million at December 31, 2008. Future taxable income and ongoing prudent and feasible tax planning strategies have been considered in assessing the need for the valuation allowance. If we later determine that it is more- likely-than-not that the net deferred tax assets would be realized, the previously provided valuation allowance would be reversed. In order to realize our deferred tax assets we must be able to generate sufficient taxable income in the tax jurisdictions in which the deferred tax assets are located. This critical accounting assumption has been historically accurate, as we have not been able to utilize our net deferred tax assets prior to 2008. Although we have utilized portion of our net operating losses and tax credits to offset a portion of 2008 taxable income, we currently believe it is more-likely-than-not that we will not be able to realize our deferred tax assets beyond 2008. We developed this estimate by more-likely-than not scenarios for our long-term goals and financial projections. These projections included our estimates of future revenues and expenses based upon historical and estimated future results, and also considered the significant business uncertainties that are implicit in such projections. However, this assumption may change in the future as the uncertainty around the use of the deferred tax assets becomes more certain.

Recent Accounting Pronouncements

See Note 2(s) of our accompanying consolidated financial statements for a full description of recent accounting pronouncements and our expectation of their impact on our results of operations and financial condition.

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Results of Operations

BioMarin Results of Operations

Net Income (Loss)

Our net income for the year ended December 31, 2008 increased by $46.6 million to $30.8 million, from a net loss of $15.8 million for the year ended December 31, 2007. The increase in net income in 2008 is primarily a result of the following (in millions):

Net loss for the year ended December 31, 2007	$ (15.8)
Increased Naglazyme gross profit	38.9
Increased Aldurazyme gross profit	52.2
Increased Kuvan gross profit	40.0
Increased Kuvan royalty and license revenues	15.3
Increased research and development expenses	(14.7)
Increased selling, general and administrative expense	(29.0)
Increased losses from BioMarin/Genzyme LLC	(32.8)
Decreased interest income	(9.5)
Impairment charge on Summit investment	(4.1)
Absence of Orapred milestone revenue	(4.0)
Increased interest expense	(2.2)
Increased income tax expense	(1.9)
Other individually insignificant fluctuations	(1.6)
Net income for the year ended December 31, 2008	$ 30.8

The increase in Naglazyme gross profit during 2008 as compared to 2007 is primarily a result of additional patients initiating therapy outside the U.S. and the E.U. as well as the favorable impact of foreign currency exchange rates on Naglazyme sales from customers outside the U.S. The increase in Aldurazyme gross profit is attributed to the restructuring of our joint venture with Genzyme effective January 1, 2008. Prior to the restructuring we recognized our 50% share of the net income of BioMarin/Genzyme LLC as Equity in the income of BioMarin/Genzyme LLC in our consolidated statements of operations. The increase in Kuvan gross profit in 2008 compared to 2007 is attributed to the FDA approval of Kuvan, in December 2007 which resulted in approximately two weeks of Kuvan sales in 2007 compared to twelve months in 2008. The increase in Kuvan royalty and license revenues is primarily attributed to the $30.0 million milestone received in 2008 from Merck Serono for the EMEA approval of Kuvan offset by the absence of the $15.0 million milestone received in 2007 for the acceptance of the Kuvan EMEA filing. The increase in selling, general and administrative expense was primarily due to the continued international expansion of Naglazyme and commercialization of Kuvan in the U.S. The increase in research and development expense was primarily due to increases in development expense for GALNS, a licensed product for the treatment of Ducherne muscular dystrophy, and other early stage programs. See below for additional information related to the primary net income (loss) fluctuations presented above, including details of our operating expense fluctuations.

Our net loss for the year ended December 31, 2007 decreased by $12.7 million, to $15.8 million, from $28.5 million for the year ended December 31, 2006. Net loss for 2007 decreased primarily as a result of the following (in millions):

Net loss for the year ended December 31, 2006	$ (28.5)
Increased Naglazyme gross profit	28.5
Milestone revenue related to the Kuvan EMEA filing	15.0
Increased profits from BioMarin/Genzyme LLC	11.3
Decreased net Orapred profits, including license revenues	(10.5)
Increased research and development expense	(11.9)
Increased selling, general and administrative expense	(29.0)
Increased interest income	13.5
Decreased other collaborative agreement revenues	(5.5)
Absence of debt conversion expense	3.3
Increase in corporate overhead and other	(2.0)
Net loss for the year ended December 31, 2007	$ (15.8)

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The increase in Naglazyme gross profit during 2007 as compared to 2006 is primarily the result of additional patients initiating Naglazyme therapy in the U.S., E.U. and other countries. The decrease in collaborative agreement revenues primarily relates to lower reimbursable development costs for Kuvan. The increase in selling, general and administrative expense was primarily due to the continued international expansion of our Naglazyme commercialization and preparation for commercializing Kuvan. The decrease in Orapred profits primarily relates to the timing of the milestone payments under the Orapred sublicense. See below for additional information related to the primary net loss fluctuations presented above, including details of our operating expense fluctuations.

Net Product Revenues and Gross Profit

The following table shows a comparison of net product revenues for the years ended December 31, 2006, 2007 and 2008 (in millions):

	Years Ended December 31,				
	2006	2007	2008	2006 vs. 2007	2007 vs. 2008
Naglazyme	$ 46.5	$ 86.2	$ 132.7	$ 39.7	$ 46.5
Kuvan		0.4	46.7	0.4	46.3
Aldurazyme			72.5		72.5
Orapred	3.1	0.2		(2.9)	(0.2)
Total net product revenues	$ 49.6	$ 86.8	$ 251.9	$ 37.2	$ 165.1

2008 as Compared to 2007

Net product revenues for Naglazyme in 2008 totaled $132.7 million, of which $111.2 million was earned from end-user customers based outside the U.S. The positive impact of foreign currency exchange rates on Naglazyme sales from customers based outside the U.S. was approximately $5.7 million in 2008 compared to $4.3 million in 2007. Gross profit from Naglazyme in 2008 was approximately $106.8 million, representing gross margins of approximately 81% as compared to $67.9 million in 2007, representing gross margins of approximately 79%. The increase in gross margins is attributed to both foreign currency benefits and improved manufacturing yields.

We received marketing approval for Kuvan in the U.S. in December 2007 and began shipping product that same month. Net product sales for Kuvan in the U.S. for 2008 were $46.7 million. Gross profit from Kuvan in 2008 was approximately $40.4 million, representing gross margins of approximately 86%, which reflect royalties paid to third parties of 11%. In accordance with our inventory accounting policy, we began capitalizing Kuvan inventory production costs after U.S. regulatory approval was obtained in December 2007. As a result, the product sold in 2008 had an insignificant cost basis. We expect that a significant portion of Kuvan sold during 2009 will be previously expensed product and will have a minimal cost basis. The cost of sales for Kuvan for 2008 is principally comprised of royalties paid to third parties based on Kuvan net sales.

Prior to the restructuring of BioMarin/Genzyme LLC effective January 2008, we did not record Aldurazyme revenue and instead recorded our share of the net profits from the joint venture. As a result of the restructuring of the joint venture, we record a 39.5% to 50% royalty on worldwide net product sales of Aldurazyme. We also recognize product transfer revenue when product is released to Genzyme and all of our obligations have been fulfilled. Genzyme s return rights for Aldurazyme are limited to defective product or product. The product transfer revenue represents the fixed amount per unit of Aldurazyme that Genzyme is required to pay us if the product is unsold by Genzyme. The amount of product transfer revenue will eventually be deducted from the calculated royalty rate when the product is sold by Genzyme. Aldurazyme net product revenues of $72.5 million for 2008 represent $60.1 million of royalty revenue on net Aldurazyme sales by Genzyme. Royalty revenue from

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Genzyme is based on 39.5% to 42% of net Aldurazyme sales by Genzyme, which totaled $151.3 million for 2008. Incremental Aldurazyme net product transfer revenue of $12.4 million for 2008 reflects incremental shipments of Aldurazyme to Genzyme to meet future product demand. In January 2008, we transferred existing finished goods on-hand to Genzyme under the restructured terms of the BioMarin/Genzyme LLC agreements, resulting in the recognition of significant incremental product transfer revenue during 2008. In the future, to the extent that Genzyme Aldurazyme inventory quantities on hand remain flat, we expect that our total Aldurazyme revenues will approximate the 39.5% to 50% royalties on net product sales by Genzyme. In 2008, Aldurazyme gross profit was $52.2 million, representing a gross margin of 72%, which reflects the profit earned on royalty revenue and net incremental product transfer revenue. Our Aldurazyme gross margins may fluctuate depending on the mix of royalty revenue, from which we earn higher gross profit, and product transfer revenue, from which we earn a lower gross profit.

Total cost of sales during 2008, was $52.5 million, a significant increase compared to $18.4 million in 2007. The increase is primarily due to the increased net product revenues discussed above, as well as the restructuring of the joint venture with Genzyme, prior to which we did not recognize Aldurazyme net product revenues and the related cost of sales that were recognized by the joint venture.

2007 as Compared to 2006

Net product revenues for Naglazyme in 2007 totaled $86.2 million, of which $68.7 million was earned from end user customers based outside the U.S. The positive impact of foreign currency exchange rates on Naglazyme sales from customers based outside the U.S. was approximately $4.3 million in 2007 compared to $2.5 million in 2006. Gross profit from Naglazyme in 2007 was approximately $67.9 million, representing gross margins of approximately 79% as compared to $39.4 million in 2006, representing gross margins of approximately 85%. The increase in gross margins is attributed to both foreign currency benefits and improved manufacturing yields.

We received marketing approval for Naglazyme in the U.S. in May 2005 and began shipping product in June 2005. In accordance with our inventory accounting policy, we began capitalizing Naglazyme inventory production costs after U.S. regulatory approval was obtained in May 2005. As a result, some of the product sold in 2006 and 2007 had an insignificant cost basis and therefore lower cost of goods sold was reported. Substantially all of the Naglazyme inventory with an insignificant cost basis was sold or used in clinical trials as of December 31, 2007.

During the year ended December 31, 2006 we recognized net product sales of $3.1 million related to the Orapred product line. In March 2006, we sublicensed rights to sell and distribute Orapred in North America for up-front and milestone payments of $18.0 million and royalties on future sales of all Orapred products, including Orapred ODT. As a result of the sublicense subsequent to March 2006, we did not record net product sales related to the Orapred product line. Current and future revenue streams related to the Orapred product will include license and royalty revenues for future sales of Orapred product by the sublicensee, which are discussed below.

Collaborative Agreement Revenues

Collaborative agreement revenues include both license revenue and contract research revenue under our agreement with Merck Serono, which was executed in May 2005. License revenues are related to amortization of the $25.0 million up-front license payment received from Merck Serono and contract research revenues are related to shared development costs that are incurred by us, of which approximately 50% is reimbursed by Merck Serono. Our performance obligations related to the initial $25.0 million up-front payment were completed as of December 2008. Therefore, future periods will not include amortization amounts related to this payment. As shared development spending increases or decreases, contract research revenues will also change proportionately. Reimbursable revenues are expected to increase if PEG-PAL, or 6R-BH4 successfully complete Phase 2 clinical trials and Merck Serono exercises its option to co-develop the program. The related costs are included in

research and development expenses.

Collaborative agreement revenues in 2006, 2007, and 2008 were $18.7 million, $28.3 million and $38.9 million, respectively. Collaborative agreement revenues are comprised of amortization of the 2005 $25.0 million

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upfront license fee received from Merck Serono, reimbursable Kuvan development costs and Kuvan milestones earned from Merck Serono in 2007 and 2008. Amortization of the upfront license fee amounted to $7.4 million, $6.9 million, and $5.2 million, in 2006, 2007 and 2008, respectively. Reimbursable Kuvan development costs incurred during 2006, 2007 and 2008, were $11.3 million, $6.4 million and $3.7 million, respectively. The milestones included in 2007 and 2008 collaborative agreement revenues are the 2007, $15.0 million milestone payment received from Merck Serono upon EMEA acceptance of the Kuvan filing and $30.0 million milestone payment received from Merck Serono upon EMEA approval of Kuvan in 2008, respectively. Kuvan development costs primarily decreased during 2008 as compared to 2007 due to reductions in Kuvan clinical trial activities subsequent to the FDA approval received in December 2007. Amortization of the up-front license fee received from Merck Serono and recognized as revenue decreased from 2007 to 2008 due primarily to the changes in the amortization period.

Royalty and License Revenues

Royalty and license revenue in 2008 totaled $5.7 million compared to $6.5 million in 2007. Royalty and license revenues in 2008 included royalty revenues from Orapred product sold by the sublicensee of $3.8 million, Kuvan royalty revenues for products sold in Japan of $0.4 million and a $1.5 million milestone payment related to the Japanese approval of Kuvan in July 2008. Royalty and license revenues in 2007 included royalty revenues from Orapred product sold by the sublicensee of $2.3 million and a $4.0 million milestone payment related to the one-year anniversary of FDA approval of the marketing application for Orapred ODT.

Royalty and license revenues, totaling $15.9 million in 2006, include a $7.5 million milestone payment related to FDA approval of the marketing application for Orapred ODT, received in June 2006 and a $4.0 million milestone payment related to the commercial launch of Orapred ODT, received in September 2006. Royalty and license revenues in 2006 also include $2.5 million related to the up-front license fee received from the third party. During 2007, we recognized $2.3 million in royalty revenues from Orapred product sold by the sublicensee, as compared to $1.6 million during 2006.

Research and Development Expense

Our research and development expense includes personnel, facility and external costs associated with the research and development of our product candidates and products. These research and development costs primarily include preclinical and clinical studies, manufacturing of our product candidates prior to regulatory approval, quality control and assurance and other product development expenses, such as regulatory costs.

Research and development expenses increased by $14.7 million to $93.3 million for the year ended December 31, 2008, from $78.6 million for the year ended December 31, 2007. The change in research and development expenses for the year ended December 31, 2008 is primarily as a result of the following (in millions):

Research and development expenses for the year ended December 31, 2007	$ 78.6
Increased GALNS for Morquio disease development expenses	11.2
Decreased PEG-PAL development costs	(2.1)
Increase in research and development expense on other early stage programs	5.7
Increased Aldurazyme development expenses	1.6
Increased stock-based compensation expense	1.6
License payment related to collaboration with Summit Corporation plc	1.4
Decreased Kuvan clinical trial and manufacturing costs	(9.1)
Decreased 6R-BH4 development costs for indications other than PKU	(0.6)

Increase in non-allocated research and development expense and other net changes	5.0
Research and development expenses for the year ended December 31, 2008	$ 93.3

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The increase in GALNS development costs is primarily attributed to an increase in pre-clinical studies and manufacturing costs. The increase in Aldurazyme development costs relate to certain development costs that are no longer charged to the joint venture. The decrease in Kuvan clinical trial and manufacturing costs is primarily related to the capitalization of these costs into inventory during 2008 whereas in 2007 these costs were expensed prior to the FDA approval in December 2007. The decrease in PEG-PAL development costs is primarily due to a decline in pre-clinical studies in 2008. However, we expect to continue incurring significant Kuvan research and development costs for the foreseeable future due to long-term clinical activities related to post-approval regulatory commitments and spending on our GALNS program for the treatment of Morquio Syndrome and our PEG-PAL program. The increase in stock-based compensation expense is a result of an increased number of options outstanding due to increased headcount and a higher average stock price on the related grant date. The increase in non-allocated research and development primarily includes increases in facilities costs, general research costs and research and development personnel.

Research and development expenses increased by $11.9 million to $78.6 million for the year ended December 31, 2007, from $66.7 million for the year ended December 31, 2006. Research and development expenses increased for the year ended December 31, 2007 primarily as a result of the following (in millions):

Research and development expenses for the year ended December 31, 2006	$ 66.7
Decreased Kuvan clinical trial and manufacturing expenses	(7.6)
Increased 6R-BH4 development costs for endothelial dysfunction	3.6
Increased PEG-PAL development costs	8.4
Increased stock-based compensation expense	3.4
Absence of milestone payments to third party co-developer for approval and launch of Orapred ODT	(3.2)
Decreased Naglazyme development costs	(1.1)
Increase in research and development expense on early stage programs	2.0
Increase in non-allocated research and development expense and other changes	6.4
Research and development expenses for the year ended December 31, 2007	$ 78.6

The increase in 6R-BH4 development costs is related to increases for the ongoing pre-clinical studies of 6R-BH4 in other indications including endothelial dysfunction and costs related to planning and conducting Phase 2 clinical trials in peripheral arterial disease and sickle cell disease. The increase in PEG-PAL development costs is related to increases for pre-clinical studies and manufacturing costs. The decrease in Kuvan clinical trial and manufacturing costs is primarily due to decreased clinical trial and manufacturing expenses incurred as Kuvan approached marketing approval, which was received in December 2007. However, we expect to continue incurring significant Kuvan research and development costs for the foreseeable future due to long-term clinical activities related to post-approval regulatory commitments. The increase in non-allocated research and development primarily includes increases in facilities costs, general research costs and non-allocated research and development personnel. We expect research and development expense to increase in future periods, primarily as a result of spending on our GALNS program and on our PEG-PAL program.

Selling, General and Administrative Expense

Our selling, general and administrative expense includes commercial and administrative personnel, corporate facility and external costs required to support our commercialized products and product development programs. These selling, general and administrative costs include: corporate facility operating expenses and depreciation; marketing and sales operations; human resources; finance, legal and support personnel expenses; and other external corporate costs such as insurance, audit and legal fees.

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Selling, general and administrative expenses increased by $29.1 million, to $106.6 million for the year ended December 31, 2008, from $77.5 million for the year ended December 31, 2007. The components of the change for the year ended December 31, 2008 primarily include the following (in millions):

Selling, general and administrative expense for the year ended December 31, 2007	$ 77.5
Increased Naglazyme sales and marketing expenses	7.6
Increased stock-based compensation expense	4.4
Increased Kuvan commercialization expenses	9.8
Increased foreign exchange losses on un-hedged transactions	2.0
Net increase in corporate overhead and other administrative costs	5.3
Selling, general and administrative expenses for the year ended December 31, 2008	$ 106.6

Naglazyme sales and marketing expenses increased in 2008, primarily due to the expansion of our international commercial activities. We also incurred increased commercialization expenses related to the Kuvan commercial launch. The increase in stock-based compensation expense was the result of an increased number of outstanding options and a higher average stock price on the related grant date. The increase in corporate overhead and other administrative costs was primarily related to increases in salaries and benefits due to our growth in administrative employee headcount, consulting fees, travel, facilities and non-income taxes. We expect selling, general and administrative expenses to increase in future periods as a result of the international expansion of Naglazyme and the U.S. commercialization activities for Kuvan.

Selling, general and administrative expenses increased by $29.0 million, to $77.5 million for the year ended December 31, 2007, from $48.5 million for the year ended December 31, 2006. The components of the increase for the year ended December 31, 2007 primarily include the following (in millions):

Selling, general and administrative expenses for the year ended December 31, 2006	$ 48.5
Increased Naglazyme sales and marketing expenses	8.4
Increased stock-based compensation expense	5.3
Increased Kuvan commercial preparation expenses	7.8
Net increase in corporate overhead and other administrative costs	7.5
Selling, general and administrative expenses for the year ended December 31, 2007	$ 77.5

We initiated commercial operations in the E.U. and South America during 2006 and incurred related costs during 2007, primarily related to the commercialization of Naglazyme. During 2007, we also incurred significant expenses related to the preparation for the commercial launch of Kuvan in the U.S. The increase in stock-based compensation expense is the result of an increased number of options outstanding and a higher average stock price on the related grant date. The increase in corporate overhead and other administrative costs is primarily related to increases in salaries and benefits due to significant growth in employee headcount. We expect selling, general and administrative expenses to increase in future periods as a result of the international expansion of Naglazyme and Kuvan.

Amortization of Intangible Assets

Amortization of intangible assets includes the current amortization expense of the intangible assets acquired in the Ascent Pediatrics transaction in May 2004, including the Orapred developed and core technology. Kuvan license payments made to third parties as a result of the FDA approval of Kuvan in December 2007 and the EMEA approval of Kuvan in December 2008. The Orapred and Kuvan intangible assets are being amortized over approximately 3.5 years, 7.0 years and 10.0 years, respectively. Amortization of acquired intangible assets for the years ended December 31, 2006, 2007 and 2008 totaled $3.7 million, $4.4 million and $4.4 million, respectively. The increase in amortization of the acquired intangible assets from 2006 to 2007 was due to the change in

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expected useful life of the Orapred intangible assets from 15.0 years to 3.5 years following the sublicense of North American rights to Orapred in March 2006. Following our expected purchase of the common stock of Ascent Pediatrics from Medicis in August 2009, the underlying intellectual property related to Orapred will be transferred to the subliensee. We expect amortization expense associated with the Orapred intangible assets to approximate $2.9 million through the end of the expected useful life in August 2009. Amortization expense related to the Kuvan intangible asset is recorded as a component of cost of sales and is expected to approximate $0.6 million annually through 2014 and $0.3 million annually thereafter through 2018.

Equity in the Income (Loss) of BioMarin/Genzyme LLC

Equity in the income (loss) of BioMarin/Genzyme LLC includes our 50% share of the joint venture s income/loss for the period. Effective January 2008, we and Genzyme restructured BioMarin/Genzyme LLC regarding the manufacturing, marketing and sale of Aldurazyme. As of January 1, 2008, instead of sharing all costs and profits equally through the 50/50 joint venture, BioMarin/Genzyme LLC s operations will consist primarily of certain research and development activities and intellectual property will continue to be managed in the joint venture with costs shared equally by BioMarin and Genzyme.

Equity in the income (loss) of the joint venture decreased $32.8 million to a loss of $2.3 million in 2008, compared to equity in the income of the joint venture of $30.5 million in 2007. The fluctuation from 2007 to 2008 is attributed to the restructuring of the joint venture which became effective on January 1, 2008. Equity in the income of the joint venture increased to $30.5 million in 2007, compared to $19.3 million for 2006. The increase in profit from BioMarin/Genzyme LLC in 2007 was principally due to increases in Aldurazyme net revenue, which totaled $123.7 million for 2007, compared to $96.3 million for 2006.

Interest Income

We invest our cash and short-term investments in government and other high credit quality securities in order to limit default and market risk. Interest income decreased to $16.4 million for 2008, from $25.9 million for 2007, primarily due to lower interest rates offset by increased average levels of cash and investments during 2008.

Interest income increased to $25.9 million for 2007, from $12.4 million for 2006, primarily due to higher interest rates and increased levels of cash and investments during 2007.

Interest Expense

We incur interest expense on our convertible debt. Interest expense also includes imputed interest expense on the discounted acquisition obligation for the Ascent Pediatrics transaction. Interest expense was $16.4 million in 2008, as compared to $14.2 million in 2007, representing an increase of $2.2 million. The increase in interest expense is attributed to the payment of a full year of interest expense related to our $324.9 million of 1.875% senior subordinate convertible notes due in 2017 that were issued in April 2007.

Interest expense was $14.2 million for 2007, as compared to $13.4 million for 2006, representing an increase of $0.8 million. The decrease in 2007 is primarily due to the lack of interest expense related to our 3.5% Senior Subordinated Convertible Notes due in 2008, which were converted into common stock in two separate transactions in September 2006 and January 2007. This decreased interest expense was partially offset by increased interest expense on our $324.9 million of 1.875% senior subordinated convertible notes due in 2017 that were issued in April 2007.

The decrease in imputed interest expense was due to a lower outstanding balance of the acquisition obligation in 2007. Imputed interest expense totaled $4.7 million, $4.5 million and $4.4 million for the years ended December 31, 2006, 2007 and 2008, respectively. Imputed interest on the outstanding balance will be incurred through August 2009 when payment is due on the Medicis obligation.

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Debt Conversion Expense

In September 2006, certain holders of our 3.50% Convertible Senior Subordinated Notes due in 2008 agreed to convert $73.6 million in aggregate principal amount of the notes to approximately 5.25 million shares of our common stock. As a result of the conversion, we agreed to pay an inducement to the holders of approximately $3.3 million, which was recognized as additional interest expense during year ended December 31, 2006. In January 2007, the remaining outstanding balance of $51.4 million for our 3.50% Convertible Senior Subordinated Notes due in 2008 was converted into approximately 3.7 million shares of common stock.

Changes in Financial Position

From December 31, 2007 to December 31, 2008, our inventory increased by approximately $40.8 million. The increase in inventory was primarily attributed to the distribution of Aldurazyme inventory from the joint venture and the capitalization of Kuvan inventory costs as a result of the FDA approval in December 2007. Our accounts receivable increased by $37.3 million due to increased sales of Naglazyme and Kuvan and receivables from Genzyme for Aldurazyme product transfer and royalty revenues. In the first quarter of 2008, we received distributions of $16.7 million of cash and $26.8 million of inventory from BioMarin/Genzyme LLC as a result of the restructuring of the joint venture. Other current assets increased approximately $43.1 million from December 31, 2007 to December 31, 2008, primarily as a result of the $30.0 million milestone earned from Merck Serono due to the EMEA approval of Kuvan and the reclassification of $6.2 million of restricted cash from long-term to short-term. Our net property, plant and equipment increased by approximately $48.2 million from December 31, 2007 to December 31, 2008, primarily as a result of the purchase of our facility at 300 Bel Marin Keys, in Novato, California, capital equipment and improvements to our other facilities practically offset by depreciation expense during the period. We expect property, plant and equipment to increase in future periods, due to several ongoing facility improvement projects. Our total current liabilities increased by approximately $68.5 million primarily due to the reclassification of amounts due to Medicis from non-current to current.

Liquidity and Capital Resources

Cash and Cash Flow

As of December 31, 2008, our combined cash, cash equivalents and short-term investments totaled $559.8 million, a decrease of $25.8 million from $585.6 million at December 31, 2007.

The decrease in our combined balance of cash, cash equivalents and short-term investments during 2008 was $25.8 million, which was $6.2 million more than the net decrease in the combined balance in 2007 of $19.6 million, excluding offering proceeds of $316.4 million. The primary items contributing to the increase in net cash outflow, excluding the net offering proceeds, in 2008 were as follows (in millions):

Increased proceeds from stock option exercises and ESPP	$ 13.2
Increased capital asset purchases	(34.0)
Cash received from the settlement of foreign currency forward contracts	5.0
Investment in Summit Corporation plc	(5.7)
Net decreased cash used in operating activities, including net payments for working capital, and other	15.3

Total increase in net cash outflow excluding net offering proceeds	$ (6.2)

The net decreased operating spend includes increases in cash receipts from net revenues partially offset by increases in cash payments made for operating activities, such as research and development and sales and marketing efforts, as discussed in the *Results of Operations* section above. Increased capital purchases include the purchase of our facility at 300 Bel Marin Keys Drive, Novato, California. Net payments for working capital in 2008 primarily include increased inventory build of $6.6 million, which excluded the inventory distribution from the joint venture, increased accounts receivable build of $35.0 million, the Merck Serono receivable of $30.0 million related to the EMEA approval of Kuvan, and decreased accounts payable and accrued liabilities build of $3.4 million.

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With respect to the restructuring of our joint venture with Genzyme, our liquidity was not materially impacted by the restructuring despite the change in the Aldurazyme transaction structure. We remain responsible for the cash outflows for the investment in inventory and continue to receive the cash inflows from sales of Aldurazyme on a quarterly basis, except we currently receive cash through the royalty from Genzyme instead of cash distributions from the joint venture prior to the restructuring. However, as we now record accounts receivable from Genzyme that include both amounts related to royalty revenue and incremental product transfer revenue, our days sales outstanding has increased as a result of the joint venture restructuring and we expect our days sales outstanding to either remain consistent with the current level or increase modestly in the future. Genzyme is required to pay the royalty due within 45 days of the quarter in which the relevant sales were made, and with respect to the incremental product transfer revenue for unsold Aldurazyme, Genzyme is required to pay within 45 days after the calendar quarter in which the unit was determined to be unsold, which is not determinable until the product is lost, destroyed or expires before a sale to a customer. Further, pursuant to the terms of the restructured joint venture, we received a cash distribution of $16.7 million and an inventory distribution of $26.8 million from the joint venture in the first quarter of 2008.

During 2007, we received $316.4 million of net proceeds from a public offering of convertible senior subordinated notes, distributions from the joint venture of $17.1 million, $4.0 million in milestone payments for the one-year anniversary of the FDA approval of Orapred ODT and $15.0 million in milestone payments for the EMEA acceptance of the Kuvan filing. During 2006, we received $127.4 million of net proceeds from a public offering of common stock, $167.0 million of net proceeds from a public offering of convertible senior subordinated notes, distributions from the joint venture of $19.8 million and $14.0 million of proceeds related to our sublicense of North American rights for Orapred.

The $296.8 million increase in cash, cash equivalents, short-term investments and restricted cash during 2007 includes net proceeds from the public offering of convertible debt of $316.4 million. Excluding the net offering proceeds, the decrease in cash, cash equivalents, and short-term investments during 2007 was $19.6 million, which was $50.8 million less than the net decrease in cash, cash equivalents, short-term investments and restricted cash during 2006 of $70.4 million, excluding net offering proceeds of $294.3 million. The primary items contributing to the decrease in net cash outflow, excluding the net offering proceeds, in 2007 were as follows (in millions):

Decreased license proceeds related to sublicense of North American Orapred rights	$ (10.0)
Absence of net repayments of equipment and facility loans	20.9
Receipt of milestone payment for acceptance of Kuvan MAA filing by the EMEA	15.0
Decreased capital asset purchases	2.2
Absence of conversion premium and accrued interest payment	4.1
Absence of milestone payment for the approval and launch of Orapred ODT	3.2
Decreased cash flows from BioMarin/Genzyme LLC	(2.7)
Increased proceeds from stock option exercises	2.1
Net decreased cash used in operating activities, including net payments for working capital, and other	16.0
Total decrease in net cash outflow excluding net offering proceeds	$ 50.8

The net decreased operating spend includes increases in cash receipts from net revenues partially offset by increases in cash payments made for operating activities, such as research and development and sales and marketing efforts, as discussed in the *Results of Operations* section above. Decreases in net payments for working capital in 2007 primarily include decreased inventory build of $6.8 million, decreased accounts receivable build of $6.5 million and increased accounts payable and accrued liabilities build of $1.2 million.

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We expect that our net cash outflow in 2009 related to capital asset purchases will increase significantly compared to 2008. The expected increase in capital asset purchases primarily includes: expansion of our manufacturing facility, increased spending on manufacturing and lab equipment, expansion of our corporate campus including leasehold improvements and the continued development of information technology systems upgrades.

We have historically financed our operations primarily by the issuance of common stock, convertible debt and by relying on equipment and other commercial financing. During 2009, and for the foreseeable future, we will be highly dependent on our net product revenue to supplement our current liquidity and fund our operations. We may in the future elect to supplement this with further debt or equity offerings or commercial borrowing.

Funding Commitments

We expect to fund our operations with our net product revenues from Naglazyme, Aldurazyme and Kuvan, cash, cash equivalents and short-term investments supplemented by proceeds from equity or debt financings, loans or collaborative agreements with corporate partners, to the extent necessary. We expect our current cash, cash equivalents and short-term investments will meet our operating and capital requirements for the foreseeable future based on our current long-term business plans and assuming that we are able to achieve our long-term goals. This expectation could also change depending on how much we elect to spend on our development programs and for potential licenses and acquisitions of complementary technologies, products and companies.

Our investment in our product development programs has a major impact on our operating performance. Our research and development expenses for the years ended December 31, 2006, 2007, and 2008 and for the period since inception (March 1997 for the portion not allocated to any major program) represent the following (in millions):

	2006	2007	2008	Since Program Inception
GALNS for Morquio disease	$ 1.6	$ 2.2	$ 12.6	$ 16.4
6R-BH4 for other indications, including endothelial dysfunction	8.9	15.0	14.7	42.1
PEG-PAL	4.5	13.2	11.0	31.2
Not allocated to specific major current projects	12.3	21.0	28.4	181.2
	$ 27.3	$ 51.4	$ 66.7	$ 270.9

We cannot estimate the cost to complete any of our product development programs. Additionally, except as disclosed under *Overview* above, we cannot estimate the time to complete any of our product development programs or when we expect to receive net cash inflows from any of our product development programs. Please see *Risk Factors* in this Form 10-K, for a discussion of the reasons that we are unable to estimate such information, and in particular the following risk factors included in our Form 10-K *If we fail to maintain regulatory approval to commercially market and sell our drugs, or if approval is delayed, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased; To obtain regulatory approval to market our products, preclinical studies and costly and lengthy preclinical and clinical trials are required and the results of the studies and trials are highly uncertain; If we are unable to successfully develop manufacturing processes for our drug products to produce sufficient quantities and at acceptable costs, we may be unable to meet demand for our products and lose potential revenue, have reduced margins or be forced to terminate a program; If we fail to compete successfully with respect to product sales, we may be unable to*

generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product and our revenue could be adversely affected; and *If we do not*

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achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

We may elect to increase our spending above our current long-term plans and may be unable to achieve our long-term goals. This could increase our capital requirements, including: costs associated with the commercialization of our products; additional clinical trials and the manufacturing of Naglazyme, Aldurazyme and Kuvan; preclinical studies and clinical trials for our other product candidates; potential licenses and other acquisitions of complementary technologies, products and companies; general corporate purposes; payment of the amounts due with respect to the Ascent Pediatrics transaction; and working capital.

Our future capital requirements will depend on many factors, including, but not limited to:

- our ability to successfully market and sell Naglazyme and Kuvan;
- Genzyme s ability to successfully market and sell Aldurazyme;
- the progress, timing, scope and results of our preclinical studies and clinical trials;
- the time and cost necessary to obtain regulatory approvals and the costs of post-marketing studies which may be required by regulatory authorities;
- the time and cost necessary to develop commercial manufacturing processes, including quality systems and to build or acquire manufacturing capabilities;
- the time and cost necessary to respond to technological and market developments;
- any changes made to or new developments in our existing collaborative, licensing and other commercial relationships or any new collaborative, licensing and other commercial relationships that we may establish; and
- whether our convertible debt is converted to common stock in the future.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that are currently material or reasonably likely to be material to our financial position or results of operations.

Borrowings and Contractual Obligations

In April 2007, we sold approximately $324.9 million of senior subordinated convertible debt due April 2017. The debt was issued at face value and bears interest at the rate of 1.875% per annum, payable semi-annually in cash. The debt is convertible, at the option of the holder, at any time prior to maturity, into shares of our common stock at a conversion price of approximately $20.36 per share, subject to adjustment in certain circumstances. There is a no call provision included and we are unable to unilaterally redeem the debt prior to maturity in 2017. We also must repay the debt if there is a qualifying change in control or termination of trading of our common stock. In March 2006, we sold approximately $172.5 million of senior subordinated convertible notes due 2013. The debt was issued at face value and bears interest at the rate of 2.5% per annum, payable semi-annually in cash. There is a no call provision included and we are unable to unilaterally redeem the debt prior to maturity in 2013. The debt is convertible, at the option of the holder, at any time prior to maturity, into shares of our common stock at a conversion price of approximately $16.58 per share, subject to adjustment in certain circumstances. However, we must repay the debt prior to maturity if there is a qualifying change in control or termination of trading of our common stock. Our $497.1 million of convertible debt will impact our liquidity due to the semi-annual cash interest payments and the scheduled repayments of the debt.

As a result of the Ascent Pediatrics transaction, we expect to pay Medicis $73.6 million in 2009, of which $8.6 million at our election is payable through the issuance of our common stock.

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We have contractual and commercial obligations under our debt, operating leases and other obligations related to research and development activities, purchase commitments, licenses and sales royalties with annual minimums. Information about these obligations as of December 31, 2008 is presented below (in thousands).

	Payments Due by Period					
	2009	2010	2011-2012	2013-2014	2015 and Thereafter	Total
Medicis obligations	$ 73,600	$	$	$	$	$ 73,600
Convertible debt and related interest	10,401	10,401	20,801	186,544	340,104	568,251
Operating leases	3,894	4,026	6,481	2,624		17,025
Research and development and purchase commitments	35,689	612	3,927	2,827	3,353	46,408
Total	$ 123,584	$ 15,039	$ 31,209	$ 191,995	$ 343,457	$ 705,284

We are also subject to contingent payments related to various development activities totaling approximately $111.7 million, which are due upon achievement of certain regulatory and licensing milestones, and if they occur before certain dates in the future.

Related Party Transactions

Our Chief Medical Officer, Emil D. Kakkis, M.D., Ph.D., formerly held an adjunct faculty position with LA Biomedical, formerly known as Harbor-UCLA Research Educational Institute, for purposes of conducting research. LA Biomedical licenses certain intellectual property and provides other research services to us. We are also obligated to pay LA Biomedical a minimum annual payment and royalties on future sales of products covered by the license agreement. Our joint venture with Genzyme is subject to a second agreement with LA Biomedical that requires our joint venture partner pay LA Biomedical a royalty on sales of Aldurazyme through November 2019. Pursuant to Dr. Kakkis agreements with LA Biomedical, which were entered into prior to his employment by us, Dr. Kakkis is entitled to certain portions of these amounts payable to LA Biomedical. The license agreements were effective before Dr. Kakkis was an officer of our company. Pursuant to Dr. Kakkis agreements with LA Biomedical, he was entitled to approximately $1.1 million, $1.4 million and $1.8 million related to Aldurazyme during 2006, 2007, and 2008, respectively.

Item 7A. Quantitative and Qualitative Disclosure About Market Risk

Interest Rate Market Risk

Our exposure to market risk for changes in interest rates relates primarily to our investment portfolio. By policy, we place our investments with highly rated credit issuers and limit the amount of credit exposure to any one issuer. As stated in our policy, we seek to improve the safety and likelihood of preservation of our invested funds by limiting default risk and market risk.

We mitigate default risk by investing in high credit quality securities and by positioning our portfolio to respond appropriately to a significant reduction in a credit rating of any investment issuer or guarantor. The portfolio includes only marketable securities with active secondary or resale markets to ensure portfolio liquidity.

As of December 31, 2008, our investment portfolio did not include any investments with significant exposure to the subprime mortgage market issues. Based on our investment portfolio and interest rates at December 31, 2008, we believe that a 100 basis point decrease in interest rates could result in a potential loss in fair value of our investment portfolio of approximately $5.7 million. Changes in interest rates may affect the fair value of our investment portfolio. However, we will not recognize such gains or losses in our consolidated statement of operations unless the investments are sold.

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The table below presents the carrying value of our cash and investment portfolio, which approximates fair value at December 31, 2008 (in thousands):

	Carrying Value
Cash and cash equivalents	$ 222,900*
Short-term investments	336,892**
Total	$ 559,792

* 94% of cash and cash equivalents invested in money market instruments and 6% of uninvested cash.

** 66% of short-term investments invested in U.S. government treasuries, 17% in corporate securities, 10% in commercial paper, and 7% in U.S. government backed commercial paper.

Our debt obligations consist of our convertible debt, which carries a fixed interest rate and, as a result, we are not exposed to interest rate market risk on our convertible debt. The carrying value of our convertible debt approximates its fair value at December 31, 2008.

Foreign Currency Exchange Rate Market Risk

We transact business in various foreign currencies, primarily in certain European countries. Accordingly, we are subject to exposure from movements in foreign currency exchange rates, primarily related to Euro and British Pound revenue from sales of our products in Europe. Our operating expenses in the United Kingdom and other European counties are in British Pounds and Euros, respectively. Both serve to mitigate a portion of the exposure related to the above-mentioned revenue in both markets.

We hedge a portion of our net position in assets and liabilities denominated in Euros and British Pounds using primarily forward contracts. We also hedge a percentage of our forecasted international revenue with forward contracts. Our hedging policy is designed to reduce the impact of foreign currency exchange rate movements.

In the second quarter of 2008, we commenced hedging a portion of our forecasted Euro-based revenue to help mitigate short-term exposure to fluctuations of the currency by entering into foreign exchange forward rate contracts. These contracts have maturities of less than 12 months.

Our hedging programs are expected to reduce, but do not entirely eliminate, the short-term impact of currency exchange rate movements in operating expenses. As of December 31, 2008, we had foreign currency forward contracts to sell approximately $61.6 million in Euros and $3.9 million in British Pounds. As of December 31, 2008, our outstanding foreign currency forward contracts had a fair value of $1.9 million, of which is $0.8 million included in other current assets, and $1.1 million is included in accrued expenses.

We do not use derivative financial instruments for speculative trading purposes, nor do we hedge foreign currency exposure in a manner that entirely offsets the effects of changes in foreign exchange rates. The counterparty to these forward contracts is a creditworthy multinational

commercial bank, which minimizes the risk of counterparty nonperformance. We currently do not use financial instruments to hedge local currency operating expenses in Europe. Instead, we believe that a natural hedge exists, in that local currency revenue substantially offsets the local currency operating expenses. We regularly review our hedging program and may, as part of this review, make changes to the program.

Based on our overall currency rate exposures at December 31, 2008, we expect that a near-term 10% fluctuation of the U.S. dollar could result in the potential change in the fair value of our foreign currency sensitive assets and investments by approximately $0.9 million. We expect to enter into new transactions based in foreign currencies that could be impacted by changes in exchange rates.

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At December 31, 2008, we had cash of approximately $9.5 million denominated in foreign country currencies, which represented approximately 1.7% of the total investment portfolio. As a result, our investment portfolio is subject to limited amounts of foreign exchange risk.

A significant portion of Aldurazyme sales by Genzyme are earned outside of the U.S. and therefore our royalty on Aldurazyme sales is subject to risk of foreign currency exchange rate fluctuations, primarily the Euro and British pound. The policies and procedures related to the management of foreign currency risk of Aldurazyme sales are established and maintained by our joint venture partner, Genzyme.

Item 8. Financial Statements and Supplementary Data

The information required to be filed in this item appears on pages F-1 to F-38 of this report.

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

An evaluation was carried out, under the supervision of and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our 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)) as of the end of the period covered by this report. Based on the evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls are effective to ensure that the information required to be disclosed by us in the reports we file or submit under the Exchange Act was recorded, processed, summarized and reported within the time periods specified in the SEC s rules and instructions for Form 10-K.

Management s Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining an adequate internal control structure and procedures for financial reporting. Under the supervision of and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, our management has assessed the effectiveness of internal control over financial reporting as of December 31, 2008. Our management s assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, Internal Control-Integrated Framework.

Based on using the COSO criteria, we believe our internal control over financial reporting as of December 31, 2008 was effective.

Our independent registered public accounting firm, KPMG LLP, has audited the financial statements included in this Form 10-K and has issued a report on the effectiveness of our internal control over financial reporting. The report of KPMG LLP is incorporated by reference from Item 8 of this Form 10-K.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the fourth quarter of 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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Scope of the Effectiveness of Controls

Our 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. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and our board of directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on our 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.

Item 9B. Other Information

Amendment to Bylaws

On February 25, 2009, our board of directors approved and adopted Amended and Restated Bylaws, or the Amended Bylaws. The Amended Bylaws were effective as of February 25, 2009. In addition to various clarifying and conforming amendments, the Amended Bylaws revise and update the procedures for stockholders to propose business or nominations for election of directors to be considered at annual or special meetings of the stockholders. Among other things, the amendments clarify that the public announcement of an adjournment or postponement of an annual or special meeting will not commence a new time period (or extend any time period) for the giving of a stockholder s notice of proposed business or nomination for election of directors.

The amendments also expand the information that must be included in a stockholder s notice to include, among other things, (i) a description of any agreement, arrangement or understanding between the stockholder and the beneficial owner, if any, on whose behalf the proposal or nomination is made that has been entered into as of the date of the notice relating to the proposed business or nomination; (ii) in the case of proposed business, a description of the reasons for conducting such business at the meeting and any material interest in such business of the stockholder and the beneficial owner, if any, on whose behalf the proposal is made; and (iii) a description of any agreement, arrangement or understanding that has been entered into by the stockholder or beneficial owner with the effect or intent to mitigate loss, manage risk or benefit from share price changes or increase or decrease the stockholder s or beneficial owner s voting power with respect to the Company s stock.

The foregoing description of the Amended Bylaws is qualified in its entirety by reference to the full text of the Amended Bylaws, which is attached hereto as Exhibit 3.3 and is incorporated herein by reference.

Amendment to Rights Plan

On September 11, 2002, our Board of Directors authorized a dividend of one preferred share purchase right, or a Right, for each share of our common stock outstanding at the close of business on September 23, 2002. In connection with the authorization of the Rights, the Company entered into a Rights Agreement, dated as of September 11, 2002, or the Original Rights Agreement, with Mellon Investor Services LLC, a New Jersey limited liability company, as Rights Agent, or the Rights Agent. In connection with an increase in the number of

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authorized shares of our common stock in June 2003, the Company and the Rights Agent amended and restated the Original Rights Agreement pursuant to an Amended and Restated Rights Agreement, dated as of August 7, 2003, or the Prior Rights Plan. On February 27, 2009, the Company and the Rights Agent entered into an Amended and Restated Rights Agreement, or the Amended Rights Plan, which amends and restates the Prior Rights Plan. The term of the Rights Agreement and the share ownership threshold discussed below have not been changed since the Rights Plan was originally adopted in 2002.

Among other things, the Amended Rights Plan provides that, at any time after a person or group of affiliated or associated persons acquires, or obtains the right to acquire, beneficial ownership of 15% or more of our common shares (such person or group being referred to herein as an Acquiring Person), we may exchange the Rights at an exchange ratio of one share of our common stock per Right (such an event being referred to herein as an Exchange).

Furthermore, the Amended Rights Plan provides that, in effecting an Exchange, we may enter into a trust agreement by which we transfer to the trust created by such trust agreement, or the Trust, all shares of our common stock issued pursuant to the Exchange. The Trust would hold the shares of our common stock for the benefit of stockholders entitled to receive them pursuant to the Exchange. Stockholders would receive shares from the Trust after complying with the relevant terms of the trust agreement.

The Amended Rights Plan also provides that, in the event a person, entity or group becomes an Acquiring Person (such an event being referred to herein as a Trigger Event), each holder of a Right will have a sixty day period (subject to adjustment in certain circumstances) thereafter to exercise his, her or its Rights.

Under the Amended Rights Plan, following a Trigger Event and the expiration of the exercise period described above, we may, at our option, redeem all of the outstanding Rights in connection with certain transactions not involving an Acquiring Person in which all holders of our common stock are treated alike. In addition, in certain circumstances, we may redeem all of the outstanding Rights following a Trigger Event and the expiration of the exercise period if the Acquiring Person s beneficial ownership has dropped below the 15% threshold.

The foregoing description of the Amended Rights Plan is qualified in its entirety by reference to the full text of the Amended Rights Plan, which is attached hereto as Exhibit 4.1 and is incorporated herein by reference.

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Part III

Item 10. Directors and Executive Officers and Corporate Governance

We incorporate information regarding our directors, executive officers and corporate governance into this section by reference from sections captioned Election of Directors and Executive Officers in the proxy statement for our 2009 annual meeting of stockholders.

Item 11. Executive Compensation

We incorporate information regarding executive compensation into this section by reference from the section captioned Executive Compensation in the proxy statement for our 2009 annual meeting of stockholders.

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

We incorporate information regarding security ownership of our beneficial owners, management and related stockholder matters into this section by reference from the section captioned Security Ownership of Certain Beneficial Owners in the proxy statement for our 2009 annual meeting of stockholders.

Item 13. Certain Relationships and Related Transactions and Director Independence

We incorporate information regarding certain relationships related to transactions and director independence into this section by reference from the section captioned Interest of Insiders in Material Transactions in the proxy statement for our 2009 annual meeting of stockholders.

Item 14. Principal Accounting Fees and Services

We incorporate information regarding our principal accountant fees and services into this section by reference from the section captioned Auditors in the proxy statement for our 2009 annual meeting of stockholders.

Part IV

Item 15. Exhibits and Financial Statement Schedules

Financial Statements

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Exhibit Index

2.1	Asset Purchase Agreement dated as of April 20, 2004, by and among BioMarin Pharmaceutical Inc., Medicis Pharmaceutical Corporation, Ascent Pediatrics, Inc. and BioMarin Pediatrics Inc., previously filed with the Commission on June 2, 2004 as Exhibit 2.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
2.2	Securities Purchase Agreement dated as of May 18, 2004, by and among BioMarin Pharmaceutical Inc., Medicis Pharmaceutical Corporation, Ascent Pediatrics, Inc. and BioMarin Pediatrics Inc., previously filed with the Commission on June 2, 2004 as Exhibit 2.2 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
2.3	License Agreement dated as of May 18, 2004, by and among BioMarin Pharmaceutical Inc., Medicis Pharmaceutical Corporation, Ascent Pediatrics, Inc. and BioMarin Pediatrics Inc., previously filed with the Commission on June 2, 2004 as Exhibit 2.3 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
2.4	Settlement Agreement and Mutual Release dated January 12, 2005, by and among BioMarin Pharmaceutical Inc., BioMarin Pediatrics Inc., Medicis Pharmaceutical Corporation and Medicis Pediatrics, Inc. (f/k/a Ascent Pediatrics, Inc.), previously filed with the Commission on March 16, 2005 as Exhibit 2.4 to the Company s Annual Report on Form 10-K, which is incorporated herein by reference.
2.5	Amendment to Securities Purchase Agreement dated January 12, 2005, by and among BioMarin Pharmaceutical Inc., BioMarin Pediatrics Inc., Medicis Pharmaceutical Corporation and Medicis Pediatrics, Inc. (f/k/a Ascent Pediatrics, Inc.), previously filed with the Commission on March 16, 2005 as Exhibit 2.5 to the Company s Annual Report on Form 10-K, which is incorporated herein by reference.
2.6	Amendment to License Agreement dated January 12, 2005, by and among BioMarin Pharmaceutical Inc., BioMarin Pediatrics Inc., Medicis Pharmaceutical Corporation and Medicis Pediatrics, Inc. (f/k/a Ascent Pediatrics, Inc.), previously filed with the Commission on March 16, 2005 as Exhibit 2.6 to the Company s Annual Report on Form 10-K, which is incorporated herein by reference.
3.1	Amended and Restated Certificate of Incorporation, as amended June 12, 2003, previously filed with the Commission on June 23, 2003 as Exhibit 3.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
3.2	Certificate of Correction to Certificate of Amendment to the Amended and Restated Certificate of Incorporation of BioMarin Pharmaceutical Inc., previously filed with the Commission on April 4, 2005 as Exhibit 3.2 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
3.3*	Amended and Restated By-Laws of BioMarin Pharmaceutical Inc.
4.1*	Amended and Restated Rights Agreement, dated as of February 27, 2009, between BioMarin Pharmaceutical Inc. and Mellon Investor Services LLC, as Rights Agent.
4.2	Indenture dated June 23, 2003, by and between BioMarin Pharmaceutical Inc. and Wilmington Trust Company, previously filed with the Commission on August 12, 2003 as Exhibit 4.1 to the Company s Quarterly report on Form 10-Q, which is incorporated herein by reference.
4.3	Indenture dated March 29, 2006, by and between BioMarin Pharmaceutical Inc. and Wilmington Trust Company, previously filed with the Commission on March 29, 2006 as Exhibit 4.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.

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4.4	First Supplemental Indenture dated March 29, 2006, by and between BioMarin Pharmaceutical Inc. and Wilmington Trust Company, previously filed with the Commission on March 29, 2006 as Exhibit 4.2 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
4.5	Form of 2.5% Senior Subordinated Convertible Notes due 2013, previously filed with the Commission on March 29, 2006 as Exhibit 4.2 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.1	Form of Indemnification Agreement for Directors and Officers, previously filed with the Commission on May 4, 1999 as Exhibit 10.1 to the Company s Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.
10.2	Severance Plan and Summary Plan Description as originally adopted on January 27, 2004 and amended and restated on March 23, 2005, previously filed with the Commission on March 29, 2005 as Exhibit 10.42 to the Company s Annual Report on Form 10-K/A, which is incorporated herein by reference.
10.3	Amendment to 1997 Stock Plan, as amended, as adopted March 20, 2002, previously filed with the Commission on March 21, 2002 as Exhibit 99.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.4	Amendment No. 2 to 1997 Stock Plan, as adopted May 5, 2004, previously filed with the Commission on August 9, 2004 as Exhibit 10.1 to the Company s Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.5	Amended and Restated BioMarin Pharmaceutical Inc. 2006 Share Incentive Plan, as adopted on June 21, 2006, previously filed with the Commission on June 16, 2006 as Exhibit 99.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.6	1998 Director Option Plan and forms of agreements thereunder, previously filed with the Commission on May 4, 1999 as Exhibit 10.3 to the Company s Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.
10.7	Amendment to 1998 Director Plan as adopted March 26, 2003 previously filed with the Commission on May 15, 2003 as Exhibit 10.1 to the Company s Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.8	Amendment No. 2 to 1998 Director Option Plan, as adopted June 12, 2003 and July 21, 2003, previously filed with the Commission on August 12, 2003 as Exhibit 10.1 to the Company s Quarterly report on Form 10-Q, which is incorporated herein by reference.
10.9	Amendment No. 3 to 1998 Director Option Plan, as adopted May 5, 2004, previously filed with the Commission on August 9, 2004 as Exhibit 10.2 to the Company s Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.10	Amended and Restated 2006 Employee Stock Purchase Plan, as adopted on June 21, 2006, previously filed with the Commission on August 3, 2006 as Exhibit 10.3 to the Company s Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.11	Amended and Restated BioMarin Pharmaceutical Inc. Nonqualified Deferred Compensation Plan, as adopted on December 1, 2005 and as amended and restated on January 1, 2009, previously filed with the Commission on December 23, 2008 as Exhibit 10.8 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.12	Amended and Restated Employment Agreement with Jean-Jacques Bienaime dated January 1, 2009 previously filed with the Commission on December 23, 2008, as Exhibit 10.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.

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10.13	Amended and Restated Employment Agreement with Stephen Aselage dated January 1, 2009 previously filed with the Commission on December 23, 2008 as Exhibit 10.2 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.14	Amended and Restated Employment Agreement with Robert A. Baffi dated January 1, 2009 previously filed with the Commission on December 23, 2008, as Exhibit 10.3 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.15	Amended and Restated Employment Agreement with Emil D. Kakkis, M.D., Ph.D. dated January 1, 2009 previously filed with the Commission on December 23, 2008 as Exhibit 10.4 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.16	Amended and Restated Employment Agreement with Jeffrey H. Cooper dated January 1, 2009 previously filed with the Commission on December 23, 2008 as Exhibit 10.5 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.17	Amended and Restated Employment Agreement with G. Eric Davis dated January 1, 2009, previously filed with the Commission on December 23, 2005 as Exhibit 10.6 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.18	Amended and Restated Employment Agreement with Mark Wood dated January 1, 2009 previously filed with the Commission on December 23, 2008 as Exhibit 10.7 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
10.19	Employment Agreement with Stuart J. Swiedler, M.D., Ph.D., dated April 9, 2007, previously filed with the Commission on May 3, 2007 as Exhibit 10.5 to the Company s Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.20	Grant Terms and Conditions Agreement between BioMarin Pharmaceutical Inc. and Harbor-UCLA Research and Education Institute dated April 1, 1997, as amended, previously filed with the Commission on July 21, 1999 as Exhibit 10.17 to the Company s Amendment No. 3 to Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
10.21	License Agreement dated July 30, 2004, between BioMarin Pharmaceutical Inc. and Daiichi Suntory Pharma Co., Ltd., as amended by Amendment No. 1 to License Agreement dated November 19, 2004, previously filed with the Commission on March 16, 2005 as Exhibit 10.25 to the Company s Annual Report on Form 10-K, which is incorporated herein by reference. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
10.22	Development, License and Commercialization Agreement dated May 13, 2005, between BioMarin Pharmaceutical Inc. and Ares Trading S.A., previously filed with the Commission on July 6, 2005 as Exhibit 10.1 to the Company s Current Report on Form 8-K/A, which is incorporated herein by reference. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
10.23	Operating Agreement with Genzyme Corporation, previously filed with the Commission on July 21, 1999 as Exhibit 10.30 to the Company s Amendment No. 2 to Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.
10.24	2009 Technical Amendments to BioMarin Pharmaceutical Inc. 2006 Share Incentive Plan, effective January 1, 2009, previously filed with the Commission on December 23, 2008, as Exhibit 10.9 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.

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10.25	Amended and Restated License Agreement between BioMarin Pharmaceutical Inc. and Women s and Children s Hospital dated February 7, 2007, previously filed with the Commission on May 3, 2007 as Exhibit 10.7 to the Company s Quarterly Report on Form 10-Q, which is incorporated herein by reference. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
10.26	Manufacturing, Marketing and Sales Agreement dated as of January 1, 2008, by and among BioMarin Pharmaceutical Inc., Genzyme Corporation and BioMarin/Genzyme LLC previously filed with the Commission on February 27, 2008 as Exhibit 10.30 to the Company s 2007 Annual Report on Form 10-K, which is incorporated herein by reference. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
10.27	Amended and Restated Collaboration Agreement dated as of January 1, 2008, by and among BioMarin Pharmaceutical Inc., Genzyme Corporation and BioMarin/Genzyme LLC previously filed with the Commission on February 27, 2007 as Exhibit 10.31 to the Company s 2007 Annual Report on Form 10-K, which is incorporated herein by reference. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
10.28	Members Agreement dated as of January 1, 2008 by and among BioMarin Pharmaceutical Inc., Genzyme Corporation, BioMarin Genetics Inc., and BioMarin/Genzyme LLC previously filed with the Commission on February 27, 2007 as Exhibit 10.32 to the Company s 2007 Annual Report on Form 10-K, which is incorporated herein by reference. Portions of this document have been redacted pursuant to a request for confidential treatment filed pursuant to the Freedom of Information Act.
10.29*	Development and Commercialization Agreement dated as of January 4, 2009 by and between BioMarin CF Limited and La Jolla Pharmaceutical Company. Portions of this document have been redacted pursuant to a request for confidential treatment filed pursuant to the Freedom of Information Act.
10.30*	Securities Purchase Agreement dated as of January 4, 2009 by and between BioMarin Pharmaceutical Inc. and La Jolla Pharmaceutical Company. Portions of this document have been redacted pursuant to a request for confidential treatment filed pursuant to the Freedom of Information Act.
10.31*	Amendment No. 1 to the Development and Commercialization Agreement dated as of January 16, 2009 by and between BioMarin CF Limited and La Jolla Pharmaceutical Company.
10.32*	Amendment No. 1 to the Securities Purchase Agreement dated as of January 16, 2009 by and between BioMarin Pharmaceutical Inc. and La Jolla Pharmaceutical Company.
10.33*	Summary of Bonus Plan
21.1*	Subsidiaries of BioMarin Pharmaceutical Inc.
23.1*	Consent of KPMG LLP, Independent Registered Public Accounting Firm for BioMarin Pharmaceutical Inc.
23.2*	Consent of PricewaterhouseCoopers, LLP, Independent Registered Public Accounting Firm for BioMarin/Genzyme LLC.
24.1*	Power of Attorney (Included in Signature Page)
25.1	Form T-One Statement of Eligibility under the Trust Indenture Act of 1939, previously filed with the Commission on March 20, 2006 as Exhibit 25.1 to the Company s Current Report on Form 8-K, which is incorporated herein by reference.
31.1*	Certification of Chief Executive Officer pursuant to Rules 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2*	Certification of Chief Financial Officer pursuant to Rules 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.

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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. This Certification accompanies this report and shall not, except to the extent required by the Sarbanes-Oxley Act of 2002, be deemed filed for purposes of §18 of the Securities Exchange Act of 1934, as amended.
99.1*	BioMarin/Genzyme LLC Consolidated Financial Statements as of December 31, 2008 and 2007, and for the years ended December 31, 2008, 2007 and 2006.

* Filed herewith
Management contract or compensatory plan or arrangement

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SIGNATURES

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

BIOMARIN PHARMACEUTICAL INC.

Dated: February 27, 2009

By: /s/ JEFFREY H. COOPER
Jeffrey H. Cooper

Senior Vice President, Chief Financial Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Jean-Jacques Bienaimé and Jeffrey H. Cooper, his or her attorney-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to the Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

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 registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ JEAN-JACQUES BIENAIMÉ **Jean-Jacques Bienaimé**	Chief Executive Officer (Principal Executive Officer)	February 27, 2009
/s/ JEFFREY H. COOPER **Jeffrey H. Cooper**	Senior Vice President, Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 27, 2009
/s/ PIERRE LAPALME **Pierre LaPalme**	Chairman and Director	February 27, 2009
/s/ ELAINE HERON **Elaine Heron**	Director	February 27, 2009
/s/ JOSEPH KLEIN, III	Director	February 27, 2009

Joseph Klein, III		
/s/ ALAN J. LEWIS	Director	February 27, 2009
Alan J. Lewis		
/s/ MICHAEL G. GREY	Director	February 27, 2009
Michael G. Grey		
/s/ RICHARD A. MEIER	Director	February 27, 2009
Richard A. Meier		
/s/ V. BRYAN LAWLIS	Director	February 27, 2009
V. Bryan Lawlis		

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INDEX TO BIOMARIN PHARMACEUTICAL INC.

CONSOLIDATED FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

BioMarin Pharmaceutical Inc.:

We have audited the accompanying consolidated balance sheets of BioMarin Pharmaceutical Inc. and subsidiaries (the Company) as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders equity (deficit) and comprehensive income (loss), and cash flows for each of the years in the three-year period ended December 31, 2008. These consolidated financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We did not audit the financial statements of BioMarin/Genzyme LLC (a 50 percent owned joint venture) for the years 2007 and 2006. The Company s investment in BioMarin/Genzyme LLC (in thousands) at December 31, 2007 was $44,881, and its equity in income of BioMarin/Genzyme (in thousands) was $30,525 and $19,274 for the years ended December 31, 2007 and 2006, respectively. The financial statements of BioMarin/Genzyme LLC for those years were audited by other auditors whose report has been furnished to us, and our opinion, insofar as it relates to the amounts included for BioMarin/Genzyme LLC for those years, is based solely on the report of the other auditors.

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 audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of BioMarin Pharmaceutical Inc. and subsidiaries as of December 31, 2008 and 2007, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company s 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), and our report dated February 24, 2009 expressed an unqualified opinion on the effectiveness of the Company s internal control over financial reporting

(signed) KPMG LLP

San Francisco, California

February 24, 2009

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

BioMarin Pharmaceutical Inc.:

We have audited BioMarin Pharmaceutical Inc. and subsidiaries (the Company) 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 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 Annual Report on Internal Control Over Financial Reporting in Item 9A. Our responsibility is to express an opinion on the Company s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit 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 audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

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 (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) 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 (3) 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.

In our opinion, BioMarin Pharmaceutical Inc. and subsidiaries 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.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of BioMarin Pharmaceutical Inc. and subsidiaries as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders equity (deficit) and comprehensive income (loss), and cash flows for each of the years in the three-year period ended December 31, 2008, and our report dated February 24, 2009 expressed an unqualified opinion on those consolidated financial statements. Our report refers to the report of other auditors.

(signed) KPMG LLP

San Francisco, California

February 24, 2009

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS

December 31, 2007 and 2008

(In thousands, except for share and per share data)

	December 31, 2007	December 31, 2008
ASSETS		
Current assets:		
Cash and cash equivalents	$ 228,343	$ 222,900
Short-term investments	357,251	336,892
Accounts receivable, net	16,976	54,298
Advances to BioMarin/Genzyme LLC	2,087	174
Inventory	32,445	73,162
Other current assets	7,195	50,270
Total current assets	644,297	737,696
Investment in BioMarin/Genzyme LLC	44,881	915
Other investments		1,633
Property, plant and equipment, net	76,818	124,979
Intangible assets, net	9,596	7,626
Goodwill	21,262	21,262
Other assets	18,425	12,584
Total assets	$ 815,279	$ 906,695
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$ 49,907	$ 58,851
Current portion of acquisition obligation, net of discount	6,309	70,741
Deferred revenue	5,327	307
Other current liabilities		182
Total current liabilities	61,543	130,081
Convertible debt	497,375	497,083
Long-term portion of acquisition obligation, net of discount	66,553	
Other long-term liabilities	2,082	2,856
Total liabilities	627,553	630,020
Stockholders equity:		
Common stock, $0.001 par value: 250,000,000 shares authorized at December 31, 2007 and December 31, 2008; 97,114,159 and 99,868,145 shares issued and outstanding at December 31, 2007 and 2008, respectively	97	100
Additional paid-in capital	794,917	852,947
Company common stock held by deferred compensation plan		(882)
Accumulated other comprehensive income	139	1,106

Accumulated deficit	(607,427)	(576,596)
Total stockholders equity	187,726	276,675
Total liabilities and stockholders equity	$ 815,279	$ 906,695

See accompanying notes to consolidated financial statements.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF OPERATIONS

Years ended December 31, 2006, 2007 and 2008

(In thousands, except for per share data)

	December 31,		
	2006	2007	2008
Revenues:			
Net product revenues	$ 49,606	$ 86,802	$ 251,851
Collaborative agreement revenues	18,740	28,264	38,907
Royalty and license revenues	15,863	6,515	5,735
Total revenues	84,209	121,581	296,493
Operating expenses:			
Cost of sales	8,740	18,359	52,509
Research and development	66,735	78,600	93,291
Selling, general and administrative	48,507	77,539	106,566
Amortization of acquired intangible assets	3,651	4,371	4,371
Total operating expenses	127,633	178,869	256,737
Income (Loss) from operations	(43,424)	(57,288)	39,756
Equity in the income (loss) of BioMarin/Genzyme LLC	19,274	30,525	(2,270)
Interest income	12,417	25,932	16,388
Interest expense	(13,411)	(14,243)	(16,394)
Debt conversion expense	(3,315)		
Impairment loss on investment			(4,056)
Income (Loss) before income taxes	(28,459)	(15,074)	33,424
Provision for income taxes	74	729	2,593
Net income (loss)	$ (28,533)	$ (15,803)	$ 30,831
Net income (loss) per share, basic	$ (0.34)	$ (0.16)	$ 0.31
Net income (loss) per share, diluted	$ (0.34)	$ (0.16)	$ 0.29
Weighted average common shares outstanding, basic	84,582	95,878	98,975
Weighted average common shares outstanding, diluted	84,582	95,878	103,572

See accompanying notes to consolidated financial statements.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS EQUITY (DEFICIT) AND COMPREHENSIVE INCOME (LOSS)

For the Years ended December 31, 2006, 2007 and 2008 (in thousands)

	Common stock		Additional Paid-in	Company Common Stock held by Deferred Compensation	Accumulated Other Comprehensive Income	Accumulated	Total Stockholders Equity
	Shares	Amount	Capital	Plan	(Loss)	Deficit	(Deficit)
Balance at January 1, 2006	74,302	$ 75	$ 485,570		$ (16)	$ (563,091)	$ (77,462)
Net loss						(28,533)	(28,533)
Fair market value adjustments of available-for-sale investments					23		23
Foreign currency translation adjustment					(32)		(32)
Comprehensive loss							(28,542)
Issuance of common stock in a public offering, net of issuance costs	10,350	10	127,422				127,432
Issuance of common stock under ESPP	326		1,405				1,405
Exercise of common stock options	1,499	2	11,679				11,681
Conversion of convertible notes	5,249	5	72,687				72,692
Stock compensation expense related to modification of awards			10,596				10,596
Balance at December 31, 2006	91,726	$ 92	$ 709,359		$ (25)	$ (591,624)	$ 117,802
Net loss						(15,803)	(15,803)
Fair market value adjustments of available-for-sale investments					62		62
Foreign currency translation adjustment					102		102
Comprehensive loss							(15,639)
Issuance of common stock under ESPP	275		1,928				1,928
Exercise of common stock options	1,443	1	13,291				13,292
Conversion of convertible notes	3,670	4	50,925				50,929
Stock-based compensation			19,414				19,414
Balance at December 31, 2007	97,114	$ 97	$ 794,917		$ 139	$ (607,427)	$ 187,726
Net income						30,831	30,831
Fair market value adjustments of available-for-sale investments					1,201		1,201
Unrealized loss on foreign currency hedges					(212)		(212)
Foreign currency translation adjustment					(22)		(22)
Comprehensive income							31,798

Issuance of common stock under ESPP	209		2,634				2,634
Exercise of common stock options	2,489	3	25,813				25,816
Excess tax benefit from exercises			960				960
Restricted stock vested during the period	39						
Common stock held by nonqualified deferred compensation plan				(882)			(882)
Conversion of convertible notes	17		288				288
Stock-based compensation			28,335				28,335
Balance at December 31, 2008	99,868	$ 100	$ 852,947	$ (882)	$ 1,106	$ (576,596)	$ 276,675

See accompanying notes to consolidated financial statements.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS

Years ended December 31, 2006, 2007 and 2008

(In thousands)

	December 31,		
	2006	**2007**	**2008**
Cash flows from operating activities:			
Net income (loss)	$ (28,533)	$ (15,803)	$ 30,831
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Depreciation and amortization	11,949	13,645	17,631
Amortization of discount on short-term investments	(2,167)	(12,453)	(6,487)
Imputed interest on acquisition obligation	4,685	4,527	4,378
Equity in the income (loss) of BioMarin/Genzyme LLC	(19,274)	(30,525)	2,270
Stock-based compensation	10,596	19,415	28,336
Impairment loss on investment			4,056
Excess tax benefit from stock option exercises			(960)
Unrealized foreign exchange gain (loss) on forward contracts		165	(228)
Other		9	(15)
Changes in operating assets and liabilities:			
Accounts receivable, net	(8,809)	(2,306)	(37,322)
Advances to BioMarin/Genzyme LLC	(526)	(491)	1,913
Inventory	(14,177)	(7,371)	(13,938)
Other current assets	(807)	(3,158)	(43,056)
Other assets	(3,091)	(4,745)	43
Accounts payable and accrued liabilities	10,490	10,850	7,433
Other liabilities	(4,795)	3	960
Deferred revenue	(7,807)	(6,788)	(5,020)
Net cash used in operating activities	(52,266)	(35,026)	(9,175)
Cash flows from investing activities:			
Purchase of property and equipment	(24,583)	(22,413)	(56,368)
Maturities and sales of short-term investments	29,906	693,814	761,178
Purchase of short-term investments	(217,724)	(838,864)	(733,131)
Investment in BioMarin/Genzyme LLC			(1,750)
Distributions from BioMarin/Genzyme LLC	19,800	17,100	16,683
Investment in Summit Corporation plc			(5,689)
Net cash used in investing activities	(192,601)	(150,363)	(19,077)
Cash flows from financing activities:			
Proceeds from ESPP and exercise of stock options	13,087	15,220	28,443
Decrease in cash balances related to long-term debt	17,049		
Repayment of equipment and facility loans	(20,909)		
Excess tax benefit from stock option exercises			960
Repayment of acquisition obligation	(7,700)	(7,000)	(6,500)
Net proceeds from public offering of common stock	127,431		
Net proceeds from convertible debt offering	166,979	316,350	
Repayment of capital lease obligations			(94)

Net cash provided by financing activities	295,937	324,570	22,809
Net increase (decrease) in cash and cash equivalents	51,070	139,181	(5,443)
Cash and cash equivalents:			
Beginning of year	38,092	89,162	228,343
End of year	$ 89,162	$ 228,343	$ 222,900
Supplemental cash flow disclosures:			
Cash paid for interest	$ 2,156	$ 7,358	$ 10,401
Cash paid for income taxes	121	296	1,277
Stock-based compensation capitalized into inventory	1,006	1,710	4,612
Depreciation capitalized into inventory	2,161	1,941	2,782
Supplemental non-cash investing and financing activities disclosures:			
Conversion of convertible notes	73,560	51,440	292
Distribution of inventory resulting from the joint venture restructure			26,780
Deferred offering costs reclassified to additional paid in capital as a result of convertible notes	868	512	9
Changes in accrued liabilities related to fixed assets	965	6,726	4,462
Equipment acquired through capital lease			546

See accompanying notes to consolidated financial statements.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

December 31, 2007 and 2008

(1) NATURE OF OPERATIONS AND BUSINESS RISKS

BioMarin Pharmaceutical Inc. (the Company or BioMarin®) develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. BioMarin selects product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market or offer a significant benefit over existing products. The Company s product portfolio is comprised of three approved products and multiple investigational product candidates. Approved products include Naglazyme® (galsulfase), Kuvan® (sapropterin dihydrochloride), and Aldurazyme® (laronidase).

There were 72 common stockholders of record at December 31, 2008. No dividends have ever been paid by the Company. The Company is incorporated in the state of Delaware.

Through December 31, 2008, the Company had accumulated losses of approximately $576.6 million. Management believes that the Company s cash, cash equivalents and short-term investments at December 31, 2008 will be sufficient to meet the Company s obligations for the foreseeable future based on management s current long-term business plans and assuming that the Company achieves its long-term goals. If the Company elects to increase its spending on development programs significantly above current long-term plans or enter into potential licenses and other acquisitions of complementary technologies, products or companies, the Company may need additional capital. Until the Company can generate sufficient levels of cash from its operations, the Company expects to continue to finance net future cash needs primarily through its current cash, cash equivalents and short-term investments, and to the extent necessary, through proceeds from equity or debt financings, loans and collaborative agreements with corporate partners. In April 2007, the Company raised approximately $324.9 million in net proceeds from a public offering of senior subordinated convertible debt due in 2017. The proceeds are intended to fund future business development transactions and for general corporate purposes.

The Company is subject to a number of risks, including the financial performance of Naglazyme, Kuvan, and Aldurazyme; the potential need for additional financings; its ability to successfully commercialize its product candidates, if approved; the uncertainty of the Company s research and development efforts resulting in successful commercial products; obtaining regulatory approval for such products; significant competition from larger organizations; reliance on the proprietary technology of others; dependence on key personnel; uncertain patent protection; dependence on corporate partners and collaborators; and possible restrictions on reimbursement, as well as other changes in the health care industry.

(2) SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Basis of Presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States (U.S. GAAP) and include the accounts of BioMarin and its wholly owned subsidiaries. All significant intercompany transactions have been eliminated.

(b) Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the dates of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

(c) Cash and Cash Equivalents

The Company treats liquid investments with original maturities of less than three months when purchased as cash and cash equivalents.

(d) Investments

The Company records its investments in debt and equity securities as either held-to-maturity or available-for-sale. Held-to-maturity investments are recorded at amortized cost. Available-for-sale investments are recorded at fair market value, with unrealized gains or losses being included in accumulated other comprehensive income/loss, exclusive of other-than-temporary impairment losses, if any. Short-term investments are comprised mainly of corporate securities, commercial paper, U.S. federal government agency securities, U.S. treasury bills and money market funds. As of December 31, 2008, the Company had no held-to-maturity investments.

Other investments as of December 31, 2008 are comprised of an equity investment denominated in British Pounds. The equity investment is accounted for under the provisions of Statement of Financial Accounting Standard (SFAS) No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* The Company classified the investment as available-for-sale and accordingly the investment is recorded at fair market value. Changes in the fair value are reported as a component of accumulated other comprehensive income, exclusive of other-than-temporary impairment losses, if any. Translation gains/losses on this non-monetary asset resulting from fluctuations in foreign exchange rates are included in accumulated other comprehensive income under the provisions of SFAS No. 52, *Foreign Currency Translation.* Losses related to changes in market value and exchange rates determined to be other-than-temporary are reported in earnings in the period in which the impairment occurs.

(e) Inventory

The Company values inventories at the lower of cost or net realizable value. The Company determines the cost of inventory using the average cost method. The Company analyzes its inventory levels quarterly and writes down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory quantities in excess of expected requirements. Expired inventory is disposed of and the related costs are written off to cost of sales.

United States regulatory approval for Kuvan was received in December 2007, and manufacturing costs for this product prior to this date were expensed as research and development expenses. The Company considers regulatory approval of product candidates to be uncertain, and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained. As such, the manufacturing costs for Kuvan prior to regulatory approval were not capitalized as inventory. When regulatory approval was obtained, the Company began capitalizing

inventory at the lower of cost or net realizable value.

In the first quarter of 2008, the Company received $26.8 million of inventory distributed by the Company s joint venture with Genzyme pursuant to the terms of the joint venture restructuring (see Note 5 for further information). The inventory distribution was recorded at the historical production cost, which represented the lower of cost or market value.

Stock-based compensation of $1.7 million and $4.6 million were capitalized into inventory for the years ended December 31, 2007 and 2008, respectively.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

See Note 7 for further information on inventory balances as of December 31, 2007 and 2008.

(f) Investment in and Advances to BioMarin/Genzyme LLC and Equity in the Income (Loss) of BioMarin/Genzyme LLC

Effective January 1, 2008, the Company restructured its relationship with Genzyme (see Note 5 for further information). The Company accounts for its remaining investment in the joint venture using the equity method. Accordingly, the Company records an increase in its investment for contributions to the joint venture and for its 50% share of the income of the joint venture, and a reduction in its investment for its 50% share of any losses of the joint venture or disbursements of profits from the joint venture. Equity in the income (loss) of BioMarin/Genzyme LLC includes the Company s 50% share of the joint venture s loss/income for the period. Advances to BioMarin/Genzyme LLC include the current receivable from the joint venture for the reimbursement related to services provided to the joint venture by the Company and the investment in BioMarin/Genzyme LLC includes the Company s share of the net equity of the joint venture.

(g) Goodwill, Intangible Assets and Impairment of Long-Lived Assets

The Company records goodwill in a business combination when the total consideration exceeds the fair value of the net tangible and identifiable intangible assets acquired. In accordance with Statement of Financial Accounting Standards (SFAS) No. 142, *Goodwill and Other Intangible Assets*, goodwill and intangible assets with indefinite lives are not amortized. Intangible assets with definite lives are amortized over their useful lives on a straight-line basis.

The Company reviews long-lived assets for impairment annually and whenever events or circumstances indicate that the carrying amount of an asset may not be recoverable. If it is determined that the full carrying amount of an asset is not recoverable, an impairment loss is recorded in the amount by which the carrying amount of the asset exceeds its fair value. See Note 4 for further discussion of the Company s intangible asset and goodwill impairment analyses.

The Company currently operates in one business segment, the biopharmaceutical development and commercialization segment. When reviewing goodwill for impairment, SFAS No. 142 requires that the Company assess whether goodwill should be allocated to operating levels lower than its single operating segment for which discrete financial information is available and reviewed for decision-making purposes. These lower levels are referred to as reporting units. As of December 31, 2007 and 2008, the Company had only one reporting unit. The Company performs an annual impairment test in the fourth quarter of each fiscal year by assessing the fair value and recoverability of its goodwill, unless facts and circumstances warrant a review of goodwill for impairment before that time. The Company determines the fair value of its reporting unit using quoted market prices.

The recoverability of the carrying value of buildings and leasehold improvements for the Company s facilities will depend on the successful execution of the Company s business initiatives and the Company s ability to earn sufficient returns on its approved products and product candidates. Based on management s current estimates, the Company expects to recover the carrying value of such assets.

(h) Property, Plant and Equipment

Property, plant and equipment are stated at cost. Depreciation is computed using the straight-line method over the related estimated useful lives, except for leasehold improvements, which are depreciated over the shorter of the useful life of the asset or the lease term. Significant additions and improvements are capitalized, while repairs and maintenance are charged to expense as incurred. Property and equipment purchased for specific

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

research and development projects with no alternative uses are expensed as incurred. See Note 8 for further information on property, plant and equipment balances as of December 31, 2007 and 2008.

Certain of the Company s operating lease agreements include scheduled rent escalations over the lease term, as well as tenant improvement allowances. The Company accounts for these operating leases in accordance with SFAS No. 13, *Accounting for Leases*, and FASB Technical Bulletin No. 85-3, *Accounting for Operating Leases with Scheduled Rent Increases*. Accordingly, the scheduled increases in rent expense are recognized on a straight-line basis over the lease term. The difference between rent expense and rent paid is recorded as deferred rent and included in other liabilities in the accompanying consolidated balance sheets. The tenant improvement allowances are recognized as a credit to rent expense over the lease term on a straight-line basis.

(i) Revenue Recognition

The Company recognizes revenue in accordance with the provisions of SEC Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104), and Emerging Issues Task Force Issue (EITF) No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*. The Company s revenues consist of net product revenues from Naglazyme, and Kuvan, Aldurazyme product transfer and royalty revenues beginning January 1, 2008, revenues from its collaborative agreement with Merck Serono and other license and royalty revenues. Milestone payments are recognized in full when the related milestone performance goal is achieved and the Company has no future performance obligations related to that payment.

Net Product Revenues The Company recognizes net product revenue when persuasive evidence of an arrangement exists, the product has been delivered to the customer, title and risk of loss have passed to the customer, the price to the buyer is fixed or determinable and collection from the customer is reasonably assured. Product sales transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents. Amounts collected from customers and remitted to governmental authorities, which are primarily comprised of value-added taxes (VAT) related to Naglazyme sales in foreign jurisdictions, are presented on a net basis in the Company s statements of operations, in accordance with EITF No. 06-3, *How Taxes Collected from Customers and Remitted to Governmental Authorities Should Be Presented in the Income Statement,* in that taxes billed to customers are not included as a component of net product revenues.

The Company began recognizing revenue related to Aldurazyme in the first quarter of 2008, effective with the restructuring of the Company s Aldurazyme joint venture with Genzyme (see Note 5 for further information). According to the terms of the restructuring, BioMarin receives a 39.5% to 50% royalty on worldwide net Aldurazyme sales by Genzyme depending on sales volume, which is included in net product revenue in the consolidated statements of operations. The Company recognizes a portion of this amount as product transfer revenue when product is released to Genzyme as all of the Company s performance obligations are fulfilled at that point and title to, and risk of loss for, the product has transferred to Genzyme. The product transfer revenue represents the fixed amount per unit of Aldurazyme that Genzyme is required to pay the Company if the product is unsold by Genzyme. The amount of product transfer revenue will eventually be deducted from the calculated royalty rate when the product is sold by Genzyme. The Company records the Aldurazyme royalty revenue based on net sales information provided by Genzyme and records product transfer revenue based on the fulfillment of Genzyme purchase orders in accordance with SAB 104 and the terms

of the related agreements with Genzyme. As of December 31, 2008, accounts receivable included $11.9 million of unbilled accounts receivable related to net incremental Aldurazyme product transfers to Genzyme.

The Company sells Naglazyme worldwide and sells Kuvan in the U.S. In the U.S., Naglazyme and Kuvan are generally sold to specialty pharmacies or end-users, such as hospitals, which act as retailers. In the E.U., Naglazyme is sold to the Company s authorized distributors or directly to hospitals, which act as the end-users.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

Because of the pricing of Naglazyme and Kuvan, the limited number of patients and the customers limited return rights, Naglazyme and Kuvan customers and retailers generally carry a limited inventory. Accordingly, the Company expects the sales related to Naglazyme and Kuvan will be closely tied to end-user demand.

The Company records reserves for rebates payable under Medicaid and other government programs as a reduction of revenue at the time product sales are recorded. The Company s reserve calculations require estimates, including estimates of customer mix, to determine which sales will be subject to rebates and the amount of such rebates. The Company updates its estimates and assumptions each period, and records any necessary adjustments to its reserves. The Company records fees paid to distributors as a reduction of revenue, in accordance with EITF Issue No. 01-09, *Accounting for Consideration given by a Vendor to a Customer (including a Reseller of a Vendor s Products).*

The Company records allowances for product returns, if appropriate, as a reduction of revenue at the time product sales are recorded. Several factors are considered in determining whether an allowance for product returns is required, including market exclusivity of the products based on their orphan drug status, the patient population, the customers limited return rights and the Company s experience with returns. The Company s products are comparable in nature and sold to similar customers with limited return rights, therefore the Company relies on historical return rates for Aldurazyme and Naglazyme to estimate returns for Kuvan, which has a limited history. Genzyme s return rights for Aldurazyme are limited to defective product. Based on these factors, management has concluded that product returns will be minimal. In the future, if any of these factors and/or the history of product returns changes, an allowance for product returns may be required. The Company maintains a policy to record allowances for doubtful accounts for estimated losses resulting from the inability of its customers to make required payments. As of December 31, 2008, the Company has experienced no significant bad debts and the recorded allowance for doubtful accounts was insignificant.

Orapred product sales The Company does not expect to report Orapred product sales in future periods because of the sublicense of North American rights to the product to Sciele Pharma Inc. (Sciele) in March 2006.

Collaborative agreement revenues Collaborative agreement revenues from Merck Serono include both license revenue and contract research revenue. Nonrefundable up-front license fees where the Company has continuing involvement through research and development collaboration are initially deferred and recognized as collaborative agreement license revenue over the estimated period for which the Company continues to have a performance obligation. The Company s performance obligation related to the $25.0 million upfront payment from Merck Serono ended in the fourth quarter of 2008. There is no cost of sales associated with the amortization of the up-front license fee received from Merck Serono. Nonrefundable amounts received for shared development costs are recognized as revenue in the period in which the related expenses are incurred. Contract research revenue included in collaborative agreement revenues represents Merck Serono s share of Kuvan development costs under the agreement, which are recorded as research and development expenses. Allowable costs during the development period must have been included in the pre-approved annual budget in order to be subject to reimbursement, or must be separately approved by both parties.

Collaborative agreement revenues include $7.4 million, $6.9 million and $5.2 million of the up-front license fee received from Merck Serono recognized as revenue during 2006, 2007 and 2008, respectively, and $11.3 million, $6.4 million and $3.7 million of reimbursable development costs for Kuvan, received during 2006, 2007 and 2008, respectively. Collaborative agreement revenues in 2007 also includes the $15.0 million

milestone payment received from Merck Serono upon acceptance of the Kuvan filing by the EMEA and recognized as

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

revenue during the period, and the $30.0 million milestone payment due from Merck Serono upon marketing approval for Kuvan in the E.U. and recognized as revenue during 2008.

Royalty and license revenues Royalty revenue includes royalties on net sales of products with which the Company has no direct involvement and is recognized based on data reported by licensees or sublicensees. Royalties are recognized as earned in accordance with the contract terms, when the royalty amount is fixed or determinable based on information received from the sublicensee and when collectibility is reasonably assured.

Due to the significant role the Company plays in the operations of Aldurazyme, primarily the manufacturing and regulatory activities, as well as the rights and responsibilities to deliver the product to Genzyme, the Company elected not to classify the Aldurazyme royalty as other royalty revenues.

Royalty and license revenues include royalty revenues from Orapred product sold by Sciele Pharma, Inc. (Sciele), the sublicensee of the Orapred product line, of $2.5 million, $2.3 million, and $3.8 million for the years ended December 31, 2006, 2007, and 2008, respectively. During the third quarter of 2008, the Company earned a $1.5 million milestone payment related to the Japanese approval of Kuvan in July 2008. There is no cost of sales associated with the royalty and license revenues recorded during the periods and no related costs are expected in future periods.

In the second quarter of 2007, the Company recognized the $4.0 million milestone as a result of the one year anniversary of the receipt of approval from the Food and Drug Administration (FDA) for the marketing application of Orapred ODT. Although the receipt of the $4.0 million payment was based solely on the passage of time from the FDA approval, the Company did not recognize the payment during the twelve-month period following approval because the fee was not considered to be fixed or determinable until it became due and payable. In making this determination, management considered the extended one-year payment term, the related uncertain future product sales, and the Company s lack of experience with Sciele. Milestone payments are recognized in full when the related milestone performance goal is achieved and the Company has no future performance obligations related to that payment.

(j) Research and Development

Research and development expenses include expenses associated with contract research and development provided by third parties, product manufacturing prior to regulatory approval, clinical and regulatory costs, and internal research and development costs. In instances where the Company enters into agreements with third parties for research and development activities, costs are expensed upon the earlier of when non-refundable amounts are due or as services are performed unless there is an alternative future use of the funds in other research and development projects. Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables. The Company accrues costs for clinical trial activities based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the vendors that perform

the activities.

The Company believes that regulatory approval of its product candidates is uncertain, and does not assume that products manufactured prior to regulatory approval will be sold commercially. As a result, inventory costs for product candidates are expensed as research and development until regulatory approval is obtained in a major market, at which time inventory is capitalized at the lower of cost or net realizable value.

(k) Net Income (Loss) Per Share

Net loss per share is calculated by dividing net loss by the weighted average shares of common stock outstanding during the period. Diluted net loss per share is calculated by dividing net loss by the weighted

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

average shares of common stock outstanding and potential shares of common stock during the period. Potential shares of common stock include dilutive shares issuable upon the exercise of outstanding common stock employee awards, restricted stock units, and contingent issuances of common stock related to convertible debt and acquisition payable. For 2006 and 2007, such potential shares of common stock were excluded from the computation of diluted net loss per share, as their effect is antidilutive.

Potentially dilutive securities for the years ended December 31, 2006 and 2007, include (in thousands):

	December 31,	
	2006	2007
Options to purchase common stock	10,374	11,413
Common stock issuable under convertible debt	14,075	26,361
Portion of acquisition payable in common stock at the option of the Company	525	243
Restricted stock units		117
Potentially issuable common stock for ESPP purchases	429	311
Total	25,403	38,445

The following represents a reconciliation from basic weighted shares outstanding to diluted weighted shares outstanding and the earnings per share for the year ended December 31, 2008 (in thousands, except per share data):

	Year Ended December 31, 2008		
	Net Income (Numerator)	Weighted Average Shares Outstanding (Denominator)	Per Share Amount
Basic Earnings Per Share:			
Net Income	$ 30,831	98,975	$ 0.31
Effect of dilutive shares:			
Stock options using the treasury method		3,837	
Nonqualified deferred compensation plan obligation using the treasury method	(308)	32	

Portion of acquisition obligation payable in common stock at the option of the Company		483	
Potentially issuable common stock for ESPP		245	
Diluted Earnings Per Share:			
Net Income	$ 30,523	103,572	$ 0.29

In addition to the options included in the above table, options to purchase approximately 5.3 million shares of common stock and 225,255 restricted stock units were outstanding during the twelve months ended December 31, 2008, but were not included in the computation of diluted earnings per share because they were anti-dilutive during the period using the treasury stock method. These options were anti-dilutive because the fair value of the Company s stock exceeded the assumed proceeds. Additionally, approximately 26.3 million of the underlying shares of the Company s convertible debt were not included in the diluted average common shares outstanding because they were antidilutive during the twelve months ended December 31, 2008 using the if-converted method whereby the related interest expense on the convertible debt is added to net income for the period.

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BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2007 and 2008

(l) Stock-Based Compensation

Stock-based compensation is accounted for in accordance with SFAS No. 123R, *Share-Based Payment,* and related interpretations. Under the fair value recognition provisions of this statement, share-based compensation cost is measured at the grant date based on the value of the award and is recognized as expense over the vesting period. Determining the fair value of share-based awards at the grant date requires judgment, including estimating future stock price volatility and employee stock option exercise behaviors. If actual results differ significantly from these estimates, stock-based compensation expense and results of operations could be materially impacted.

Expected volatility is based upon proportionate weightings of the historical volatility of the Company s stock and the implied volatility of traded options on the Company s stock. The expected life of options is based on observed historical exercise patterns, which can vary over time.

As stock-based compensation expense recognized in the consolidated statement of operations is based on awards ultimately expected to vest, the amount of expense has been reduced for estimated forfeitures. SFAS No. 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Forfeitures are estimated based on historical experience.

If factors change and different assumptions are employed in the application of SFAS No. 123R, the compensation expense recorded in future periods may differ significantly from what was recorded in the current period. See Note 3 for further discussion of the Company s accounting for stock-based compensation.

(m) Deferred Compensation Plan

Other non-current assets include $0.5 million and $0.9 million, respectively, of investments held in trust related to our nonqualified deferred compensation plan for certain employees and directors as of December 31, 2007 and 2008, respectively. All of the investments held in the Company s nonqualified deferred compensation plan are classified as trading securities and recorded at fair value in accordance with SFAS No. 115 with changes in the investments fair values recognized in earnings in the period they occur. Changes in the fair value are recorded in earnings in the period incurred. In accordance with EITF 97-14, *Accounting for Deferred Compensation Arrangements Where Amounts Earned Are Held in a Rabbi Trust and Invested,* restricted stock issued into the deferred compensation plan are accounted for similarly to treasury stock in that, the value of the employer stock is determined on the date the restricted stock vests and the shares are issued into the plan. The restricted stock issued into the plan is recorded in equity and changes tin their fair value is not recognized. Additionally, the Company has recorded a corresponding liability for the deferred compensation plan in other liabilities. See Note 18 for additional discussion regarding deferred compensation.

The plan allows eligible employees, including management and certain highly-compensated employees as designated by the Plan s Administrative Committee and the members of the Board to make voluntary deferrals of compensation to specified dates, retirement or death. Participants are permitted to defer portions of their salary, annual cash bonus and restricted stock. The Company is not allowed to make additional direct contributions to the plan on behalf of the participants without further action by the Board.

(n) Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred taxes are determined based on the difference between the financial statement and tax bases of assets and

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liabilities using tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is recorded to reduce deferred tax assets to the amount that is more likely than not to be realized. There is a full valuation allowance against net deferred tax assets of $294.7 million at December 31, 2008. Future taxable income and ongoing prudent and feasible tax planning strategies have been considered in assessing the need for the valuation allowance. An adjustment to the valuation allowance would increase or decrease income in the period such adjustment was made. For the years ended December 31, 2006, 2007 and 2008, the Company recognized $0.1 million, $0.7 million and $2.6 million of income tax expense primarily related to income earned in certain of the Company s international subsidiaries and in 2008, included California state income tax and U.S. federal Alternative Minimum Tax expense. See Note 13 for further discussion of the Company s income taxes.

(o) Foreign Currency and Other Hedging Instruments

The Company has transactions denominated in foreign currencies and, as a result, is exposed to changes in foreign currency exchange rates. The Company manages some of these exposures on a consolidated basis, which results in the netting of certain exposures to take advantage of natural offsets and through the use of forward contracts. Gains or losses on net foreign currency hedges are intended to offset losses or gains on the underlying net exposures in an effort to reduce the earnings and cash flow volatility resulting from fluctuating foreign currency exchange rates.

The Company accounts for its derivative instruments as either assets or liabilities on the balance sheet and measures them at fair value. Derivatives that are not defined as hedges in SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities,* are adjusted to fair value through earnings. Gains and losses resulting from changes in fair value are accounted for depending on the use of the derivative and wither it is designated and qualifies for hedge accounting. See Note 11 for further discussion of the Company s derivative instruments.

(p) Fair Value of Financial Instruments

SFAS No. 107, *Disclosures about Fair Value of Financial Instruments*, requires the Company to disclose the fair value of financial instruments for assets and liabilities for which it is practicable to estimate that value.

The carrying amounts of all cash equivalents and forward exchange contracts approximate fair value based upon quoted market prices or discounted cash flows. The fair value of trade accounts receivables, accounts payable and other financial instruments approximates carrying value due to their short-term nature.

(q) Comprehensive Income (Loss) and Accumulated Other Comprehensive Income (Loss)

Comprehensive income (loss) includes net income/loss and certain changes in stockholders equity that are excluded from net loss, such as changes in unrealized gains and losses on the Company s available-for-sale securities and changes in the Company s cumulative foreign currency translation account. Comprehensive income (loss) for the years ended December 31, 2006, 2007, and 2008 is included in the Company s consolidated statements of stockholders equity. There were no tax effects allocated to any components of other comprehensive income (loss) during 2006, 2007, and 2008.

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In 2008, the Company s comprehensive income was approximately $31.8 million compared to comprehensive net loss of $15.6 million for the year ended December 31, 2007. The fluctuation in accumulated other comprehensive income (loss) is comprised of the following (in thousands):

	Year ended December 31,	
	2007	2008
Net unrealized gain on available-for-sale securities	$ (22)	$ 1,201
Net unrealized loss on foreign currency hedges		(212)
Net foreign currency translation gain (loss)	186	(22)
Accumulated other comprehensive income	$ 164	$ 967

(r) Restricted Cash

The Company s balance of restricted cash amounted to $2.9 million and $7.3 million at December 31, 2007 and 2008, respectively. The 2007 restricted cash balance is included in other assets, and $6.2 million and $1.1 million of the 2008 balance are included in other current assets and other assets, respectively. The 2007 and 2008 balances include $2.4 million and $6.2 million related to cash received for royalties pursuant to the Orapred sublicense agreement, respectively, which are restricted until August 2009. Restricted cash also includes investments of $0.5 million and $0.9 million held by the Company s Nonqualified Deferred Compensation Plan as of December 31, 2007 and 2008, respectively. See Note 18 for further discussion on the Company s Nonqualified Deferred Compensation Plan.

(s) Recent Accounting Pronouncements

In December 2007, the Financial Accounting Standards Board released Statement Financial Accounting Standard No. 141(R), *Business Combinations.* This Statement revises previous business combination accounting requirements and applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008, which would impact the Company for business combinations completed after January 1, 2009. The effect of this Statement on the Company s consolidated financial position, results of operations or cash flows will depend on the potential future business combinations entered into by the Company that will be subject to the Statement.

In December 2007, the FASB released SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements an amendment of ARB No. 51*. This Statement is effective for fiscal years, and interim periods within those fiscal years, beginning on or after December 15, 2008, which for the Company is the year ending December 31, 2009, and the interim periods within that fiscal year. The Company does not expect the adoption of SFAS No. 160 to have a material effect on its consolidated financial statements.

In December 2007, the Securities and Exchange Commission (SEC) issued Staff Accounting Bulletin 110 (SAB 110). SAB 110 amends and replaces Question 6 of Section D.2 of Topic 14, Share-Based Payment, of the Staff Accounting Bulletin series. The Company does not expect that SAB 110 will have an impact on its financial statements.

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In February 2008, the FASB Emerging Issues Task Force issued EITF Issue No. 08-1, *Revenue Recognition for a Single Unit of Accounting*. The staff at EITF recommends that this issue be effective for fiscal years beginning after December 15, 2008, which for the Company is the year ending December 31, 2009. The adoption of this issue is not expected to have material effect on the Company s financial position, cash flows or results of operations.

In March 2008, the FASB issued SFAS No. 161, *Disclosures about Derivative Instruments and Hedging Activities*, an amendment to SFAS No. 133 (SFAS No. 161), which changes the disclosure requirements for derivative instruments and hedging activities. This statement s disclosure requirements are effective for the Company as of January 1, 2009. The adoption of this statement will not impact the Company s consolidated balance sheets, results of operations or cash flows because the statement only requires additional disclosures relating to the Company s derivative instruments.

In April 2008, the FASB issued FASB Staff Position No. FAS 142-3, *Determination of the Useful Life of Intangible Assets* (FSP FAS 142-3), which amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under FASB Statement No. 142, *Goodwill and Other Intangible Asset*. FSP FAS 142-3 also requires expanded disclosure related to the determination of intangible asset useful lives. This Statement is effective for fiscal years beginning on or after December 15, 2008, which for the Company is the year ending December 31, 2009. The Company is currently evaluating the potential impact the adoption of FSP FAS 142-3 will have on its consolidated financial statements.

In May 2008, the FASB issued SFAS No. 162, *The Hierarchy of Generally Accepted Accounting Principles*. SFAS No. 162 identifies the sources of accounting principles and the framework for selecting the principles used in the preparation of financial statements that are presented in conformity with generally accepted accounting principles. SFAS No. 162 becomes effective 60 days following the SEC s approval of the Public Company Accounting Oversight Board amendments to Statement on Auditing Standards No. 69, *The Meaning of Present Fairly in Conformity With Generally Accepted Accounting Principles*, for periods completed after January 1, 2009. The Company does not expect that the adoption of SFAS No. 162 to have a material effect on its consolidated financial statements.

In June 2008, the FASB issued FSP EITF 03-6-1, *Determining Whether Instruments Granted in Share-Based Payment Transactions Are Participating Securitie*s. FSP EITF 03-6-1 clarifies that share-based payment awards that entitle their holders of unvested awards to receive non-forfeitable dividends or dividend equivalents should be considered participating securities. The Company has some grants of restricted stock that contain non-forfeitable rights to dividends and will be considered participating securities once the Company adopts FSP EITF 03-6-1. As participating securities, the Company will be required to include these instruments in the calculation of earnings per share (EPS) using the two-class method. The two-class method of computing EPS is an earnings allocation formula that determines EPS for each class of common stock and participating security according to dividends declared and participation rights in undistributed earnings. FSP EITF 03-6-1 is effective for the first quarter of the Company s fiscal year beginning January 1, 2009. The Company is currently evaluating the potential impact, if any, the adoption of FSP EITF 03-6-1 could have on its calculation of EPS.

In January 2009, the FASB issued FASB Staff Position No. EITF 99-20-1, *Amendments to the Impairment Guidance of EITF Issue No. 99-20, (FSP EITF 99-20-1)*. This FSP amends the impairment guidance in EITF Issue No. 99-20, Recognition of Interest Income and Impairment on Purchased Beneficial Interests and Beneficial Interests That Continue to Be Held by a Transferor in Securitized Financial Assets, to align it with the impairment guidance within Statement No. 115 by removing from EITF 99-20 the requirement to place exclusive

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reliance on market participants assumptions about future cash flows when evaluating an asset for other-than-temporary impairment. Both standards will now require that assumptions about future cash flows consider reasonable management judgment about the probability that the holder of an asset will be unable to collect all amounts due The FSP is effective for interim and annual reporting periods ending after December 15, 2008, which for the Company is the year ending December 31, 2009. The application of this guidance is not expected to have a significant impact on the Company s financial condition, results of operations or cash flows.

In October 2008, the FASB issued Staff Position No. FAS 157-3, *Determining the Fair Value of a Financial Asset in a Market That Is Not Active,* (FSP FAS 157-3). FSP FAS 157-3 clarifies the application of FAS 157 in a market that is not active and defines additional key criteria in determining the fair value of a financial asset when the market for that financial asset is not active. FSP FAS 157-3 applies to financial assets within the scope of accounting pronouncements that require or permit fair value measurements in accordance with FAS 157. FSP FAS 157-3 was effective upon issuance and the application of FSP FAS 157-3 did not have a material impact on the Company s consolidated financial statements.

In November 2007, EITF issued EITF 07-1, *Accounting for Collaborative Arrangements,* (EITF 07-1). EITF 07-1, which will be applied retrospectively, requires expanded disclosures for contractual arrangements with third parties that involve joint operating activities and may require reclassifications to previously issued financial statements. EITF 07-1 is effective for the Company on January 1, 2009. The Company is currently evaluating the impact EITF 07-1 may have on its financial statements.

(t) Reclassifications

Certain items in the prior years consolidated financial statements have been reclassified to conform to the current presentation.

(3) STOCKHOLDERS EQUITY

(a) Share Incentive Plan

BioMarin s 2006 Share Incentive Plan (Share Incentive Plan), which was approved in June 2006 and replaces the Company s previous stock option plans, provides for grants of options to employees to purchase common stock at the fair market value of such shares on the grant date, as well as other forms of equity compensation. As of December 31, 2008, awards issued under the 2006 Share Incentive Plan include both stock options and restricted stock units. Stock option awards granted to employees generally vest over a four-year period on a cliff basis six months after the grant date and then monthly thereafter. The term of the outstanding options is generally ten years. Options assumed under past business

acquisitions generally vest over periods ranging from immediately upon grant to five years from the original grant date and have terms ranging from two to ten years. Restricted stock units granted to employees generally vest in a straight-line, annually over a four-year period after the grant date. Restricted stock units granted to directors generally vest in full one year after the grant date. As of December 31, 2008, options to purchase approximately 8.3 million and 3.8 million shares were outstanding under the Share Incentive Plan, and the Company s old plans, respectively.

(b) Employee Stock Purchase Plan

Under BioMarin s Employee Stock Purchase Plan (ESPP), which was approved in June 2006 and replaces the Company s previous plan, employees meeting specific employment qualifications are eligible to participate and can purchase shares on established dates semi-annually through payroll deductions at the lower of 85% of the fair market value of the stock at the commencement or each purchase date of the offering period. Each offering

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period will span up to two years. The ESPP permits eligible employees to purchase common stock through payroll deductions for up to 10% of qualified compensation, up to an annual limit of $25,000. The ESPP is intended to qualify as an employee stock purchase plan under Section 423 of the Internal Revenue Code. As of December 31, 2008, approximately 807,000 shares had been issued under the Employee Stock Purchase Plan, and approximately 1.8 million shares had been reserved for future issuance.

(c) Board of Director Grants

An initial option is granted to each new outside member of BioMarin s Board of Directors to purchase 30,000 shares of common stock at the fair value on the date of the grant. Until January 2007, on each anniversary date of becoming a director, each outside member was granted options to purchase 30,000 shares of common stock at the fair market value on such date. Effective June 7, 2007, on the date of each annual meeting of stockholders, other than newly elected directors, each outside director other than a newly elected director is granted options for the purchase of 15,000 shares of common stock and 2,500 restricted stock units. The options vest over one year and have a term of ten years. The restricted stock units vest on the one year anniversary of the date of grant.

(d) Stock-based Compensation

A summary of stock option activity under all plans, including plans that were suspended upon adoption of the 2006 Share Incentive Plan, for the year ended December 31, 2008 is presented as follows:

	Options	Weighted Average Exercise Price	Weighted Average Fair Value of Options Granted	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
					(in thousands)
Balance as of December 31, 2007	11,413,452	$ 13.65			
Granted	3,573,658	$ 33.55	$ 15.71		
Exercised	(2,488,672)	$ 10.39			$ 61,749
Expired and Forfeited	(423,286)	$ 21.25			
Balance as of December 31, 2008	12,075,152	$ 19.94		6.63	$ 32,152
Options expected to vest as of December 31, 2008	6,187,689	$ 24.37			$ 5,696

Exercisable as of December 31, 2008	5,696,089	$ 14.98	$ 26,280

The aggregate intrinsic value for outstanding options is calculated as the difference between the exercise price of the underlying awards and the quoted price of the Company s common stock as of the last trading day of fiscal 2008. There were 8.0 million options that were in-the-money at December 31, 2008. The aggregate intrinsic value of options exercised was determined as of the date of option exercise. Upon the exercise of the options the Company issues new common stock from its authorized shares.

At December 31, 2008, an aggregate of approximately 14.4 million unissued shares were authorized for future issuance under the Share Incentive Plan.

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The following table presents the composition of options outstanding and exercisable as of December 31, 2008:

	Options Outstanding			Options Exercisable	
Range of exercise prices	Number of Options Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number of Options Exercisable	Weighted Average Exercise Price
$ 0.00 to 7.34	826,531	5.50	$ 6.22	789,042	$ 6.22
7.35 to 10.55	941,082	4.91	8.79	898,794	8.78
10.56 to 14.06	2,042,524	6.66	12.24	1,400,153	12.24
14.07 to 17.58	4,066,383	8.08	17.13	1,805,058	17.12
17.59 to 21.10	965,358	9.26	18.04	123,997	18.28
21.11 to 24.61	352,427	5.46	22.43	200,044	22.12
24.62 to 28.13	224,418	9.00	26.79	41,793	26.51
28.14 to 31.65	38,650	9.57	28.94	1,173	29.12
31.66 to 35.17	103,050	9.17	33.68	21,415	33.85
35.17 to 40.99	2,514,729	9.36	38.51	414,620	38.50
	12,075,152			5,696,089	

The weighted average grant date fair value of options granted during the years ended December 31, 2006, 2007, and 2008, was $7.66, $9.22 and $15.71 per share, respectively.

The fair value of each option award is estimated on the grant date using the Black-Scholes valuation model and the assumptions noted in the table below. The expected life of options is based on observed historical exercise patterns. Groups of employees that have similar historical exercise patterns were considered separately for valuation purposes, but none were identified that had distinctly different exercise patterns as of December 31, 2008. The expected volatility of stock options is based upon proportionate weightings of the historical volatility of BioMarin stock and the implied volatility of traded options on the Company s stock for fiscal periods in which there is sufficient trading volume in options on the Company s stock. The risk free interest rate is based on the implied yield on a U.S. Treasury zero-coupon issue with a remaining term equal to the expected term of the option. The dividend yield reflects that BioMarin has not paid any cash dividends since inception and does not intend to pay any cash dividends in the foreseeable future. The weighted-average assumptions for options granted under the Share Incentive Plan for the years ended December 31, 2006, 2007, and 2008, respectively are as follows:

	Year Ended December 31,

Stock Option Valuation Assumptions	2006	2007	2008
Expected volatility	52.2-57.9%	44.4-50.8%	44.7-51.4%
Dividend yield	0.0%	0.0%	0.0%
Expected life	4.9-5.3 years	5.2-5.5 years	5.2-5.8 years
Risk-free interest rate	4.4-5.1%	3.7-5.1%	1.4-3.2%

The Company recorded $9.0 million, $16.8 million and $21.2 million of compensation costs related to current period vesting of stock options for the years ended December 31, 2006, 2007, and 2008, respectively. As of December 31, 2008, there was $73.0 million of total unrecognized compensation cost related to unvested stock options. These costs are expected to be recognized over a weighted average period of 2.7 years.

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The fair value of each award granted under the ESPP is estimated on the date of grant using the Black-Scholes valuation model and the assumptions noted in the table below. The expected volatility of ESPP shares is based on the implied volatility of traded options on the Company s stock for periods in which there is sufficient trading volume in those options. Otherwise, historical volatility is utilized. The risk free interest rate is based on the implied yield on a U.S. Treasury zero-coupon issue with a remaining term equal to the expected term of the option. The dividend yield reflects that BioMarin has not paid any cash dividends since inception and does not intend to pay any cash dividends in the foreseeable future.

	Year Ended December 31,		
Employee Stock Purchase Plan Valuation Assumptions	**2006**	**2007**	**2008**
Expected volatility	44-55%	44-54%	47-51%
Dividend yield	0.0%	0.0%	0.0%
Expected life	6-24 months	6-24 months	6- 24 months
Risk-free interest rate	2.7-5.2%	3.8-5.2%	1.1-2.4%

The Company recorded $0.6 million, $1.4 million, and $1.1 million of compensation costs related to options granted under the ESPP for the years ended December 31, 2006, 2007, and 2008, respectively. As of December 31, 2008, there was $2.3 million of total unrecognized compensation cost related to unvested stock options. These costs are expected to be recognized over a weighted average period of 1.4 years.

A summary of non-vested restricted stock unit activity under the plan for the year ended December 31, 2008 is presented as follows:

	Shares	Weighted Average Grant Date Fair Value
Non-vested units as of December 31, 2007	116,625	$ 17.39
Granted	160,755	38.08
Vested	(39,125)	16.66
Forfeited	(13,000)	28.78
Non-vested units as of December 31, 2008	225,255	$ 31.06

The Company recorded $0.3 million and $1.4 million of compensation costs related to restricted stock units for the years ended December 31, 2007 and 2008, respectively. Prior to 2007, the Company did not grant restricted stock units, as such there was no stock-based compensation associated with restricted stock in 2006. As of December 31, 2008, there was $5.7 million of total unrecognized compensation cost related to unvested restricted stock units. These costs are expected to be recognized over a weighted average period of 3.1 years.

The compensation expense that has been included in the Company s consolidated statement of operations for stock-based compensation arrangements were as follows (in thousands):

	December 31,		
	2006	2007	2008
Cost of sales	$	$ 578	$ 1,521
Selling, general and administrative expense	5,348	10,727	15,145
Research and development expense	4,242	6,978	8,584
Total stock-based compensation expense	$ 9,590	$ 18,283	$ 25,250

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There was no income tax benefit associated with stock-based compensation for 2007 and 2008 because the deferred tax asset resulting from stock-based compensation was offset by an additional valuation allowance for deferred tax assets.

Stock-based compensation of $1.7 million and $4.6 million was capitalized into inventory for the years ended December 31, 2007 and 2008, respectively. Capitalized stock-based compensation is recognized into cost of sales when the related product is sold.

At December 31, 2008, an aggregate of approximately 25.9 million unissued shares were authorized for future issuance under the Company s stock plans, which include shares issuable under the Share Incentive Plan and the Company s ESPP. Under the Share Incentive Plan, awards that expire or are cancelled without delivery of shares generally become available for issuance under the plan. Awards that expire or are cancelled under the Company s suspended 1997 Stock Plan or 1998 Director Option Plan may not be reissued.

(e) Common Stock

In March 2006, the Company completed a public offering of its common stock concurrent with its public offering of senior subordinated convertible debt (see Note 10). In the common stock offering, the Company sold 10,350,000 shares at a price to the public of $13.00 per share, or a total offering price of $134.6 million. The net proceeds were approximately $127.4 million.

(f) Stockholders Rights Plan

In 2002, the Board of Directors authorized a stockholders rights plan, which was amended and restated on February 27, 2009. Terms of the plan provide for stockholders of record at the close of business on September 23, 2002 to receive one preferred share purchase right (a Right) for each outstanding share of common stock held. The Rights will be exercisable if a person or group acquires 15% or more of the Company s common stock or announces a tender offer or exchange offer for 15% or more of the common stock. Depending on the circumstances, the effect of the exercise of the Rights will be to permit each holder of a Right to purchase shares of the Company s Series B Junior Participating Preferred Stock that have significantly superior dividend, liquidation, and voting rights compared to the Company s common stock. The Company will be entitled to redeem the Rights at $0.001 per Right at any time before a person has acquired 15% or more of the outstanding common stock. The stockholders rights plan expires in 2012. As of December 31, 2008 no stock rights have been granted under this plan.

(4) INTANGIBLE ASSETS AND GOODWILL

As of December 31, 2007 and December 31, 2008, intangible assets consisted of the following (in thousands):

	December 31,	
	2007	2008
Orapred	$ 20,437	$ 20,437
Kuvan	2,327	5,093
Less: Accumulated amortization	(13,168)	(17,904)
Net carrying value	$ 9,596	$ 7,626

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(a) Orapred

In 2004, the Company acquired the Orapred product line from Ascent Pediatrics, a wholly owned subsidiary of Medicis Pharmaceutical Corporation (Medicis). The acquisition was accounted for as a purchase business combination. Under the purchase method of accounting, the assets acquired and liabilities assumed are recorded at the date of acquisition, at their respective fair values. The total consideration has been allocated based on an estimate of the fair value of assets acquired and liabilities assumed.

The amended transaction agreements entered into with Medicis following the settlement of a dispute in January 2005 in the Company s favor, provided for total acquisition payments of $169.0 million payable to Medicis in specified amounts through 2009. At December 31, 2008 remaining payments to Medicis include a payment due in 2009 of $73.6 million, of which $8.6 million can be paid in cash or the Company s common stock, at the Company s option. The number of shares issuable in 2009, if the Company elects to pay in common stock, will be based on the per share stock price at that time.

The transaction resulted in a purchase price allocation of $21.3 million to goodwill, representing the financial, strategic and operational value of the transaction to BioMarin. Goodwill is subject to an annual impairment analysis under the provisions of SFAS No.142, *Goodwill and Other Intangible Assets* (SFAS 142). The entire amount of goodwill is expected to be deductible for tax purposes.

The product technology is the only intangible asset subject to amortization and represents the rights to the proprietary knowledge associated with Orapred. These rights include the right to develop, use, and market Orapred. The product technology is being amortized over Orapred s estimated economic life of 3.5 years using the straight-line method of amortization and includes no estimated residual value.

The Orapred intangible assets consist of the Orapred product technology as of December 31, 2007 and 2008. The gross and net carrying value of the Orapred product technology was as follows (in thousands):

	December 31,	
	2007	2008
Gross value	$ 20,437	$ 20,437
Accumulated amortization	(13,152)	(17,524)
Net carrying value	$ 7,285	$ 2,913

The Company completed its 2008 annual impairment test during the fourth quarter of 2008, according to the provisions of SFAS 142, and determined that no impairment of goodwill or the Orapred intangible asset existed as of December 31, 2008.

Amortization expense related to the Orapred intangible for the years ended December 31, 2006, 2007 and 2008 was $3.7 million, $4.4 million, and $4.4 million, respectively. The remaining $2.9 million Orapred intangible asset balance will be amortized in 2009.

The imputed discount on the purchase obligation represents the gross value of the future cash payments to Medicis, discounted to their present value at a rate of 6.1%. The discount is being amortized and recorded as interest expense over the life of the obligation using the effective interest rate method.

In March 2006, the Company entered into a license agreement with a third party for the continued sale and commercialization of Orapred and other Orapred formulations then under development. Through the agreement,

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the third party acquired exclusive rights to market these products in North America, and BioMarin retained exclusive rights to market these products outside of North America. BioMarin and the third party are individually responsible for the costs of commercializing the products within their respective territories. The third party will also pay BioMarin royalties on its net sales of these products. BioMarin will also transfer the North American intellectual property to the third party in August 2009, following the purchase of the stock of Ascent Pediatrics from Medicis.

(b) Kuvan Intangible Assets

Kuvan intangible assets relate to license payments made to third parties as a result of the FDA approval of Kuvan in December 2007 and the EMEA approval in December 2008, which resulted in a $2.7 million addition to the Kuvan intangible assets. At December 31, 2008, Kuvan intangible assets totaled a gross value of $5.1 million. Amortization expense related to the Kuvan intangible assets is included as a component of cost of sales in the consolidated statements of operations, and totaled $0.4 million for the year ended December 31, 2008. Amortization expense for the year ended December 31, 2007 was insignificant. The Company completed its 2008 annual impairment test during the fourth quarter of 2008, according to the provisions of SFAS 142, and determined that no impairment of the Kuvan intangible assets existed as of December 31, 2008.

The following table summarizes the annual amortization of the Kuvan intangible assets through 2018 (in thousands):

	Net Balance at December 31, 2008	Remaining Life	Annual Amortization
License payment for FDA Approval	$ 1,979	6 years	$ 332
License payment for EMEA Approval	2,733	10 years	277
Total	$ 4,712		$ 609

(5) JOINT VENTURE

Effective January 2008, the Company and Genzyme restructured BioMarin/Genzyme LLC. Under the revised structure, the operational responsibilities for BioMarin and Genzyme did not significantly change, as Genzyme continues to globally market and sell Aldurazyme and BioMarin continues to manufacture Aldurazyme. The restructuring had two significant business purposes. First, since each party now has full control over its own operational responsibilities, without the need to obtain the approval of the other party, and the parties do not need to review

and oversee the activities of the other, it reduces management s time and effort and therefore improves overall efficiencies. Second, since each party will realize 100% of the benefit of their own increased operational efficiencies, it increases the incentives to identify and implement cost saving measures. Under the previous 50/50 structure, each company shared 50% of the expense associated with the other s inefficiencies and only received 50% of the benefit of its own efficiencies. Specifically, the Company will be able to realize the full benefit of any manufacturing cost reductions and Genzyme will be able to realize the full benefit of any sales and marketing efficiencies.

As of January 1, 2008, instead of sharing all costs and profits equally through the 50/50 joint venture, Genzyme records sales of Aldurazyme to third party customers and pays BioMarin a tiered payment ranging from approximately 39.5% to 50% of worldwide net product sales depending on sales volume, which is recorded by BioMarin as product revenue. The Company recognizes a portion of this amount as product transfer revenue when product is released to Genzyme as all of the Company s performance obligations are fulfilled at this point

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and title to, and risk of loss, for the product has transferred to Genzyme. The product transfer revenue represents the fixed amount per unit of Aldurazyme that Genzyme is required to pay the Company if the product is unsold by Genzyme. The amount of product transfer revenue is deducted from the calculated royalty rate when the product is sold by Genzyme. Genzyme s return rights for Aldurazyme are limited to defective product. Certain research and development activities and intellectual property related to Aldurazyme continues to be managed in the joint venture with the costs shared equally by BioMarin and Genzyme. Pursuant to the terms of the joint venture restructuring, the Company received distributions of $16.7 million of cash and $26.8 million of inventory from the joint venture in the first quarter of 2008.

The Company presents the related cost of sales and its Aldurazyme-related operating expenses as operating expenses in the consolidated statements of operations. Equity in the income (loss) of BioMarin/Genzyme LLC subsequent to the restructuring includes BioMarin s 50% share of the net income/loss of BioMarin/Genzyme LLC related to intellectual property management and ongoing research and development activities.

The results of the joint venture s operations for the years ended December 31, 2006, 2007 and 2008, are presented in the table below (in thousands). Equity in the income (loss) of BioMarin/Genzyme LLC for the years ended December 31, 2006 and 2007 represents the Company s 50% share of the joint venture s income for the periods presented prior to the restructuring.

	Year ended December 31,		
	2006	2007	2008 (unaudited)
Revenue	$ 96,291	$ 123,671	$
Cost of goods sold	23,173	26,877	
Gross profit	73,118	96,794	
Operating expenses	35,262	36,510	4,738
Income (loss) from operations	37,856	60,284	(4,738)
Other income	692	766	198
Net income (loss)	$ 38,548	$ 61,050	$ (4,540)
Equity in the income (loss) of BioMarin/Genzyme LLC	$ 19,274	$ 30,525	$ (2,270)

At December 31, 2007 and 2008, the summarized assets and liabilities of the joint venture and the components of the Company s investment in the joint venture are as follows (in thousands):

	December 31,	
	2007	2008 (unaudited)
Assets	$ 98,340	$ 2,991
Liabilities	(8,577)	(1,161)
Net equity	$ 89,763	$ 1,830
Investment in BioMarin/Genzyme LLC (50% share of net equity)	$ 44,881	$ 915

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(6) SHORT-TERM INVESTMENTS

At December 31, 2008, the principal amounts of short-term investments by contractual maturity are summarized in the table below (in thousands).

	Contractual Maturity Date For the Years Ending December 31,	December 31, 2008		
	2009	Total Book Value	Unrealized Gain	Aggregate Fair Value
Corporate securities	$ 57,270	$ 57,270	$ 232	$ 57,502
Commercial paper	33,076	33,076	48	33,124
U.S. Government backed commercial paper	24,370	24,370	5	24,375
U.S. Government agency securities	220,914	220,914	977	221,891
Total	$ 335,630	$ 335,630	$ 1,262	$ 336,892

At December 31, 2007, the principal amounts of short-term investments by contractual maturity are summarized in the table below (in thousands). All short-term investments were classified as available-for-sale at December 31, 2007.

	Contractual Maturity Date For the Years Ending December 31,	December 31, 2007		
	2008	Total Book Value	Unrealized Gain (Losses)	Aggregate Fair Value
Corporate securities	$ 88,324	$ 88,324	$ (99)	$ 88,225
Commercial paper	259,067	259,067	155	259,222
U.S. Government agency securities	9,798	9,798	6	9,804
Total	$ 357,189	$ 357,189	$ 62	$ 357,251

At December 31, 2008, the aggregate amount of unrealized losses and related fair value of investments with unrealized losses were as follows (in thousands):

	Less Than 12 Months To Maturity		Total	
	Aggregate Fair Value	Unrealized Losses	Aggregate Fair Value	Unrealized Losses
Corporate securities	$ 44,941	$ (147)	$ 44,941	$ (147)
Commercial paper	1,992	(6)	1,992	(6)
U.S. Government backed commercial paper	9,947	(31)	9,947	(31)
U.S. Government agency securities	6,928	(12)	6,928	(12)
Total	$ 63,808	$ (196)	$ 63,808	$ (196)

The Company completed an evaluation of its short-term investments and determined that it did not have any other-than-temporary impairments as of December 31, 2008. The investments are placed in financial institutions with strong credit ratings and management expects full recovery of the amortized cost.

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At December 31, 2007, the aggregate amount of unrealized losses and related fair value of investments with unrealized losses were as follows (in thousands):

	Less Than 12 Months To Maturity		Total	
	Aggregate Fair Value	Unrealized Losses	Aggregate Fair Value	Unrealized Losses
Corporate securities	$ 44,826	$ (135)	$ 44,826	$ (135)
Commercial paper	4,948	(1)	4,948	(1)
Total	$ 49,774	$ (136)	$ 49,774	$ (136)

(7) SUPPLEMENTAL BALANCE SHEET INFORMATION

As of December 31, 2007 and December 31, 2008, inventory consisted of the following (in thousands):

	December 31, 2007	December 31, 2008
Raw materials	$ 5,695	$ 10,314
Work in process	14,458	29,998
Finished goods	12,292	32,850
Total inventory	$ 32,445	$ 73,162

As of December 31, 2007 and December 31, 2008, other current assets consisted of the following (in thousands):

	December 31, 2007	December 31, 2008

Approval milestone receivable from Merck Serono	$	$ 30,000
Non-trade receivables	4,475	4,828
Prepaid expenses	1,850	3,013
Deferred cost of goods sold		3,879
Short-term restricted cash		6,202
Other	870	2,348
Total other current assets	$ 7,195	$ 50,270

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As of December 31, 2007 and December 31, 2008, accounts payable and accrued liabilities consisted of the following (in thousands):

	December 31, 2007	December 31, 2008
Accounts payable	$ 1,169	$ 922
Accrued accounts payable	27,377	26,214
Accrued vacation	2,820	3,798
Accrued compensation	9,931	11,737
Accrued interest and taxes	2,533	2,684
Accrued royalties	1,329	3,401
Other accrued expenses	1,154	6,094
Accrued rebates	1,816	3,194
Acquired rebates and returns reserve	743	621
Short-term portion of deferred compensation liability	859	19
Other	176	167
Total accounts payable and accrued liabilities	$ 49,907	$ 58,851

As of December 31, 2007 and December 31, 2008, other long-term liabilities consisted of the following (in thousands):

	December 31, 2007	December 31, 2008
Long-term portion of deferred rent	$ 1,635	$ 1,176
Long-term portion of capital lease liability		270
Long-term portion of deferred compensation liability	447	1,410
Total other long-term liabilities	$ 2,082	$ 2,856

A roll forward of significant estimated revenue dilution reserves is as follows (in thousands):

	Balance at Beginning	Provision for Current	Provision/ (Reversals)	Actual Charges Related to	Actual Charges Related to	Balance at End of Period

	of Period	period Sales	for Prior Period Sales	Current Period Sales	Prior Period Sales	
Year ended December 31, 2006:						
Returns reserve	$ 6,014	$ 42	$ 118	$	$ (3,541)	$ 2,633
Accrued rebates	1,751	1,187	(1,323)	(603)	(193)	819
Acquired rebate reserve	100		590		(449)	241
Acquired returns reserve	1,546		(389)		(491)	666
Reserve for cash discounts	24	167		(150)	(20)	21
Year ended December 31, 2007:						
Returns reserve	$ 2,633	$	$ (106)	$	$ (2,466)	$ 61
Accrued rebates	819	2,023		(941)	(85)	1,816
Acquired rebate reserve	241		(11)		(108)	122
Acquired returns reserve	666				(45)	621
Reserve for cash discounts	21	298		(267)	(18)	34
Year ended December 31, 2008:						
Returns reserve	$ 61		1		(62)	
Accrued rebates	1,816	3,357		(1,684)	(295)	3,194
Acquired rebate reserve	122		(122)			
Acquired returns reserve	621					621
Reserve for cash discounts	34	1,412		(1,182)	(21)	243

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(8) PROPERTY, PLANT AND EQUIPMENT

Property, plant and equipment at December 31, 2007 and December 31, 2008, consisted of (in thousands):

Category	December 31, 2007	December 31, 2008	Estimated Useful Lives
Leasehold improvements	$ 33,583	$ 27,544	Shorter of life of asset or lease term
Building and improvements	26,784	61,183	20 years
Manufacturing and laboratory equipment	19,403	26,996	5 years
Computer hardware and software	9,657	13,088	3 years
Office furniture and equipment	3,991	4,602	5 years
Land	4,259	10,056	Not applicable
Construction-in-progress	13,952	27,589	Not applicable
	$ 111,629	$ 171,058	
Less: Accumulated depreciation	(34,811)	(46,079)	
Total property, plant and equipment, net	$ 76,818	$ 124,979	

Depreciation for the years ended December 31, 2006, 2007, and 2008 was, $6.8 million, $7.8 million and $11.4 million, respectively. Depreciation capitalized into inventory for the years ended December 31, 2007 and 2008 was $1.2 million and $2.8 million, respectively.

Capitalized interest related to the Company s fixed asset purchases during the years ended December 31, 2007 and 2008 was insignificant.

In January 2008, the Company purchased its previously leased laboratory/office building located at 300 Bel Marin Keys Drive, Novato, California for approximately $12.0 million. As a result of the purchase, the Company capitalized certain pre-existing deferred rent liabilities of approximately $0.5 million as a reduction to the acquisition cost of the building.

(9) INVESTMENT IN SUMMIT CORPORATION PLC

On July 21, 2008, the Company entered into an exclusive worldwide licensing agreement with Summit Corporation plc (Summit) related to Summit s preclinical candidate SMT C1100 and follow-on molecules, which are being developed for the treatment of Duchenne muscular dystrophy (DMD). The Company paid Summit $7.1 million for an equity investment in Summit shares and licensing rights to SMT C1100. The initial equity investment represents the acquisition of approximately 5.1 million Summit shares with a fair value of $5.7 million, based on publicly available quotes. The Company s investment in Summit represents less than 10% of Summit s outstanding shares. The $1.4 million paid in excess of the fair value of the shares acquired was allocated to the license fee using the residual method and expensed under the provisions of SFAS No. 2, *Accounting for Research and Development Costs*, in the third quarter of 2008. The Company is also obligated to make future development and regulatory milestone payments totaling $51.0 million contingent on future development and regulatory milestones, as well as tiered royalties based on future net sales. All payments pursuant to the Company s investment in, and license from Summit are denominated in British pounds.

The Company accounts for the Summit shares, which are traded on the London Stock Exchange, under the provisions of SFAS No. 115. The investment is classified as available-for-sale, with changes in the fair value reported as a component of accumulated other comprehensive income/loss, exclusive of other-than-temporary impairment losses, if any. Losses determined to be other-than-temporary are reported in earnings in the period in which the impairment occurs.

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In 2008, the Company recorded an impairment charge of $4.1 million for the decline in the investment s value determined to be other-than-temporary. The determination that the decline was other-than-temporary is, in part, subjective and influenced by several factors including: the length of time and to the extent to which the market value had been less than the value on the date of purchase, Summit s financial condition and near-term prospects, including any events which may influence their operations, and the Company s intent and ability to hold the investment for a period of time sufficient to allow for the anticipated recovery in market value. Based on the current market conditions, the low volume of trading in Summit securities and their current financial condition, the Company determined that its investment in Summit was other-than-temporarily impaired and adjusted the recorded amount of the investment to the stock s market price on December 31, 2008.

(10) CONVERTIBLE DEBT

In April 2007, the Company sold approximately $324.9 million of senior subordinated convertible notes due on April 23, 2017. The debt was issued at face value and bears interest at the rate of 1.875% per annum, payable semi-annually in cash. The debt is convertible, at the option of the holder, at any time prior to maturity or redemption, into shares of Company common stock at a conversion price of approximately $20.36 per share, subject to adjustment in certain circumstances. There is no call provision included and the Company is unable to unilaterally redeem the debt prior to maturity on April 23, 2017. The Company also must repay the debt if there is a qualifying change in control or termination of trading of its common stock.

In connection with the placement of the April 2007 debt, the Company paid approximately $8.5 million in offering costs, which have been deferred and are included in other assets. These costs are being amortized as interest expense over the life of the debt, and the Company recognized $0.6 million and $0.9 million of amortization expense during the year ended December 31, 2007 and 2008, respectively.

In March 2006, the Company sold $172.5 million of senior subordinated convertible debt due on March 29, 2013. The debt was issued at face value and bears interest at the rate of 2.5% per annum, payable semi-annually in cash. The debt is convertible, at the option of the holder, at any time prior to maturity or redemption, into shares of Company common stock at a conversion price of approximately $16.58 per share, subject to adjustment in certain circumstances. There is no call provision included and the Company is unable to unilaterally redeem the debt prior to maturity in 2013. The Company also must repay the debt if there is a qualifying change in control or termination of trading of its common stock.

In connection with the placement of the 2006 debt, the Company paid approximately $5.5 million in offering costs, which have been deferred and are included in other assets. These costs are being amortized as interest expense over the life of the debt, and the Company recognized $0.6 million, $0.8 million and $0.8 million of amortization expense during the year ended December 31, 2006, 2007, and 2008, respectively.

Interest expense for the years ended December 31, 2006, 2007 and 2008 was, $13.4 million, $14.2 million, and $16.4 million, respectively, and included $4.7 million, $4.5 million and $4.4 million in imputed interest expense related to the Company s acquisition obligation, respectively. Capitalized interest related to the Company s fixed asset purchases during the years ended December 31, 2006, 2007 and 2008 was insignificant.

(11) DERIVATIVE FINANCIAL INSTRUMENTS

Foreign Currency and Other Hedging Instruments

The Company follows the provisions of SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities*, as amended. SFAS No. 133 establishes accounting and reporting standards for derivative instruments

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and hedging activities and requires the Company to recognize these as either assets or liabilities on the balance sheet and measure them at fair value. The accounting for gains and losses resulting from changes in fair value is dependent on the use of the derivative and whether it is designated and qualifies for hedge accounting.

Economic and Accounting Hedging Hedges of Forecasted Transactions

The Company uses forward foreign exchange contracts to hedge certain operational exposures resulting from changes in foreign currency exchange rates. Such exposures result from portions of our forecasted revenues being denominated in currencies other than the U.S. dollar, primarily the Euro. These foreign exchange contracts have durations of six months or less and are entered into in the normal course of business; as such they are not speculative.

All hedging relationships are formally documented at the inception of the hedge and must meet the definition of highly effective in offsetting changes to future cash flows within the meaning of SFAS No. 133 to be a qualifying hedge. The effectiveness of the qualifying hedge contract, excluding the time value of money, is assessed quarterly using regression analysis. The Company records changes in the fair value of the derivative instruments designated as qualifying hedges of forecasted non-U.S. dollar revenue from product sales in other current assets and other current liabilities. Gains or losses resulting from changes in the fair value of qualifying hedges is initially reported as a component of accumulated other comprehensive income/loss in stockholders equity, until the forecasted transaction occurs. When the forecasted transaction occurs this amount is reclassified into revenue. As of December 31, 2008, the Company expects the entire amount in other comprehensive income to be reclassified to earnings within twelve months. Any non-qualifying portion of the gains or losses resulting from changes in fair value, if any, is reported in the Company s consolidated statement of operations in operating expenses.

In the event the underlying forecasted transaction does not occur, or it becomes probable that the forecasted transaction will not occur, the gain or loss on the related hedge is reclassified from accumulated other comprehensive income/loss to other income on the consolidated statement of income at that time. During 2008, there were no such net gains or losses recognized.

As of December 31, 2008, the Company had open contracts totaling $43.2 million that qualified for hedge accounting and $0.2 million in other comprehensive income representing the anticipated loss to be reclassified to earnings over the next twelve months as the forecasted transactions occur. During 2008, the Company recognized a net gain of $1.9 million in revenue relating to hedged transactions which occurred. The ineffective portion of the gains or losses resulting from changes in fair value was insignificant. The loss representing time value excluded from the assessment of the hedge effectiveness was immaterial and is included in operating expense on the Company s consolidated statement of operations.

The Company did not enter into any derivative transactions which qualified for hedge accounting under SFAS No. 133, as amended, prior to the second quarter of 2008.

(12) FAIR VALUE MEASUREMENTS

In January 2008, the Company adopted SFAS No. 157, *Fair Value Measurements*, for financial assets and liabilities. SFAS No. 157 utilizes a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value into three broad levels. Level one involves observable inputs such as unadjusted quoted prices in active markets for identical assets or liabilities. Level two involves inputs other than quoted prices that are observable for the asset or liability, either directly or indirectly, which include quoted prices for similar assets or

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liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active. Level three involves unobservable inputs that reflect the reporting entity s own assumptions. The Company measures certain financial assets and liabilities at fair value on a recurring basis, including available-for-sale fixed income and equity securities, other equity securities and foreign currency derivatives. The table below presents the fair value of these certain financial assets and liabilities determined using the inputs defined at December 31, 2008, by SFAS No. 157.

In February 2008, the FASB issued FASB FSP 157-2, which delays the effective date of SFAS No. 157 for all nonfinancial assets and nonfinancial liabilities, except those that are recognized or disclosed at fair value in the financial statements at least annually until fiscal years beginning after November 15, 2008, and interim periods within those fiscal years. The partial adoption of SFAS No. 157 for financial assets and liabilities did not have a material impact on the Company s consolidated financial position, results of operations or cash flows.

	Fair Value Measurements (in thousands) at Reporting Date Using:			
	Total	Quoted Price in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market instruments and overnight deposits (1)	$ 222,900	$ 12,959	$ 209,941	$
Corporate equity securities (2)	59,135	2,332	56,803	
Government agency securities (2)	221,891		221,891	
Government backed commercial paper (2)	24,370		24,370	
Commercial paper (2)	33,124		33,124	
Foreign currency derivatives (3)	803		803	
Total	$ 562,223	$ 15,291	$ 546,932	$
Liabilities:				
Deferred compensation liability (4)	$ 1,428	$	$ 1,428	$
Foreign currency derivatives (5)	1,129		1,129	
Total	$ 2,557	$	$ 2,557	$

(1) Included in cash and cash equivalents investments in the Company s consolidated balance sheet.
(2) 99.5% and 0.5% included in short-term investments and other investments, respectively, in the Company s consolidated balance sheet.
(3) Included in other current assets on the Company s consolidated balance sheet. Foreign currency derivatives include forward foreign exchange contracts for the Euro and British Pound.

(4) Included in other long-term liabilities on the Company s consolidated balance sheet.
(5) Included in accounts payable and accrued liabilities on the Company s consolidated balance sheet.

(13) INCOME TAXES

The Company generated net losses since its inception in 1997 until 2008. As of December 31, 2008, the Company had federal operating loss carryforwards of approximately $299.2 million and state operating loss carryforwards of approximately $148.5 million. The Company also had federal research and development and orphan drug credit carryforwards of approximately $93.6 million as of December 31, 2008, and state research

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credit carryovers of approximately $22.9 million. The federal net operating loss and credit carryforwards expire at various dates beginning in the year 2019 through 2027, if not utilized. The state net operating loss carryforwards will begin to expire in 2020 and will completely expire in 2029 if not utilized. Certain state research credit carryovers will begin to expire in 2020 if not utilized with others carrying over indefinitely. The Company also has Canadian net operating loss carryforwards of $3.7 million and research credit carryovers of $5.5 million that it currently does not expect to utilize.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets for financial reporting and the amount used for income tax purposes. Significant components of the Company s net deferred tax assets for federal and state income taxes are as follows (in thousands):

	December 31,	
	2007	2008
Net deferred tax assets:		
Net operating loss carryforwards	$ 124,512	$ 114,536
Credit and contribution carryforwards	118,208	117,254
Capitalized research expenses	4,240	3,664
Property, plant and equipment	8,280	8,041
Accrued expenses, reserves, and prepaids	3,906	11,130
Intangible assets	35,263	33,356
Deferred revenue	2,137	425
Stock-based compensation	19	6,275
Impairment on investment		1,882
Other	116	(222)
Gross deferred tax assets	$ 296,681	$ 296,341
Deferred tax liability related to joint venture basis difference	(2,280)	(1,601)
Valuation allowance	(294,401)	(294,740)
Net deferred tax assets	$	$

A full valuation allowance is maintained to reduce the Company s deferred tax assets to zero, as management believes that it is more likely than not that the deferred tax assets will not be realized, because ultimate long-term profitability of the Company is uncertain as of December 31, 2008. The net valuation allowance increased by $1.4 million in 2007 and $0.3 million in 2008. The decrease in the gross amount of net deferred tax assets and net valuation allowance during 2008 is primarily attributed to the expected usage of approximately $12.5 million of federal NOLs and state tax credits offset expected 2008 federal taxable income and state income taxes payable.

As of December 31, 2008, approximately $65.1 million of the federal net operating loss carryforwards and $46.7 million of the state net operating loss carryforwards arose from the exercise of employee stock options which will be accounted for as an increase to additional paid-in-capital if and when realized.

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For the years ended December 31, 2006, 2007 and 2008, the Company recognized $0.1 million, $0.7 million and $2.6 million of income tax expense, respectively, primarily related to income earned in several of the Company s international subsidiaries, and in 2008 included California state income tax and U.S. federal Alternative Minimum Tax. In addition, the Company recognized income tax expense as a result of accounting for income taxes under the provisions of SFAS 109. The Company had no current U.S. federal income tax expense and current state income tax expense for the years ended December 31, 2006 and 2007. The reconciliations between the U.S. federal statutory tax rates to the Company s effective tax rates are as follows:

	December 31,		
	2006	2007	2008
Federal tax	35.0%	35.0%	35.0%
State tax			3.1%
Permanent items	(10.4)%	(55.0)%	(29.1)%
General business credits	26.9%	95.4%	4.4%
Foreign income tax	(0.3)%	(4.8)%	2.4%
Alternative minimum tax	(0.4)%		2.1%
Valuation allowance	(51.1)%	(75.4)%	(10.3)%
Effective income tax rate	(0.3)%	(4.8)%	7.6%

	December 31,		
	2006	2007	2008
Federal income tax expense	$	$	$ 716
State income tax expense			1,055
Foreign income tax expense	74	729	822
Total income tax expense	$ 74	$ 729	$ 2,593

The Company adopted the provisions of FASB Interpretation No. 48 *Accounting for Uncertainty in Income Taxes An Interpretation of FASB Statement No. 109,* (FIN 48) on January 1, 2007. As a result of the adoption of FIN 48, there was no effect to the opening balance of retained earnings, deferred taxes, and net assets in the balance sheet of fiscal year 2007. The Company had no material unrecognized tax benefits before or after the adoption of FIN 48.

The Company s deferred tax assets as of December 31, 2008 may include potential uncertain tax positions, which if recognized would affect the Company s effective tax rate; however no benefits have been recognized from the deferred tax assets due to a full valuation allowance.

The Company s policy for classifying interest and penalties associated with unrecognized income tax benefits is to include such items in the income tax expense. No interest or penalties have been recorded by the Company to date through December 31, 2008.

The Company or one of its subsidiaries files income tax returns in the U.S. federal jurisdiction, and various states and foreign jurisdictions. For income tax returns filed before 2003, the Company is no longer subject to audit by the U.S. federal, state, local, or non-U.S. tax authorities. However, carryforward tax attributes that were generated prior to 2003 may still be adjusted upon examination by tax authorities. Currently the Company has no pending or open tax return audits.

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In accordance with APB 23, deferred taxes have not been provided on the cumulative undistributed earnings approximating $0.4 million as of December 31, 2008, of certain foreign subsidiaries as such earnings have been permanently reinvested. The Company has also elected to treat certain foreign entities as disregarded entities for U.S. tax purposes, which results in their net income or loss being recognized currently in the Company s U.S. tax return. As such, the tax benefit of net operating losses available for foreign statutory tax purposes has already been recognized for U.S. purposes.

(14) REVENUE AND CREDIT CONCENTRATIONS

The Company considers there to be revenue concentration risks for regions where net product revenue exceeds 10% of consolidated net product revenue. The concentration of the Company s revenue within the regions below may expose the Company to a material adverse effect if sales in the respective regions were to experience difficulties. The table below summarizes product revenue concentrations based on patient location for the years ended December 31, 2006, 2007 and 2008.

	December 31,		
	2006	2007	2008
Region:			
United States	37%	21%	56%
Europe	56%	60%	25%
Latin America	1%	7%	10%
Rest of World	6%	12%	9%
Total Net Product Revenue	100%	100%	100%

As of December 31, 2008, accounts receivable related to net product sales of Naglazyme and Kuvan and Aldurazyme product transfer and royalty revenues. On a consolidated basis, four customers accounted for 66% of our net product revenues in 2008. On a consolidated basis, two customers accounted for 17% and 50% of the December 31, 2008, accounts receivable balance, respectively. The Company does not require collateral from its customers, but performs periodic credit evaluations of its customers financial condition and requires immediate payment in certain circumstances.

(15) COLLABORATIVE AGREEMENTS

(a) Merck Serono

In May 2005, the Company entered into an agreement with Merck Serono S.A. (Merck Serono) for the further development and commercialization of BH4, both in Kuvan for PKU and for other indications, and PEG-PAL (phenylalanine ammonia lyase). Through the agreement and subsequent amendment, Merck Serono acquired exclusive rights to market these products in all territories outside the U.S., Canada and Japan, and BioMarin retained exclusive rights to market these products in the U.S. and Canada. The Company and Merck Serono will generally share equally all development costs following successful completion of Phase 2 trials for each product candidate in each indication. BioMarin and Merck Serono are individually responsible for the costs of commercializing the products within their respective territories. Merck Serono will also pay BioMarin royalties on its net sales of these products.

Pursuant to the agreement, Merck Serono paid BioMarin $25.0 million as consideration for executing the agreement, and is required to make additional milestone payments of up to $232.0 million based on the successful development and approval of both products in multiple indications, including $45.0 million associated

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with Kuvan for the treatment of PKU. The $45.0 million in Kuvan approval milestones were received in two payments of $15.0 million and $30.0 million during 2007 and 2008, respectively, when the EMEA filing was accepted and E.U. marketing approval was obtained. The term of the agreement is the later of 10 years after the first commercial sale of the products or the period through the expiration of all related patents within the territories. As of December 31, 2007 deferred revenue included $5.2 million related to the remaining unamortized up-front license fee which was recognized in 2008, when our performance obligations were satisfied. As of December 31, 2007 and 2008 accounts receivable included $0.9 million due from Merck Serono for reimbursable development costs for Kuvan.

(b) Other Agreements

The Company is engaged in research and development collaborations with various other entities. These provide for sponsorship of research and development by the Company and may also provide for exclusive royalty-bearing intellectual property licenses or rights of first negotiation regarding licenses to intellectual property development under the collaborations. Typically, these agreements can be terminated for cause by either party upon 90 days written notice.

In September 2007 the Company licensed to Asubio Pharma Co., Ltd. (a subsidiary of Daiichi Sankyo) exclusive rights to data and intellectual property contained in the Kuvan new drug application. The Company will receive a milestone payment for approval and royalties on net sales of the product.

(16) COMMITMENTS AND CONTINGENCIES

(a) Lease Commitments

The Company leases office space and research, testing and manufacturing laboratory space in various facilities under operating agreements expiring at various dates through 2019. Certain of the leases provide for options by the Company to extend the lease for multiple five-year renewal periods and also provide for annual minimum increases in rent, usually based on a Consumer Price Index or annual minimum increases. Minimum lease payments for future years are as follows (in thousands):

2009	$ 3,894
2010	4,026
2011	3,562
2012	2,919

2013	2,584
Thereafter	40
Total	$ 17,025

Rent expense for the years ended December 31, 2006, 2007 and 2008 was $3.1 million, $3.9 million, and $3.6 million, respectively. Deferred rent accruals at December 31, 2008 totaled $1.3 million, of which $0.2 million was current. At December 31, 2007, deferred rent accruals totaled $1.7 million, of which $0.1 million was current.

(b) Research and Development Funding and Technology Licenses

The Company uses experts and laboratories at universities and other institutions to perform certain research and development activities. These amounts are included as research and development expenses as services are provided.

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The Company has also licensed technology, for which it is required to pay royalties upon future sales, subject to certain annual minimums. As of December 31, 2008, such minimum annual commitments are approximately $0.3 million.

(c) Contingencies

From time to time the Company is involved in legal actions arising in the normal course of its business. The Company is not presently subject to any material litigation nor, to management s knowledge, is any litigation threatened against the Company that collectively is expected to have a material adverse effect on the Company s cash flows, financial condition or results of operations. The Company is also subject to contingent payments totaling approximately $111.7 million upon achievement of certain regulatory and licensing milestones if they occur before certain dates in the future.

There have been several lawsuits filed in Brazil alleging that the Company s joint venture with Genzyme and/or the affiliates of the joint venture are contractually obligated to provide Aldurazyme at no cost to several patients in Brazil. The joint venture and/or its affiliates are vigorously defending against these actions. The joint venture and management of the Company are not able to predict the outcome of these cases or estimate with certainty the amount or range of any possible loss the joint venture might incur if the joint venture and/or its affiliates do not prevail in the final, non-appealable determination of these matters.

(17) RELATED-PARTY TRANSACTIONS

The Company s Chief Medical Officer, formerly held an adjunct faculty position with LA Biomedical, formerly known as Harbor-UCLA Research Educational Institute, for purposes of conducting research. LA Biomedical licenses certain intellectual property and provides other research services to the Company. The Company is also obligated to pay LA Biomedical royalties on future sales of products covered by the license agreement. The Company s joint venture with Genzyme is subject to a second agreement with LA Biomedical that requires the Company s joint venture partner to pay LA Biomedical a royalty on sales of Aldurazyme through November 2019. Pursuant to the officer s agreements with LA Biomedical, which were entered into on or to his employment with the Company, the officer is entitled to certain portions of these amounts payable to LA Biomedical. The license agreements were effective before the officer was a BioMarin employee. Pursuant to these agreements, the officer was entitled to approximately $1.1 million, $1.4 million and $1.8 million from Genzyme related to Aldurazyme during 2006, 2007 and 2008, respectively.

(18) COMPENSATION AGREEMENTS AND PLANS

(a) Employment Agreements

The Company has entered into employment agreements with certain officers. Generally, these agreements can be terminated without cause by the Company upon written prior notice, or by the officer upon four weeks prior written notice to the Company.

(b) 401(k) Plan

The Company sponsors the BioMarin Retirement Savings Plan (401(k) Plan). Most employees (Participants) are eligible to participate following the start of their employment, at the beginning of each calendar month. Participants may contribute up to the lesser of 100% of their current compensation to the 401(k) Plan or an amount up to a statutorily prescribed annual limit. The Company pays the direct expenses of the 401(k) Plan and matches 100% of Participant s contributions up to a maximum of the lesser of 2% of the employee s annual

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compensation or $4,000 per year. The Company s matching contribution vests over four years from employment commencement and was approximately $0.6 million, $0.8 million and $1.3 million for the years ended December 31, 2006, 2007 and 2008, respectively. Employer contributions not vested upon employee termination are forfeited.

(c) Deferred Compensation Plan

In December 2005, the Company adopted the BioMarin Pharmaceutical Inc. Nonqualified Deferred Compensation Plan (the Deferred Compensation Plan). The Deferred Compensation Plan allows eligible employees, including management and certain highly-compensated employees as designated by the Plan s Administrative Committee, and members of the Board the opportunity to make voluntary deferrals of compensation to specified future dates, retirement or death. Participants are permitted to defer portions of their salary, annual cash bonus and restricted stock. The Company may not make additional direct contributions to the Deferred Compensation Plan on behalf of the participants, without further action by the Board. Deferred compensation is held in trust and generally invested to match the investment benchmarks selected by participants. The recorded cost of any investments will approximate fair value. Investments of $0.5 million and $0.9 million and the related deferred compensation liability of $0.5 million and $1.4 million were recorded as of December 31, 2007 and 2008, respectively. The change in market value was insignificant for the years ended December 31, 2006 and 2007 and amounted to a gain of approximately $0.3 million in 2008.

(19) SUBSEQUENT EVENT

On January 6, 2009, the Company entered into a co-exclusive worldwide (excluding Asia Pacific) licensing agreement with La Jolla Pharmaceutical Company (La Jolla) to develop and commercialize Riquent, La Jolla s investigational drug for lupus nephritis. Riquent was being evaluated by La Jolla in an international double blind, placebo controlled randomized phase 3 clinical study for lupus nephritis (Phase 3 ASPEN Study). On February 12, 2009, the results of the first interim efficacy analysis for the Phase 3 ASPEN Study clinical trial were announced, and the Independent Data Monitoring Board determined that the continuation of the trial was futile. Based on the results of this interim efficacy analysis, the Company and La Jolla have decided to stop the study, unblind all of the data and evaluate all of the clinical results, including the secondary endpoints.

Under the terms of the agreement, the Company made an initial upfront payment of $15.0 million in exchange for the license rights and 339,104 shares of La Jolla s Series B Preferred Stock. The Company expects to recognize up to $15.0 million of expense related to the upfront payment in the first quarter of 2009, which includes both the research and development expense and an expected impairment of the Company s investment in La Jolla.