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

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2005

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 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

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

Securities registered under Section 12(g) of the Act:
Common Stock, $.001 par value
Preferred Share Purchase Rights
(Title of Class)

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (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 ☒ 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, or a non-accelerated filer. See definition of "accelerated filer" in Rule 12b-2 of the Exchange Act. (as defined in Rule 12b-2 of the Act).
Large accelerated filer ☐ Accelerated filer ☒ Non-accelerated filer ☐

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

The aggregate market value of the voting stock held by non-affiliates of the Registrant as of June 30, 2005 was $483.7 million. The number of shares of common stock, $0.001 par value, outstanding on February 21, 2006 was 74,641,983.

The documents incorporated by reference are as follows:

Portions of the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held June 21, 2006, are incorporated by reference into Part III.

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" and similar expressions. These forward-looking statements may be found in "*Risk Factors*," "*Description of 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.

Item 1. Description of Business

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 Aldurazyme® (laronidase), Naglazyme™ (galsulfase) and Orapred® (prednisolone sodium phosphate oral solution).

Aldurazyme has been approved for marketing in the United States (U.S.) by the U.S. Food and Drug Administration (FDA), in the European Union (E.U.) by the European Commission (EC) and in other countries for the treatment of mucopolysaccharidosis I (MPS I), for which no other drug treatment currently exists. MPS I is a progressive and debilitating life-threatening genetic disease, which frequently results in death during childhood or early adulthood. It is caused by the deficiency of alpha-L-iduronidase, an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs). As the first drug approved for the treatment of MPS I, 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. We developed Aldurazyme through a 50/50 joint venture with Genzyme Corporation (Genzyme). Aldurazyme net revenue recorded by our joint venture for 2005 totaled $76.4 million, compared to $42.6 million for 2004.

In May 2005, the FDA granted marketing approval for Naglazyme for the treatment of mucopolysaccharidosis VI (MPS VI), a debilitating life-threatening genetic disease for which no other drug treatment currently exists. MPS VI is caused by the deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B), an enzyme normally required for the breakdown of GAGs. Naglazyme net product sales recorded for 2005 totaled $6.1 million. In January 2006, the EC granted marketing approval for Naglazyme in the E.U. Naglazyme has been granted orphan drug status in the U.S. and the E.U., which gives Naglazyme 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. Product launch in the E.U. is underway on a country-by-country basis.

In May 2004, we completed the transaction to acquire the business of Ascent Pediatrics from Medicis Pharmaceutical Corp. (Medicis). This business includes Orapred, a drug primarily used to treat asthma exacerbations in children and other inflammatory conditions, and two additional proprietary formulations of Orapred, including Orapred ODT™ (prednisolone sodium phosphate orally disintegrating tablets). Orapred net product sales for 2005 totaled $6.9 million, compared to $18.6 million for 2004.

There are a number of products that have the same active ingredient as our liquid Orapred formulation and are competitive in the marketplace. Some of these products are less expensive than Orapred. In the third quarter of 2004 and in 2005, the FDA approved several generic products that have the same strength and active ingredient as Orapred. Although there are several other products on the market that have the same or similar ingredients, these products have the exact same drug substance and concentration as Orapred. In many states, the generic products may be substituted at pharmacies without consulting the prescribing physician. Since the introduction of these new generic products to Orapred, we have experienced an additional decrease in the Orapred share of the oral liquid prednisolone market, from 22% in December 2004 to 8% in December 2005. Please see our accompanying consolidated financial statements for our revenues and losses for the last three fiscal years.

In October 2005, we announced that the FDA had accepted for filing the New Drug Application for Orapred ODT for the treatment of inflammatory conditions. We expect to receive a response from the FDA by June 1, 2006. There is currently no generic competition with this new formulation. We continue to explore strategic alternatives for the Orapred product line, which may include the sublicense of part or all of the franchise.

We are developing several investigational product candidates for the treatment of genetic diseases including: Phenoptin™ (sapropterin dihydrochloride), a proprietary oral form of tetrahydrobiopterin (6R-BH_4, also commonly referred to as BH_4), for the treatment of phenylketonuria (PKU); and Phenylase™ (phenylalanine ammonia lyase), an enzyme substitution therapy for the treatment of phenylketonurics who are not 6R-BH_4-responsive and for classic PKU, the more severe form of the disease.

In December 2004, we announced that we initiated our Phase 2 clinical trial of Phenoptin for PKU. Patients enrolled in the Phase 2 clinical trial who met certain criteria were eligible to enroll in the Phase 3 trial, which began in April 2005. The Phase 3 clinical trial of Phenoptin is a six-week, multi-center, international, double-blind, placebo-controlled study. Phase 3 clinical trial enrollment is complete and we expect to announce top-line results from the Phase 3 clinical trial in late March 2006. As a primary efficacy endpoint, the trial measures the changes in blood phenylalanine (Phe) level in patients receiving Phenoptin compared to patients receiving placebo. Following the double-blind Phase 3 clinical trial, we expect that the patients in the Phase 3 clinical trial will continue to receive treatment in a 22-week open-label extension study. We also plan to conduct a supplemental diet study in children between 4 to 12 years of age. We have received orphan drug designation for Phenoptin for the treatment of PKU in both the U.S. and E.U., which if approved, will have seven years of market exclusivity in the U.S. and ten years of market exclusivity in the E.U. In January 2006, the FDA designated Phenoptin as a fast-track product for the treatment of PKU.

PKU is an inherited metabolic disease that affects at least 50,000 diagnosed patients under the age of 40 in the developed world, an estimated 30% to 50% of whom have a moderate to mild form of the disease. We believe those with the moderate to mild form of the disease could benefit from treatment with Phenoptin, if approved. PKU is caused by a deficiency of an enzyme, phenylalanine hydroxylase (PAH), which is required for the metabolism of Phe. Phe is an amino acid found in most 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. Currently, the only way to manage PKU is through an extremely restricted diet that patients find very difficult to follow. Phenoptin, our lead product candidate for the treatment of PKU, is a proprietary, synthetic oral form of 6R-BH_4, a small-molecule therapeutic that is a co-factor for PAH. If approved, Phenoptin could become the first drug for the treatment of PKU.

Phenylase is an investigational enzyme substitution therapy currently in preclinical development. It is being developed as a subcutaneous injection and is intended for those who suffer from classic PKU and for those who are not 6R-BH_4 responsive, and do not respond to Phenoptin.

In May 2005, the Company entered into an agreement with Serono S.A. (Serono) for the further development and commercialization of Phenoptin and Phenylase for PKU, and 6R-BH_4, the active ingredient in Phenoptin, for other indications including endothelial dysfunction. Through the agreement, Serono acquired exclusive rights to market these products in all territories outside the U.S. and Japan, and BioMarin retained exclusive rights to market these products in the U.S. BioMarin and Serono will generally share equally all development costs following successful completion of Phase 2 clinical trials for each product candidate in each indication. BioMarin and Serono are individually responsible for the costs of commercializing the products within their respective territories. Serono will also pay BioMarin royalties on its net sales of these products and milestone payments for the successful completion of certain development and approval milestones.

Data from preclinical and clinical trials suggests that treatment for endothelial dysfunction with BH_4 is generally safe and well tolerated. We plan to conduct additional preclinical and clinical studies of BH_4 for endothelial dysfunction in 2006.

We are evaluating other enzyme-based therapies for serious medical conditions including Vibrilase™ (vibriolysin), an investigational topical enzyme therapy for use in the debridement of serious burns. In August 2004, we announced positive data from a Phase 1b clinical trial of Vibrilase. Data from the trial suggest that treatment with Vibrilase is generally safe and well-tolerated. Additionally, we are evaluating preclinical development of several other enzyme product candidates for genetic and other diseases as well as an immune tolerance platform technology designed to overcome limitations associated with the delivery of existing pharmaceuticals.

In May 2005, we announced the appointment of Jean-Jacques Bienaimé as Chief Executive Officer and as a director. In June 2005, we announced that Stephen Aselage was appointed as Senior Vice President of Global Commercial Operations. In August 2005, we announced the promotion of Jeffrey Cooper to the position of Chief Financial Officer. Mr. Cooper succeeds Louis Drapeau who retired at the end of October 2005. Chris Starr, Senior Vice President and Chief Scientific Officer, retired at the end of December 2005. In January 2006, Emil Kakkis, formerly Senior Vice President of Business Operations, was promoted to Chief Medical Officer.

In July 2005, we announced that we were reducing the Orapred sales force through the elimination of 52 positions. Severance and related costs and payments of approximately $0.9 million, associated with eliminating the 52 sales force positions, plus six non-sales force positions, were recognized in the third quarter of 2005. No additional costs related to the sales force reduction are anticipated in future periods. We continue to market Orapred through non-personal promotion activities.

Also in July 2005, we completed a public offering of our common stock. In the offering, we sold 8,500,000 shares at a price to the public of $7.05 per share, or a total offering price of $59.9 million. The net proceeds were approximately $56.3 million.

Our principal executive offices are located at 105 Digital Drive, Novato, California 94949 and our telephone number is (415) 506-6700. “BioMarin,” “Naglazyme,” “Phenoptin,” “Neutralase,” “Vibrilase,” and “Phenylase” are our trademarks. “Aldurazyme” is a registered trademark of BioMarin/Genzyme LLC. “Orapred” is a registered trademark of Medicis Pediatrics, Inc., and is used under license. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, 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 on our website as soon as reasonably practicable after electronically filing such reports with the SEC. 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 report.

Recent Developments

Marketing Authorization for Naglazyme in the E.U.

On January 30, 2006, we announced that we received European marketing authorization for Naglazyme, including being granted orphan drug status, which gives 10 years of market exclusivity in the E.U. Naglazyme has been approved in the 25 member states of the European Union, Iceland and Norway for long-term enzyme replacement therapy in patients with a confirmed diagnosis of MPS VI. BioMarin is in the process of launching Naglazyme in the E.U. on a country-by-country basis.

FDA Fast-Track Designation for Phenoptin for PKU

On January 25, 2006, we announced that the FDA granted fast-track designation for Phenoptin for PKU. Phenoptin, an investigational oral small molecule therapeutic, is currently in Phase 3 clinical development. The FDA's fast-track program is designed to facilitate the development of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

Establishment of European Operations

On January 10, 2006, we announced that we established commercial operations in Europe in anticipation of receiving European marketing approval for Naglazyme. BioMarin Europe Ltd. is headquartered in London, with branch offices located in Spain, Switzerland and Italy.

FDA Acceptance of Orapred ODT Filing

On October 19, 2005, we announced that the FDA accepted for filing the New Drug Application (NDA) for Orapred ODT, a new formulation of Orapred. Prednisolone is commonly used to reduce inflammation seen in numerous medical conditions including asthma, arthritis and cancer. The FDA will take action on the application, under the Prescription Drug User Fee Act (PDUFA), by June 1, 2006.

Commercial Products

Aldurazyme

Our first commercial product, Aldurazyme, an enzyme replacement therapy, is approved in the U.S. by the FDA, in the E.U. by the EC and in other countries for the treatment of MPS I. Marketing applications are planned or are currently under review in several additional countries. The genetic disease MPS I is caused by the deficiency of alpha-L-iduronidase, a lysosomal enzyme. Patients with MPS I 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, delayed and regressed mental development (in the severe form), enlarged liver and spleen, joint deformities and reduced range of motion, impaired cardiovascular and heart function, upper airway obstruction, reduced pulmonary function, frequent ear and lung infections, impaired hearing and vision, sleep apnea, malaise and reduced endurance. Most patients with MPS I die from complications associated with the disease during childhood or early adulthood. Aldurazyme net revenue, which is recorded by our joint venture with Genzyme, during 2005 totaled $76.4 million, compared to $42.6 million in 2004. There were approximately 370 commercial patients as of December 31, 2005, compared to approximately 270 as of December 31, 2004.

Aldurazyme is produced, marketed and sold through a 50/50 joint venture with Genzyme. We are responsible for product development, manufacturing and U.S. regulatory submissions. Genzyme is responsible for sales, marketing, distribution, obtaining reimbursement for Aldurazyme worldwide and international

regulatory submissions. See *"Management's Discussion and Analysis of Financial Condition and Results of Operations—BioMarin/Genzyme LLC"* for discussion of the financial results of Aldurazyme.

The FDA has granted Aldurazyme orphan drug designation, which provides our joint venture with exclusive rights to market Aldurazyme for the treatment of MPS I in the U.S. until 2010. In addition, the EC has granted Aldurazyme orphan drug designation, giving it market exclusivity in the E.U. until 2013. However, different drugs can be approved for the same condition.

Naglazyme

We developed Naglazyme as an enzyme replacement therapy for the treatment of MPS VI, a debilitating genetic disease for which no other drug treatment currently exists, similar to MPS I. Naglazyme is a recombinant form of *N*-acetylgalactosamine 4-sulfatase (arylsulfatase B). MPS VI is caused by the deficiency of N-acetylgalactosamine 4-sulfatase, an enzyme normally required for the breakdown of GAGs. In May 2005, the FDA granted marketing approval for Naglazyme for the treatment of MPS VI. Naglazyme has been granted orphan drug status by the FDA, conferring upon it seven years of market exclusivity in the U.S., until 2012. Following marketing approval for Naglazyme in the U.S., we began shipping product in late June 2005. We have established a specialty sales force and commercial organization in the U.S. to market Naglazyme, and potentially other products. Net product sales for Naglazyme for 2005 were $6.1 million.

In January 2006, we announced that we received marketing approval from the EC for Naglazyme for MPS VI in the E.U. We are in the process of launching Naglazyme in the E.U. on a country-by-country basis. This launch is being implemented by our recently established European sales force and commercial organization. In other markets, we are evaluating the option of using local partners as an alternative to direct marketing of Naglazyme. Naglazyme has been granted orphan drug status in the E.U., which gives it 10 years of market exclusivity, until 2016. However, different drugs can be approved for the same condition if they are determined to have a better safety and efficacy profile than Naglazyme.

Orapred

In May 2004, we obtained rights to market and sell Orapred, a drug primarily used to treat asthma exacerbations in children as well as the exclusive rights to the Orapred intellectual property. Orapred was approved by the FDA in December 2000. Orapred prescription and sales volumes are subject to seasonal fluctuations, specifically the winter season when the number of asthma incidents is significantly higher than other seasons of the year.

Orapred net product sales during 2005 totaled $6.9 million, compared to $18.6 million in 2004 following the acquisition in May 2004. In the third quarter of 2004, the FDA approved a generic product that has the same strength and route of administration as Orapred. Because of the AA equivalence rating to Orapred, when this product was introduced to the market in the fourth quarter of 2004, many pharmacies and managed care organizations, began to substitute the new generic product for Orapred. Since the introduction of this new generic product and several other generic competitors introduced during 2005, we have experienced an additional decrease in the Orapred share of the oral liquid prednisolone market from 22% in December 2004 to 8% in December 2005.

We also obtained the exclusive rights to two additional proprietary formulations of Orapred, including an oral disintegrating tablet (Orapred ODT) and a room temperature version (Orapred RT) of the oral solution. In October 2005, we announced that the FDA had accepted for filing the New Drug Application for Orapred ODT for the treatment of inflammatory conditions. We expect to receive a response from the FDA on this filing in by June 1, 2006. We continue to explore strategic alternatives for the Orapred product line, which may include the sublicense of part or all of the franchise.

Lead Product Candidates

Phenoptin

We are developing Phenoptin as a potential treatment for patients with PKU, a genetic disease in which the body cannot properly metabolize phenylalanine (Phe), an essential amino acid found in most protein-containing foods. If left untreated, elevated blood Phe levels can lead to a variety of neurological complications, including severe mental retardation and brain damage, mental illness, seizures and tremors and other cognitive problems. Phenoptin is intended to treat patients with the mild to moderate forms of PKU, which represents approximately 30-50% of the PKU cases. The total PKU population is estimated to currently be approximately 50,000 individuals in the developed world. Sapropterin dihydrochloride, the active ingredient in Phenoptin, is a synthetic form of 6R-BH_4, an essential enzyme cofactor required for the metabolism of Phe. In December 2004, we announced that we initiated our Phase 2 clinical trial of Phenoptin for PKU. Patients identified in the Phase 2 clinical trial that met certain criteria were eligible to enroll in the Phase 3 clinical trial, which was initiated in April 2005. The Phase 3 clinical trial of Phenoptin is a six-week, multi-center, international, double-blind, placebo-controlled study. Phase 3 clinical trial enrollment is complete and we expect to announce preliminary results from this trial in late March 2006. As a primary efficacy endpoint, the trial measures the changes in blood Phe levels in patients receiving Phenoptin compared to patients receiving placebo. We have received orphan drug designation for Phenoptin for the treatment of PKU in both the U.S. and the E.U. In January 2006, the FDA granted Phenoptin fast-track designation for the treatment of PKU.

Currently there are no approved drug therapies for the treatment of PKU. 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 critical period to ensure 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. Phenoptin is intended to provide PKU patients with a more convenient and effective way to manage their disease and potentially enable them to eat a more normal diet.

In May 2005, the Company entered into an agreement with Serono S.A. (Serono) for the further development and commercialization of two BioMarin product candidates, Phenoptin and Phenylase for PKU. This agreement also included the further development and commercialization of BH_4, the active ingredient in Phenoptin, for other indications including endothelial dysfunction. Through the agreement, Serono acquired exclusive rights to market these products in all territories outside the U.S. and Japan, and BioMarin retained exclusive rights to market these products in the U.S. BioMarin and Serono will generally share equally all development costs following successful completion of Phase 2 clinical trials for each product candidate in each indication. BioMarin and Serono are individually responsible for the costs of commercializing the products within their respective territories. Serono will pay BioMarin royalties on its net sales of these products and milestone payments for the successful completion of certain development and approval milestones.

Endothelial dysfunction is a condition characterized by the inability of the endothelium (the single cell layer lining that forms the barrier between blood vessel walls and the blood) to respond to physiological changes correctly. In preclinical and investigator-sponsored studies, BH_4 administration has improved vascular endothelial function in animal models and in patients with diabetes and other cardiovascular diseases. BH_4 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. We plan to conduct additional preclinical and clinical studies of BH_4 for endothelial dysfunction in 2006.

Other Product Development Programs

Phenylase

We are developing Phenylase as an injectable enzyme substitution therapy for PKU. Phenylase is currently in preclinical development and is intended for those who suffer from classic PKU, the more severe form of the disease and those who suffer from the mild to moderate form of the disease but do not respond to Phenoptin. In preclinical models, Phenylase produced a rapid, dose-dependent reduction in blood Phe levels. We plan to conduct additional preclinical studies of Phenylase in 2006.

Vibrilase

We have developed Vibrilase through Phase 1b as a topically applied enzyme for the debridement of serious burns. In August 2004, we announced positive data from our European Phase 1b clinical trial. Data from the study suggest that treatment with Vibrilase is generally safe and well tolerated. Although the trial was designed to measure safety and tolerability, the preliminary efficacy data suggest that Vibrilase is effective in debriding partial-thickness burns. We are currently evaluating options for this program and are in the process of applying for an Orphan Drug designation.

Immune Tolerance Technology

We are evaluating the potential of our proprietary immune tolerance technology, a platform technology that may address pathologic immune responses, which occur in autoimmune diseases, and unwanted immune responses induced by protein-based therapies, including those used for the treatment of lysosomal storage disorders, hemophilia A, and other medical conditions. The immune response induced by certain protein-based drugs can reduce the efficacy and safety of treatment and is an increasingly common medical problem caused by the emergence of protein-based drugs used to treat chronic diseases. In December 2003, we announced the results of preclinical studies demonstrating the induction of immune tolerance to enzyme therapy that were published in the Proceedings of the National Academy of Sciences of the United States of America. The studies demonstrated a substantial prevention of immune responses to enzyme therapy in an animal model of MPS I, without the continuous use of immunosuppressive drugs. We continue to develop this technology and expect to conduct additional preclinical studies in 2006.

Manufacturing

We are manufacturing Aldurazyme and Naglazyme, which are both recombinant enzymes, in our current Good Manufacturing Practices (GMP) production facility located in Novato, California (Galli Drive). Our Galli Drive facility is approximately 70,000 square feet and includes clean rooms for bulk drug production, utilities, laboratories and other support areas. Vialing and packaging of Aldurazyme are performed by either our joint venture partner or contract manufacturers, and vialing and packaging of Naglazyme are performed by contract manufacturers. We also have approximately 16,000 square feet of GMP warehouse space and quality control laboratories located near Galli Drive. We believe that Galli Drive and our GMP warehouse have ample operating capacity to support the commercial demand of both Aldurazyme and Naglazyme through at least the remainder of this decade because relatively low doses are required for treatment and because the targeted patient populations are small.

In general, we expect to contract with outside service providers for certain manufacturing services, including final product vialing and packaging operations for our recombinant enzymes and bulk production for clinical and early commercial production of our other product candidates. Orapred is manufactured by Lyne Laboratories, and Orapred ODT is manufactured by CIMA Labs, through agreements with these entities. In December 2005, we entered into a long-term supply agreement with Groupe Novasep for the production of BH_4. We are in the process of qualifying additional manufacturers for BH_4.

Our Galli Drive and our GMP warehouse facilities have been licensed by the FDA, EC and health agencies in other countries for the commercial production of Aldurazyme and by the FDA and the EC for the commercial production of 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. Failure to comply with these requirements could result in the shutdown of our facilities or the assessment of fines or other penalties.

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 sales and marketing organization to support our product lines directly in the U.S. and E.U. For other markets, we are evaluating options for marketing support, including local partners to assist in commercial development. Our U.S. sales force consisted of 11 employees as of December 31, 2005. We also had 3 employees overseeing sales activities in the E.U. as of December 31, 2005. We believe that the size of our sales force is appropriate to effectively reach our target audience in markets where Naglazyme is directly marketed. We utilize a third-party logistics company to store and distribute Naglazyme from its warehouse in the United Kingdom (U.K.) for customers in the E.U. and from a second warehouse in Tennessee for customers outside of the E.U.

We use a variety of techniques to promote Naglazyme, including advertising and promotional materials, website information and the publication of clinical data.

We continue to market Orapred through non-personal promotion activities, such as website information. We have and will continue to implement strategies designed to compete with our Orapred liquid generic competition. We utilize a third-party logistics company to store and distribute Orapred from its warehouse in Tennessee. If we do not sub-license Orapred ODT, we expect to use a variety of marketing techniques to promote Orapred ODT including contract sales support, sampling, advertising and promotional materials, specialty publications, coupons, and website information.

Pursuant to our joint venture agreement, Genzyme is responsible for sales, marketing, distribution, obtaining reimbursement worldwide and international regulatory submissions of Aldurazyme.

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 230, including approximately 35 patents issued by the U.S. Patent and Trademark Office (USPTO). Furthermore, our portfolio of pending patent applications totals approximately 145 applications, including approximately 35 pending U.S. applications.

The issuance of four core patents has strengthened our patent position for Aldurazyme. U.S. Patent No: 6,426,208 covers our ultra-pure alpha-L-iduronidase composition of Aldurazyme and U.S. Patent No. 6,585,971 describes methods of treating deficiencies of alpha-L-iduronidase by administering pharmaceutical compositions comprising such ultra-pure alpha-L-iduronidase. The third U.S. Patent, No. 6,569,661, details a method of purifying such ultra-pure alpha-L-iduronidase. A fourth patent, U.S. Patent No. 6,858,206 B1, issued on February 22, 2005 covers the use of biologically active fragments of the ultra-pure alpha-L-iduronidase composition of Aldurazyme. In addition, our South African Patent No. 2002/3619 and Australian Patent No. 84635/01 cover composition, methods of production, purification and treatment.

Transkaryotic Therapies Inc. (TKT), which was acquired by Shire PLC, has announced that three U.S. patents on alpha-L-iduronidase had been issued and that these patents had been exclusively licensed to TKT. 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, but the Canadian and Japanese applications are still pending and are being prosecuted by the applicants. 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 venture with Genzyme to market Aldurazyme with commercial diligence, in order to provide MPS I patients with the benefits of Aldurazyme.

In October 2003, Genzyme and TKT announced their collaboration to develop and commercialize an unrelated drug product. In connection with the collaboration agreement, Genzyme and TKT signed a global legal settlement involving an exchange of non-suits between the companies. As part of this exchange, TKT has agreed not to initiate any patent litigation against Genzyme or our joint venture relating to 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 refiled.

With respect to Naglazyme™, U.S. Patent No. 6,866,844 issued on March 15, 2005 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 purifying such ultrapure *N*-acetylgalactosamine-4-sulfatase compositions. A second U.S. Patent No. 6,972,124 issued on December 6, 2005 covers the use of any recombinant human *N*-acetylgalactosamine-4-sulfatase to treat MPS VI at approved doses.

With respect to Orapred, we obtained the exclusive rights to the Orapred intellectual property from Medicis.

Customers

Our Naglazyme customers include a limited number of specialty pharmacies and end-users, such as hospitals, which act as retailers. We also sell Naglazyme to certain larger pharmaceutical wholesalers, which, with respect to Naglazyme, act as intermediaries between us and end-users and generally do not stock quantities of Naglazyme. During 2005, these customers accounted for the following portions of our Naglazyme net product sales:

	2005
AmerisourceBergen	20%
Caremark	13%
Hospices Civils de Lyon	11%
	44%

Despite the significant concentration of customers, the demand for Naglazyme is driven by patient therapy requirements and we are not dependent upon any individual distributor with respect to Naglazyme sales. Due to the pricing of Naglazyme and the limited number of patients, the specialty pharmacies carry a very limited inventory, resulting in sales of Naglazyme being closely tied to end-user demand. In the E.U., starting in mid-December 2005, hospital customers are serviced by an authorized distributor, which will be our primary customer in the E.U.

Our Orapred customers include certain of the nation's leading wholesale pharmaceutical wholesalers, such as Cardinal Health, Inc. (Cardinal), McKesson Corporation (McKesson) and AmerisourceBergen Corporation (AmerisourceBergen). During 2005, these customers accounted for the following portions of our Orapred net product sales:

	2005
McKesson	32%
Cardinal	30%
AmerisourceBergen	20%
	82%

Despite the significant concentration of customers, the demand for Orapred is driven by prescriptions and we are not dependent on any individual wholesaler or any specific combination of wholesalers with respect to Orapred sales.

Government Regulation

Food and Drug Administration Modernization Act of 1997 (Modernization Act)

The Modernization Act was enacted, in part, to ensure the availability of safe and effective drugs and medical devices by expediting the FDA review process for new products. The Modernization Act establishes a statutory program for the approval of fast-track products. The fast-track provisions essentially codify the FDA's accelerated approval regulations for drugs. A fast-track product is defined as a new drug intended for the treatment of a serious or life-threatening condition that demonstrates the potential to address unmet medical needs for that condition. Under the fast-track program, the sponsor of a new drug may request that the FDA designate the drug as a fast-track-product at any time during the clinical development of the product. The Modernization Act specifies that the FDA must determine if the product qualifies for fast-track designation within 60 days of receipt of the sponsor's request.

Approval of a license application for a fast-track product can be based on a clinical endpoint or on a surrogate endpoint that is reasonably likely to predict clinical benefit. Approval of a license application for a fast-

track product may be subject to post-approval studies to validate or confirm the effect on the clinical endpoint, or, if based on a surrogate endpoint, to validate or confirm the surrogate endpoint, plus the FDA must review all promotional materials prior to drug approval. If a preliminary review of the clinical data suggests that the product is effective, the FDA may initiate review of sections of a license application for a fast-track product before the application is complete. This rolling review is available if the applicant provides a schedule for submission of remaining information and pays applicable user fees. However, the time period specified in the Prescription Drug User Fees Act (PDUFA), which governs the time period goals the FDA has committed to reviewing a license application, does not begin until the complete application is submitted.

Because fast-track products are intended to treat serious or life-threatening conditions and must demonstrate the potential to address unmet medical needs for such conditions, a license application for a product in a fast-track drug development program ordinarily will be eligible for priority review wherein the PDUFA timeframe for the review is 6 months instead of 10 months. As a result, we cannot predict the ultimate impact, if any, of the fast-track process on the timing or likelihood of FDA approval of any of our potential products, which may receive this designation.

The FDA has designated Phenoptin as a fast-track product for the treatment of PKU. We cannot predict the ultimate impact, if any, of the fast-track process on the timing or likelihood of FDA approval of Phenoptin or any of our other potential products.

Orphan Drug Designation

Aldurazyme, Naglazyme and Phenoptin 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 license 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. A similar system for orphan drug designation exists in the E.U. Aldurazyme, Naglazyme and Phenoptin received orphan medicinal product designation by the European Committee for Orphan Medicinal Products.

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. and 10 years in the E.U. 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.

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:

Aldurazyme

Other than Aldurazyme, there are currently no approved drugs for the treatment of MPS I. 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.

Naglazyme

We know of no active competitive program for enzyme replacement therapy for MPS VI that has entered clinical trials.

There are other developing technologies which are potential competitive threats to enzyme replacement therapies for both MPS I and MPS VI. We know of no competitive program using other developing technologies for the treatment of either MPS I or MPS VI that has entered clinical trials.

Orapred

There are a number of products that are direct competitors with Orapred. Some of these products are less expensive than Orapred. In the third quarter of 2004 and in 2005, the FDA approved several generic products that have the same strength and active ingredient as Orapred. Although there are several other products on the market that have the same or similar ingredients, these generic products have the exact same drug substance and concentration as Orapred. Furthermore, the generic products have an AA equivalence rating to Orapred and therefore may be substituted at pharmacies without consulting the prescribing physician. Since the introduction of these new generic products to Orapred, we have experienced an additional decrease in the Orapred share of the oral liquid prednisolone market from 22% in December 2004 to 8% in December 2005. We have and expect to continue to implement strategies designed to compete with our generic competition.

There is currently no generic competition with Orapred ODT, and we do not anticipate generic competition for Orapred ODT in the near term.

Phenoptin and Phenylase

There are currently no 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 Phenoptin and Phenylase 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 Phenoptin and Phenylase. However, because LNAA is a dietary supplement, the FDA has not evaluated any claims of efficacy of LNAA.

With respect to Phenoptin, we are aware of two other companies that produce forms of 6R-BH_4, and that 6R-BH_4 has been used in certain instances for the treatment of PKU. We do not believe that either of these companies are currently actively developing 6R-BH_4 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 BH_4 as a drug product to treat PKU in the U.S. and E.U., these companies 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 the therapy is in an early stage of preclinical development.

With respect to BH_4 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 endothelial dysfunction through other active ingredients, which are currently on the market. We believe that the BH_4 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 developing BH_4 for the treatment of endothelial dysfunction.

Employees

As of February 21, 2006, we had 314 full-time employees, 168 of whom are in operations, 73 of whom are in research and development, 25 of whom are in sales and marketing and 48 of whom are in administration.

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.

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 primarily in research and development and have operated at a net loss for the entire time. Our first product, Aldurazyme, was approved for commercial sale in the U.S. and the E.U. and has generated approximately $130.5 million in net sales revenue to our joint venture from the product's launch in May 2003 through December 31, 2005. We acquired exclusive rights to Orapred in May 2004 and reported $25.5 million in Orapred net product sales following the acquisition through December 31, 2005. On June 1, 2005 we announced that the FDA granted marketing approval for Naglazyme for the treatment of MPS VI. We reported $6.1 million in Naglazyme net product sales during 2005. We have no revenues from sales of our product candidates. As of December 31, 2005, we had an accumulated deficit of $563.1 million. We expect to continue to operate at a net loss for the foreseeable future. Our future profitability depends on our marketing and selling of Orapred and Naglazyme, the successful commercialization of Aldurazyme by our joint venture partner, Genzyme, our receiving regulatory approval of our product candidates and our ability to successfully manufacture and market any approved drugs, either by ourselves or jointly with others. 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 will 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 when 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 as we need such funds, we will 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 joint venture partner's ability to successfully commercialize Aldurazyme;

- the progress, timing and scope of our preclinical studies and clinical trials;
- our ability to successfully market and sell Orapred, including our ability to protect our existing market share and regain market share against generic competition;
- 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;
- our ability to maintain compliance with our debt covenants;
- the time and cost necessary to respond to technological and market developments;
- any changes made 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.

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

- additional licenses and collaborative agreements;
- additional contracts for consulting, maintenance and administrative services;
- additional contracts for product manufacturing; and
- additional financing facilities.

We believe that our cash, cash equivalents, short-term investment securities and cash balances related to long-term debt at December 31, 2005, plus funds contractually committed to us will be sufficient to meet our operating and capital requirements into the first quarter of 2007. These estimates are based on assumptions and estimates, including the availability of a $25 million loan from Medicis. These assumptions and estimates may prove to be wrong. Additionally, we are required to maintain a total unrestricted cash balance of at least $25.0 million under our credit facility with Comerica. We will need to sell equity or debt securities to raise additional funds 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.

If we fail to maintain regulatory approval to commercially market or 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. Aldurazyme, Naglazyme and Orapred have received regulatory approval to be commercially marketed and sold in the U.S., and Aldurazyme and Naglazyme have received regulatory approval to be commercially marketed and sold in the 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 of 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 FDA 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 FDA's regulations, the range of possible sanctions includes FDA issuance of adverse publicity, product recalls or seizures, fines, total or partial suspensions of production and/or distribution, suspension of FDA's review of marketing applications, enforcement actions, including injunctions and civil or criminal prosecution. The FDA can withdraw a product's approval under some circumstances, such as the failure to comply with existing or future regulatory requirements or unexpected safety issues. Further, the FDA may condition approval of our product candidates 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 safety. If data we collect from post-marketing studies suggest that one of our approved products may present a risk to safety, the FDA 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, our management's credibility, 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.

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 on animals 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. 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 on animals, the results in humans may be significantly different. After we have conducted preclinical studies in animals, 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.

The fast-track designation for our product candidates, if obtained, may not actually lead to a faster review process and a delay in the review process or in the approval of our products will delay revenue from the sale of the products and will increase the capital necessary to fund these programs.

Our product candidates may not receive fast-track designation or a six-month review timeframe. Even with fast-track designation, it is not guaranteed that the total review process will be faster or that approval will be obtained, if at all, earlier than would be the case if the product had not received fast-track designation.

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 must obtain regulatory approval of our manufacturing facilities, processes and quality systems; and the manufacture of our drugs must comply with GMP regulations. The GMP regulations govern facility compliance, quality control and documentation policies and procedures. In addition, our 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 facility in Novato, California (Galli Drive) and GMP warehouse facilities have been inspected and licensed by the State of California for clinical pharmaceutical manufacture and have been approved by the FDA, the EC and health agencies in other countries for the commercial manufacture of Aldurazyme and by the FDA and EC for the commercial manufacture of Naglazyme. We have entered into contracts with third-party manufacturers to produce Orapred and Phenoptin.

Due to the complexity of the processes used to manufacture Aldurazyme, Naglazyme and our 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 Aldurazyme, Naglazyme or our product candidates may be unable to comply with GMP regulations in a cost effective manner. As anticipated by GMP requirements, manufacturing deviations and deviations from GMP can and do occur from time to time. When a deviation occurs, we take corrective actions, which may not always be successful. Continued or extensive deviations can cause a manufacturing facility to be out of compliance with GMP. If we, or our 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 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 a drug intended to treat a rare disease or condition, defined as a patient population of less 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 particularly 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 Orphan Drug Act designation to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have 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 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 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.

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.

Aldurazyme and Naglazyme both target diseases with small patient populations. As a result, our per-patient prices must be relatively high in order to recover our development costs and achieve profitability. Aldurazyme targets patients with MPS I and Naglazyme targets patients with MPS VI. We believe that we will need to market worldwide to achieve significant market penetration of each product. In addition, we are developing other drug candidates to treat conditions, such as other genetic diseases, with small patient populations. Due to the expected costs of treatment for Aldurazyme and Naglazyme, we may be unable to maintain or obtain sufficient market share for Aldurazyme or Naglazyme at a price high enough to justify our product development efforts.

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 July 2002 PhRMA Code on Interactions with Healthcare Professionals.

Neither the government nor the courts have provided substantial 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, 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.

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 Aldurazyme and Naglazyme 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 Aldurazyme or Naglazyme 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.

We currently have limited expertise in obtaining reimbursement. We rely on the expertise of our joint venture partner, Genzyme, to obtain reimbursement for the costs of Aldurazyme. We are developing our own reimbursement capabilities for Naglazyme and have initiated the process for obtaining reimbursement in the E.U. 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 and for Naglazyme outside the U.S., 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, our products may not be commercially viable or our future revenues and gross margins may be adversely affected.

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), providing 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 will receive their 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. 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. 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. Other cost containment measures have been adopted or proposed by federal, state, and local 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.

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 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. Other parties have published the structure of the enzymes and compounds, the methods for purifying or producing the enzymes and compounds or the methods of treatment. The composition and genetic sequences of animal and/or human versions of Aldurazyme, Naglazyme and many of our product candidates, including BH_4, have been published and are believed to be in the public domain. Publication of this information may prevent us from obtaining composition-of-matter patents, which are generally believed to offer the strongest patent protection.

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 on patents as a means of protecting our products or product candidates, including Aldurazyme, Naglazyme, Orapred or BH_4.

We own or license patents and patent applications related to Aldurazyme, Naglazyme, Orapred, 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. As a company, 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.

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 United States Patent and Trademark Office (USPTO) has issued three patents to a third-party that relate to alpha-L-iduronidase. If we are not able to successfully challenge these patents, we may be prevented from producing Aldurazyme in the U.S. unless and until we obtain a license.

The USPTO has issued three patents to a third-party that include 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. Our lead drug product, Aldurazyme, is based on human, recombinant alpha-L-iduronidase. We believe that these patents are invalid or not infringed on a number of grounds. 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. However, corresponding applications are still pending in Canada and Japan, and these applications are being prosecuted by the applicants. We do not know whether any of these applications will issue as patents or the scope of the claims that would issue from these applications. In addition, under U.S. law, issued patents are entitled to a presumption of validity, and our challenges to the U.S. patents may be unsuccessful. Even if we are successful, challenging the U.S. 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.

The holder of the patents described above has granted an exclusive license for products relating to these patents to one of our competitors, Transkaryotic Therapies Inc. (TKT), which was acquired by Shire PLC in 2005. If we are unable to successfully challenge the patents, we may be unable to produce Aldurazyme in the U.S. (or in Canada or Japan, should patents issue in these countries) unless we can reach an accommodation with the patent holder and licensee. Neither the current licensee nor the patent holder is required to grant us a license or other accommodation and even if a license or other accommodation is available, we may have to pay substantial license fees, which could adversely affect our business and operating results.

On October 8, 2003, Genzyme, our joint venture partner, and TKT announced their collaboration to develop and commercialize an unrelated drug product. In connection with the collaboration agreement, Genzyme and TKT signed a global legal settlement involving an exchange of non-suits between the companies. As part of this exchange, TKT has agreed not to initiate any patent litigation against Genzyme or our joint venture relating to Aldurazyme. If any or all of the TKT-licensed patents are deemed (or ruled) to cover Aldurazyme, our joint venture may be required to reach additional accommodations with the holder of the patents, who is not party to the TKT-Genzyme settlement discussed above.

If our joint venture with Genzyme were terminated, we could be barred from commercializing Aldurazyme or our ability to successfully commercialize Aldurazyme would be delayed or diminished.

We rely on Genzyme to apply the expertise it has developed through the launch and sale of other enzyme-based products to the marketing of Aldurazyme. We have very limited experience selling, marketing or obtaining reimbursement for orphan pharmaceutical products. In addition, without Genzyme we would be required to pursue foreign regulatory approvals. We have limited experience in seeking foreign regulatory approvals.

Either Genzyme or we may terminate the joint venture 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 the joint venture agreement and we believe that Genzyme is not currently in breach of the joint venture 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 joint venture is terminated for breach, the non-breaching party would be granted, exclusively, all of the rights to Aldurazyme and any related intellectual property and regulatory approvals and would be obligated to buy out the breaching party's interest in the joint venture. If we are the breaching party, we would lose our rights to Aldurazyme and the related intellectual property and regulatory approvals. If the joint venture 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 the joint venture and obtain all rights to Aldurazyme exclusively. 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 equally between Genzyme and us.

If the joint venture is terminated by either party because the other declared bankruptcy and is also in breach of the agreement, the terminating party would be obligated to buy out the other and would obtain all rights to Aldurazyme exclusively. If the joint venture 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 the joint venture for a stated amount set by the terminating party at its discretion. The offeree must then either accept this offer or agree to buy the terminating party's interest in the joint venture on those same terms. The party who buys out the other would then have exclusive rights to Aldurazyme.

If we were obligated, or given the option, to buy out Genzyme's interest in the joint venture, 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.

If our license agreement with Ascent Pediatrics is terminated or becomes non-exclusive we could be barred from commercializing Orapred or our ability to successfully commercialize Orapred could be diminished.

The license agreement with Ascent Pediatrics is terminable upon specified material breaches by Ascent Pediatrics or us. If the license agreement were terminated, we would no longer have the ability to manufacture, market, sell, or distribute Orapred.

Ascent Pediatrics has the right under the license agreement to cause the license to become non-exclusive in the event of certain specified breaches by us. If the license becomes non-exclusive, Ascent Pediatrics would be able to commercialize Orapred itself or license it to others, which could reduce our competitive advantage and which could reduce our revenue significantly.

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

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 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 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 Serono by giving notice or by us for a material breach by 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 Serono does not own. Upon a termination of the agreement by 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 Serono under the agreement become irrevocable and fully-paid upon the payment of amounts due by 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 Serono to us under or pursuant to the agreement will automatically terminate. Under the terms of our agreement with Serono, 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, Serono can opt out of this responsibility. If Serono opts out, or if the agreement is terminated by either Serono or us, and we continue the development of products related to that agreement, we would be responsible for 100% of future development costs, and our expenses could increase and our operating performance could be adversely affected.

If the option under the securities purchase agreement with Medicis to purchase all of the issued and outstanding capital stock of Ascent Pediatrics is accelerated by Medicis, we may not have sufficient funds to exercise the option, which could result in a termination of the license agreement and our revenue could decrease significantly.

We are obligated to exercise the option under our securities purchase agreement with Medicis to purchase all issued and outstanding capital stock of Ascent Pediatrics in approximately three years unless our product sales from the Ascent Pediatrics business for the 12 months ending March 31, 2009 exceed 150% of the Ascent Pediatrics business product sales in the 12 months ended March 31, 2004, in which event we would have the right not to exercise the option. The exercise of the option is subject to acceleration on specified material breaches of our license agreement with Ascent Pediatrics or a bankruptcy or insolvency proceeding involving Medicis or Ascent Pediatrics, and if such acceleration is due to a specified breach of the license by us, then the option exercise price together with an amount equal to all license payments remaining under our license agreement with Ascent Pediatrics will become due on the accelerated closing date for the purchase of shares under the option.

If the option were accelerated, we may not have sufficient funds at that time to exercise the option and/or to make the license payments, and may not be able to obtain the financing to do so, in which case we would not be able to consummate the transaction to acquire such shares and would be in breach of the license agreement and the securities purchase agreement. If we are in breach of the license agreement, Ascent Pediatrics may terminate the license and we would no longer have the ability to manufacture, market, sell, or distribute Orapred and our revenue could decrease significantly.

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.

Although we manufacture Aldurazyme and Naglazyme at commercial scale and within our cost parameters, due to the complexity of manufacturing our products we may not be able to manufacture any other drug product successfully with a commercially viable process or at a scale large enough to support their respective commercial markets or at acceptable margins.

Our manufacturing processes may not meet initial expectations and we may encounter problems with any of the following if we attempt to increase the scale or size, or improve the commercial viability of our manufacturing processes:

- design, construction and qualification of manufacturing facilities that meet regulatory requirements;
- schedule;
- reproducibility;

- production yields;
- purity;
- costs;
- quality control and assurance systems;
- raw material suppliers;
- shortages of qualified personnel; and
- compliance with regulatory requirements.

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, and other events that cannot always be prevented or anticipated.

The availability of suitable contract manufacturing capacity at scheduled or optimum times is not certain. The cost of contract manufacturing is generally greater than internal manufacturing and therefore our manufacturing processes must be of higher productivity to result in equivalent margins.

Although we have entered into contractual relationships with third-party manufacturers to produce Orapred and Phenoptin, 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, regulatory approval for Phenoptin or Orapred ODT could be significantly delayed and we may lose potential revenue.

We have built-out approximately 60,000 square feet at our Galli Drive facility for manufacturing capability for Aldurazyme and Naglazyme, including related quality control laboratories, materials capabilities, and support areas. We expect to add additional capabilities in stages over time, which could create additional operational complexity and challenges. We expect that developing manufacturing processes for all of our product candidates will require significant time and resources before we can begin to manufacture them (or have them manufactured by third parties) in commercial quantity at an acceptable cost.

In order to achieve our product cost targets, we must develop efficient manufacturing processes either by:

- improving the product yield from our current cell lines, which are populations of cells that have a common genetic makeup;
- improving the manufacturing processes licensed from others; or
- developing more efficient, lower cost recombinant cell lines and production processes.

A recombinant cell line is a cell line with foreign DNA inserted that is used to produce an enzyme or other protein that it would not otherwise produce. The development of a stable, high production cell line for any given enzyme or other protein is difficult, expensive and unpredictable and may not result in adequate yields. In addition, the development of protein purification processes is difficult and may not produce the high purity required with acceptable yield and costs or may not result in adequate shelf-lives of the final products. If we are not able to develop efficient manufacturing processes, the investment in manufacturing capacity sufficient to satisfy market demand will be much greater and will place heavy financial demands upon us. If we do not achieve our manufacturing cost targets we may be unable to meet demand for our products and lose potential revenue, have reduced margins or be forced to terminate a program.

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 our manufacturing processes have a higher than expected failure rate, we may be unable to meet demand for our products and lose potential revenue, have reduced margins, or be forced to terminate a program.

The processes we use to manufacture our product and product candidates are extremely complex. 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 Aldurazyme and Naglazyme, have been within our expectations, which are based on industry norms.

In order to produce product within our time and cost parameters, we must continue to produce product within expected failure parameters. 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 and timely take corrective action in response to any failure.

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 sole manufacturing facility for Aldurazyme and Naglazyme 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 Aldurazyme and Naglazyme or our third-party manufacturer's ability to manufacture Orapred or Phenoptin.

Our Galli Drive facility is our only manufacturing facility for Aldurazyme and Naglazyme. 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, our ability to manufacture Aldurazyme and Naglazyme, or to have Orapred manufactured for us, could be seriously, or potentially completely impaired, and our Aldurazyme, Naglazyme and Orapred commercialization efforts, revenue from the sale of Aldurazyme, Naglazyme and Orapred and our development efforts with respect to Phenoptin could be seriously impaired. The insurance we maintain 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 cause a loss of our market share and reduce 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.

We try to maintain inventory levels that are no greater than necessary to meet our current projections. Any interruption in the supply of finished products could hinder our ability to timely distribute finished products. With respect to Orapred, if we are unable to obtain adequate product supplies to satisfy our customers' orders, we may lose those orders and our customers may cancel other orders and stock and sell competing products. This, in turn, could cause a loss of our market share and reduce our revenues.

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.

Fluctuations in demand for our products create inventory maintenance uncertainties.

We sell our products primarily to major wholesalers and retail pharmacy chains. Consistent with pharmaceutical industry patterns, most of our Orapred revenues are derived from three major drug wholesale concerns. While we attempt to estimate inventory levels of Orapred at our major wholesale customers, using historical prescription information and purchase patterns, this process is inherently imprecise. We rely wholly upon our wholesale and drug chain customers to effect the distribution allocation of Orapred. There can be no assurance that these customers will adequately manage their local and regional inventories to avoid spot outages.

We cannot control or influence greatly the purchasing patterns of wholesale and retail drug chain customers. These are highly sophisticated customers that purchase our products in a manner consistent with their industry practices and, presumably based upon their projected demand levels. From time to time, we offer sales incentives, such as price discounts and extended payment terms, in the ordinary course of business. These incentives may impact the level of inventory held by wholesalers. Additionally, the buying practices of the wholesalers include occasional speculative purchases of product in excess of the current market demand, at their discretion, in anticipation of future price increases. Purchases by any given customer, during any given period, may be above or below actual prescription volumes of any of our products during the same period, resulting in fluctuations in product inventory in the distribution channel. In addition, if wholesaler inventories substantially exceed retail demand, we could experience reduced revenue from sales in subsequent periods, or product returns from the distribution channel due to overstocking, low end-user demand or product expiration.

Our recent reduction in our sales force could adversely affect our ability to market our current and future products and could adversely affect our revenues.

During the third quarter, we reduced our sales force by 52 employees or approximately 83% of the sales force. We believe that the current size of the sales force is appropriate based on the nature of our products being sold, the expected revenues and the competitive marketplace. We also believe that, to the extent necessary, we could increase the size of our sales force in the future to accommodate demands required by future products. However, if our assessments are incorrect, our ability to market our current and future products could be adversely affected. If this were to happen, the revenues generated by our current and future products would 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.

There are a number of competitive products with Orapred that have the same active ingredient. Some of these products are less expensive than Orapred. Additionally, in the third quarter of 2004 and the first nine months of 2005, the FDA approved several generic products that have the same strength and active ingredient as Orapred. Although there are several other products on the market that have the same or similar ingredients, these products have the same drug substance and concentration as Orapred. These generic products also have an AA equivalence rating to Orapred and therefore may be substituted at pharmacies without consulting the prescribing physician. Our revenue from Orapred has been adversely affected by these generic products and will be further adversely affected if we are not able to implement effective defensive strategies or if our existing defensive strategies are not effective.

If we fail 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.

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 Phenylase, and several of our product programs have been developed through licensing or collaborative arrangements, such as Aldurazyme, Naglazyme, Orapred, Phenoptin and Vibrilase. These collaborations include licensing proprietary technology from, and other relationships with, academic research institutions. If our competitors successfully enter into partnering arrangements 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 enzyme therapeutics, including Genzyme, our joint venture partner. These companies 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 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.

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 have no experience commercializing drug products in the E.U. and, if we are unable to successfully market and sell Naglazyme in the E.U., our revenues and profitability will be adversely affected.

As an organization, we have no experience commercializing drug products outside of the U.S. We have established operations in the E.U. and are in the process of initiating commercialization of Naglazyme ourselves. However, establishing and maintaining a complete and effective commercial structure is a complicated and difficult process. This includes establishing sales, marketing, regulatory, distribution, and reimbursement functions. In order to successfully commercialize Naglazyme, we will need to effectively maintain or contract for all of these functions.

Commercialization in the E.U. is significantly different from commercialization in the U.S. Each country in the E.U. has a different healthcare system and different policies and procedures for funding and reimbursing expensive orphan products, such as Naglazyme, and for treating rare and complicated diseases such as MPS VI. Obtaining reimbursement for these types of drugs can be particularly difficult and requires direct and effective negotiations with the government organizations and private third-party organizations.

If we are not successful with these activities, our revenues from sales of Naglazyme in the E.U. will be adversely affected. Further, establishing and maintaining an effective commercial organization requires significant attention of senior management. An adverse affect on revenue from the E.U. or the attention required by senior management to correct an ineffective organization could reduce our overall revenues and profitability.

We depend upon our key personnel and our ability to attract, train 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 their 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 rapid growth has strained our managerial, operational, financial and other resources. We expect this growth to continue. Based on the FDA and EC approval of Naglazyme for the treatment of MPS VI, we expect to devote additional resources in the immediate future to support the commercialization of Naglazyme.

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.

Growth in our business may also contribute to fluctuations in our operating results, which may cause the price of our securities to decline. Our revenue may fluctuate due to many factors, including changes in:

- wholesaler buying patterns;
- reimbursement rates;
- physician prescribing habits; and
- the availability or pricing of competitive products.

We may also experience fluctuations in our quarterly results due to price changes and sales incentives. For example, purchasers of our products, particularly wholesalers, may increase purchase orders in anticipation of a price increase and reduce order levels following a price increase. We occasionally offer sales incentives, such as price discounts and extended payment terms, in the ordinary course of business, that could have a similar impact. In addition, some of our products are subject to seasonal fluctuation in demand.

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

Even if our drug products are approved, doctors must use treatments that require using those products. If doctors elect a different course of treatment from that which includes our drug products, this decision would reduce demand for our drug products and adversely affect revenues. For example, if in the future gene therapy becomes widely used as a treatment of genetic diseases, the use of enzyme replacement therapy, like Aldurazyme and Naglazyme 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. BioMarin/Genzyme LLC maintains product liability insurance for Aldurazyme with aggregate loss limits of $5.0 million. We have also obtained insurance against product liability lawsuits for commercial sale of our products and for the clinical trials of our product candidates with aggregate loss limits of $15.0 million plus additional clinical liability coverage with lower loss limits in other countries where clinical studies are conducted. 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 Aldurazyme and Naglazyme, our clinical trials for Phenoptin and Vibrilase, or our clinical trials for our terminated program for Neutralase, 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 take, and 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 liabilities 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.

We will incur increased costs as a result of recently enacted and proposed changes in laws and regulations.

We face burdens relating to the recent trend toward stricter corporate governance and financial reporting standards. New legislation or regulations that follow the trend of imposing stricter corporate governance and financial reporting standards, including compliance with Section 404 of the Sarbanes-Oxley Act of 2002, have led to an increase in our costs of compliance. The new rules could make it more difficult or more costly for us to obtain certain types of insurance, including directors' and officers' liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our Board committees or as executive officers. A failure to comply with these new laws and regulations may impact market perception of our financial condition and could materially harm our business. Additionally, it is unclear what additional laws or regulations may develop, and we cannot predict the ultimate impact of any future changes in law.

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 Aldurazyme, Naglazyme and Orapred;
- manufacture, supply or distribution of Aldurazyme, Naglazyme or Orapred;
- 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 both the Nasdaq National Market and the Swiss Main Board. Listing on both exchanges 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.

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 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. 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

Our real estate strategy is to lease and develop property that will allow us to maintain our research and development, clinical and commercial manufacturing, sales and marketing, and administrative activities in line with our current organizational strategies and anticipated needs in the future. In addition to the small office suite we occupy in London, we are currently occupying a total of five buildings, all of which are located in Novato, California, each within a half-mile radius. The five buildings, each named for their location, are:

- 46 Galli Drive facility;
- 79 Digital Drive facility;

- 90 Digital Drive facility;
- 95 Digital Drive facility; and
- 105 Digital Drive facility

The 46 Galli Drive facility consists of approximately 70,000 square feet. It houses our Aldurazyme and Naglazyme manufacturing facility, including limited storage and warehouse functions and a small research and development laboratory. The lease expires in August 2010 and we have the option to extend for two additional five-year periods.

The 79 Digital Drive facility, with approximately 25,700 square feet, provides warehousing support for our entire organization. Its primary focus is to provide controlled access warehousing and the required segregation and testing of all cGMP raw materials used in our manufacturing operations. In addition, the 79 Digital Drive facility serves as the primary shipping, receiving and storage point for all other materials used throughout our organization. Within the 25,700 square feet, about 10,400 square feet is administrative space, which is utilized by our Quality Control and IT departments. The lease expires in July 2006, and we are currently negotiating an extension.

The 95 Digital Drive facility serves as our primary research and development facility with the recent construction of approximately 20,000 square feet of laboratory space and support areas. An additional 16,000 square feet of undeveloped space within the building remains available for future development. The lease on this building expires in January 2014.

The 90 and 105 Digital Drive facilities provide approximately 74,800 square feet dedicated to housing administrative and research offices, common areas and additional warehouse space. These two facilities serve as the corporate headquarters and are part of a four-building complex, comprised of the 79, 90, 95 and 105 Digital Drive facilities. We began occupying the 90 and 105 Digital Drive space in November 2004. The lease for both the 90 and 105 Digital Drive facilities expires in October 2013 and we have the option to extend for two additional five-year periods.

Our administrative office space is expected to be adequate for the foreseeable future. We may need to supplement the capacity of our production facilities in order to meet future market demands. We believe that, to the extent required, we will be able to lease 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. We expect to further develop our internal clinical manufacturing capabilities in 2006.

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, 2005.

Part II

Item 5. Market for Common Equity and Related Stockholder Matters

Our common stock is listed under the symbol "BMRN" on both the Nasdaq National Market and the Swiss SWX Main Board. The following table sets forth the high and low sales prices for our common stock for the periods noted, as reported by Nasdaq National Market.

		Prices	
Year	Period	High	Low
2004	First Quarter	$ 8.87	$7.09
2004	Second Quarter	$ 8.12	$5.53
2004	Third Quarter	$ 6.66	$4.50
2004	Fourth Quarter	$ 6.49	$3.87
2005	First Quarter	$ 6.41	$4.40
2005	Second Quarter	$ 7.77	$4.75
2005	Third Quarter	$ 9.47	$7.02
2005	Fourth Quarter	$11.70	$6.94

On February 21, 2006, the last reported sale price on the Nasdaq National Market for our common stock was $11.79. We have never paid any cash dividends on our common stock and we do not anticipate paying cash dividends in the foreseeable future.

Holders

As of February 21, 2006, there were 91 holders of record of 74,641,983 outstanding shares of our common stock. Additionally, on such date, options to acquire 8,162,842 shares of our common stock were outstanding.

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 statement of operations data for the years ended December 31, 2001, 2002, 2003, 2004 and 2005 and balance sheet data as of December 31, 2001, 2002, 2003, 2004 and 2005 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)				
	2001	2002	2003	2004	2005
Consolidated statements of operations data:					
Net product sales	$ —	$ —	$ —	$ 18,641	$ 13,039
Collaborative agreement revenue	—	—	12,100	—	12,630
Total revenues	—	—	12,100	18,641	25,669
Operating expenses:					
Cost of sales (excludes amortization of developed product technology)	—	—	—	3,953	2,629
Research and development	22,144	26,811	53,932	49,784	56,391
Selling, general and administrative	6,828	17,347	15,278	37,606	41,556
Amortization of acquired intangible assets	—	—	—	3,987	1,144
Acquired in-process research and development	11,647	11,223	—	31,453	—
Impairment of acquired intangible assets	—	—	—	68,251	—
Total operating expenses	40,619	55,381	69,210	195,034	101,720
Equity in the (loss)/income of BioMarin/Genzyme LLC	(18,663)	(23,466)	(18,693)	(2,972)	11,838
Loss from operations	(59,282)	(78,847)	(75,803)	(179,365)	(64,213)
Interest income	1,871	2,017	2,559	2,466	1,861
Interest expense	(17)	(542)	(3,131)	(10,544)	(11,918)
Net loss from continuing operations	(57,428)	(77,372)	(76,375)	(187,443)	(74,270)
Income (loss) from discontinued operations	(2,266)	135	—	—	—
Gain (loss) on disposal of discontinued operations	(7,912)	(224)	577	—	—
Net loss	$(67,606)	$(77,461)	$(75,798)	$(187,443)	$ (74,270)
Net loss per share, basic and diluted:					
Net loss from continuing operations	$ (1.40)	$ (1.45)	$ (1.23)	$ (2.91)	$ (1.08)
Loss from discontinued operations	(0.06)	—	—	—	—
Gain (loss) on disposal of discontinued operations	(0.19)	—	0.01	—	—
Net loss per share, basic and diluted	$ (1.65)	$ (1.45)	$ (1.22)	$ (2.91)	$ (1.08)
Weighted average common shares outstanding	41,083	53,279	62,125	64,354	68,830

	December 31, (in thousands)				
	2001	2002	2003	2004	2005
Consolidated balance sheet data:					
Cash, cash equivalents and short-term investments	$131,097	$ 73,978	$206,357	$ 48,815	$ 47,792
Total current assets	136,783	78,254	213,262	85,159	68,941
Total assets	171,811	110,616	256,340	232,966	195,303
Long-term liabilities	3,961	5,226	125,672	230,890	232,398
Total stockholders' equity (deficit)	159,548	98,543	117,853	(67,978)	(77,462)

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

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.

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 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 Aldurazyme, Naglazyme and Orapred. Aldurazyme has been approved for marketing in the U.S. by the FDA, in the E.U. by the EC and in other countries for the treatment of MPS I.

We have developed Aldurazyme through a joint venture with Genzyme. Aldurazyme net revenue recorded by our joint venture for 2005 totaled $76.4 million, compared to $42.6 million for 2004.

In May 2004, we completed the transaction to acquire the business of Ascent Pediatrics from Medicis. The Ascent Pediatrics business includes Orapred, a drug primarily used to treat asthma exacerbations in children and other inflammatory conditions and two additional proprietary formulations of Orapred in development. Orapred net product sales for 2005 totaled $6.9 million, compared to $18.6 million in 2004. In October 2005, we announced that the FDA had accepted for filing the New Drug Application for Orapred ODT for the treatment of inflammatory conditions. We expect to receive a response from the FDA by June 1, 2006.

In May 2005, the FDA granted marketing approval for Naglazyme for the treatment of MPS VI, a debilitating life-threatening genetic disease for which no other drug treatment currently exists. Naglazyme net product sales for 2005 totaled $6.1 million. In January 2006, we announced that we received marketing approval from the EC for Naglazyme for MPS VI in the E.U. We are in the process of launching the product in the E.U. on a country-by-country basis.

We are developing several product candidates for the treatment of genetic diseases including: Phenoptin, a proprietary oral form of tetrahydrobiopterin (6R-BH_4 or BH_4), for the treatment of moderate to mild forms of PKU; and Phenylase, a preclinical enzyme substitution therapy for the treatment of the more severe form of PKU. We are developing Phenoptin for the treatment of 6R-BH_4-responsive phenylketonurics and Phenylase for phenylketonurics who are not 6R-BH_4-responsive.

Our research and development expense during 2005, primarily related to the development of Naglazyme and Phenoptin, totaled $56.4 million compared to $49.8 million in 2004. Our net loss totaled $74.3 million for 2005 compared to $187.4 million in 2004. Our cash, cash equivalents, short-term investments, restricted cash and cash balances related to long-term debt totaled $64.8 million as of December 31, 2005 compared to $90.4 million as of December 31, 2004.

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 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 our financial statements included with this report.

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

We account for our joint venture investment using the equity method. Accordingly, we record an increase in our investment for contributions to the joint venture and a reduction or increase in our investment for our 50% share of the loss or income of the joint venture, respectively.

Equity in the (Loss)/Income of BioMarin/Genzyme LLC includes our 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 our services provided to the joint venture and the investment in BioMarin/Genzyme LLC includes our share of the joint venture's net equity.

Impairment of Long-Lived Assets

Our long-lived assets include our investment in BioMarin/Genzyme LLC, property, plant and equipment, and the acquired Orapred intangible assets and goodwill. We regularly review long-lived assets for impairment. The recoverability of long-lived assets, other than goodwill, is measured by comparing the asset's carrying amount to the expected undiscounted future cash flows that the asset is expected to generate. 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 year ended December 31, 2005. In December 2004, we recognized an impairment loss related to the acquired Orapred intangible assets, totaling approximately $68.3 million, which was recorded as an impairment of acquired intangible assets in the consolidated statement of operations for the year ended December 31, 2004.

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 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 the Orapred business as a separate reporting unit, which includes all of our intangible assets and goodwill and is a component of our single operating segment. 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 a discounted cash flow model, unless facts and circumstances warrant a review of goodwill for impairment before that time.

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 discounted 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.

We believe that our investment in the joint venture will be recovered because we project that the joint venture will maintain sustained positive earnings and cash flows in the future. The joint venture recorded net income of $23.7 million during 2005. We and our joint venture partner maintain the ability and intent to fund the joint venture's operations, as necessary.

The recoverability of the carrying value of leasehold improvements for our administrative facilities 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 (SAB) No. 104: *Revenue Recognition*, and Emerging Issues Task Force Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*. Our revenues consist of Naglazyme and Orapred product sales and revenues from our collaborative agreements with Serono and Genzyme.

Naglazyme product sales—We recognize revenue from Naglazyme 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. Naglazyme product sales transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents.

Naglazyme is generally sold to specialty pharmacies or end-users, such as hospitals, which act as retailers. Because of the pricing of Naglazyme, the limited number of patients and the customers' limited return rights, the specialty pharmacies generally carry a very limited inventory. We also sell Naglazyme to certain larger pharmaceutical wholesalers, which, with respect to Naglazyme, act as intermediaries between us and end-users and generally do not stock quantities of Naglazyme. Accordingly, we expect that sales related to Naglazyme in the U.S. will be closely tied to end-user demand.

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 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' limited return rights and our joint venture's experience of returns for Aldurazyme, which is a similar product. Based on these factors, management has concluded that Naglazyme 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.

As Naglazyme was approved for commercial sale in the U.S. during the second quarter of 2005, we have limited historical experience with rebates and returns specific to Naglazyme. Until adequate historical experience is obtained to serve as a reasonable basis for our estimates of rebates and returns, management will use, 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. The nature and amount of our current estimates of the applicable revenue dilution item that are applied to gross sales of Naglazyme to derive net sales are described in the table below.

Revenue Dilution Item	Percentage of Gross Sales	Description
Rebates	6-8%	Rebates offered to state Medicaid and other government programs
Cash Discounts	1-2%	Discounts offered to customers for prompt payment of accounts receivable
Total	7-10%	

Orapred product sales—We recognize revenue from Orapred product sales when persuasive evidence of an arrangement exists, the product has been shipped, 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. Orapred product sales transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents.

The timing of customer purchases and the resulting product shipments have a significant impact on the amount of revenue from Orapred product sales that we recognize in a particular period. Also, the majority of Orapred sales are made to wholesalers, which, in turn, resell the product to retail outlets. Orapred inventory in the distribution channel consists of inventory held by wholesalers, which are our principal customers, and inventory held by retailers. Our revenue from Orapred sales in a particular period is impacted by increases or decreases in wholesalers' inventory levels. The buying practices of the wholesalers include occasional speculative purchases of Orapred in excess of the current market demand, at their discretion, in anticipation of future price increases. During 2005, continued decreases in Orapred retail demand due to increased generic competition has contributed to high levels of inventory held by wholesalers. If wholesaler inventories of Orapred continue to substantially exceed retail demand, we could experience further reduced revenue from sales in subsequent periods, or additional product returns from the distribution channel due to overstocking, low end-user demand or product expiration.

We establish and maintain reserves for amounts payable to managed care organizations and state Medicaid programs for the reimbursement of a portion of the retail price of prescriptions filled that are covered by the respective plans. The amounts estimated to be paid relating to products sold are recognized as revenue reductions and as additions to accrued expenses at the time of the original sale. The rebate reserves are based on our best estimate of the expected prescription fill rate to these managed care organizations and state Medicaid patients, as well as the rebate rates associated with eligible prescriptions. The estimates are developed using the product's rebate history adjusted to reflect known and forecasted changes in the factors that impact such reserves. These factors include changes in the mix of prescriptions that are eligible for rebates, changes in the contract rebate rates and the lag time related to the processing of rebate claims by our customers and managed care organizations. The length of time between the period of prescriptions and the processing of the related rebates has been consistent historically at between three and six months, depending on the nature of the rebate. The length of time between the period of original sale by us and the processing of the related rebate is dependent upon both the length of time that the product is in the distribution channel and the lag time related to rebate processing by third parties. Additionally, we have experienced longer than usual rebate processing lag times as a

result of the transition of the product from Medicis after the acquisition and high levels of Orapred inventory held by wholesalers. Rebate rates are sensitive to changes resulting from new Medicaid and managed care contracts entered into by us, and rebate rates may increase in the future. In the fourth quarter of 2005, we revised our estimates of future rebates payable to Medicaid programs and managed care organizations, which have decreased significantly due to a lower-than-anticipated number of rebate contracts executed by us. The decrease in estimated future rebates resulted in reserve reversals and an increase in 2005 net revenue of approximately $2.1 million, which was recorded during the fourth quarter of 2005. To the extent actual rebates differ from our estimates, additional reserves may be required or reserves may need to be reversed.

Provisions for sales discounts and estimates for chargebacks and product returns are established as a reduction of product sales at the time such revenues are recognized. These revenue reductions are established by our management as its best estimate at the time of the original sale based on the product's historical experience adjusted to reflect known changes in the factors that impact such reserves. These revenue reductions are generally reflected either as a direct reduction to gross sales and accounts receivable through an allowance or as an addition to accrued expenses. We generally permit product returns only if the product is damaged or if it is returned near or after expiration.

Our estimates for future product returns are primarily based on the actual return history for the product and estimates of future demand related to estimated wholesaler inventory levels. Although we are unable to quantify wholesaler inventory levels of Orapred with any certainty, to the extent necessary based on the expiration date and our estimates of quantity of product in the distribution channel, we adjust our estimate for future returns as appropriate. We estimate wholesaler inventory levels, to the extent possible, based on limited information obtained from certain of our wholesale customers and through other internal analyses. Our internal analyses utilize information such as historical sales to wholesalers, product shelf-life based on expiration dating, estimates of the length of time product is in the distribution channel and historical prescription data, which are provided by a third-party vendor. We also evaluate the current and future commercial market for Orapred and consider factors such as Orapred's performance compared to its existing competitors.

The amount of Orapred returns in the normal course of business compared to sales has been reasonably consistent historically. Our experience is that the length of time between the period of original sale and the product return is between one and two years. Because the product has been on the market for approximately four years and the product expiration dating is two to three years, we are continuing to obtain and analyze the returns history. During 2005, continued decreases in Orapred retail demand resulting from increased generic competition have contributed to excess wholesaler Orapred inventories. As a result, we estimate that Orapred returns upon product expiration will significantly increase from our previous estimates, and we have increased the related reserves and reduced 2005 net revenue by approximately $2.0 million, which was recorded during the fourth quarter of 2005. If there are additional changes in Orapred retail demand that impact the wholesaler inventory levels, additional reserves or reserve reversals may be required. Additionally, in the Ascent Pediatrics transaction we acquired liabilities for certain Orapred product returns and unclaimed rebates for the period prior to our acquisition of the product. In the fourth quarter of 2005, we adjusted our estimates of these liabilities, which are recorded as operating expenses because they relate to sales made by the previous owner, based on the circumstances described above, resulting in an increase to the returns reserve of $2.9 million and an decrease in the rebates reserve of $0.7 million, for a net impact of $2.2 million. We may need to further adjust our estimates of these liabilities in the future based on further changes in the market demand for Orapred and changes to our rebate contracts.

As discussed above, our estimates of revenue dilution items are based primarily on the historical experience for the product, as adjusted to reflect known and forecasted changes in the factors that impact the revenue dilutions. The nature and amount of our current estimates of the applicable effective rates for revenue dilution items that are applied to gross sales of Orapred to derive net sales are described in the table below. As discussed above, the estimated rebate allowance rates disclosed below have decreased in 2005 and the estimated rates for product returns have increased. During 2005, the effective rate of the returns provision was approximately

11-12%, after adjusting our returns reserves for the significant amount of inventory that we expect will be returned due to decreased retail demand resulting from increased generic competition. However, our product returns rate in the normal course of business absent excess levels of inventory at specific wholesalers remains consistent with previous periods, at approximately 3-4%. There are no additional material revenue dilution items other than those disclosed below and there have been no material revisions to our estimates of our revenue dilution items to date, except as discussed above.

Revenue Dilution Item	Percentage of Gross Sales	Description
Sales Returns	3-4%	Provision for returns of product sales
Rebates	8-9%	Rebates offered to managed care organizations and state Medicaid programs
Cash Discounts	2%	Discounts offered to customers for prompt payment of accounts receivable
Total	13-15%	

We periodically evaluate the need to maintain allowances for doubtful accounts for estimated losses resulting from the inability of our customers to make required payments. When making this evaluation, we make judgments about the creditworthiness of customers based on ongoing credit evaluations and the aging profile of customer accounts receivable and assess current economic trends that might impact the level of credit losses in the future. Historically, the Orapred product has not experienced significant credit losses and our allowance for doubtful accounts as of December 31, 2005 is insignificant. This is due to a significant portion of Orapred sales that are made to a limited number of financially viable distributors, because we offer discounts that encourage the prompt payment of outstanding receivables and because we require immediate payment in certain circumstances. 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.

Collaborative agreement revenues—Collaborative agreement revenues from 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 includes the portion of the $25.0 million up-front license fee received from Serono recognized as revenue during the development period.

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 have deferred the up-front license fee received from Serono and will recognize it as revenue on a straight-line basis over approximately 3.25 years, which represents an assumption of the time from inception of the agreement until European regulatory approval of Phenoptin for the treatment of PKU, at which point the Company's performance obligations for developing Phenoptin for the treatment of PKU will end. Our assumption of the Phenoptin commercialization period is based on several underlying assumptions about uncertain events, including actions by European regulatory authorities, results of our ongoing clinical trials and successful commercial scale manufacturing of Phenoptin. As Phenoptin advances through the clinical development and regulatory process, our estimates of our performance obligation period may change. The estimate was revised during the fourth quarter of 2005, from 2.75 years to 3.25 years, based on updated information regarding the estimated timing of European regulatory approval. The change in estimate did not have a significant impact on revenues during 2005, but is expected to have a material impact in future periods. Changes in our estimates of our performance obligation period will be recognized prospectively

over the remaining estimated performance obligation period. We regularly review our estimates of the period over which we have an ongoing performance obligation.

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 Serono's share of Phenoptin development costs under the agreement.

Collaborative agreement revenue from Genzyme included $12.1 million received in 2003, related to the FDA marketing approval for Aldurazyme. 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.

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, of approximately $261.2 million at December 31, 2005. 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, and we do not expect changes to this assumption as we expect to incur losses for the foreseeable future.

Inventory

We value inventories at the lower of cost or fair 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 in excess of expected requirements. Expired inventory is disposed of and the related costs are written off. 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. During 2005, increased generic competition to Orapred has resulted in continued decreases in end-user demand. As a result, we revised our estimates of expected inventory requirements and recognized additional Orapred inventory write-offs of approximately $1.5 million, of which $1.3 million was recorded during the fourth quarter of 2005. Actual results may differ from those estimates and additional inventory write-offs may be required.

Regulatory approval for Naglazyme was not received until May 2005, and costs related to the manufacturing of Naglazyme prior to this date 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 were not capitalized as inventory. When regulatory approval was obtained in May 2005, we began capitalizing inventory at the lower of cost or fair value. Naglazyme inventory as of December 31, 2005 includes a portion of the zero cost basis quantities. Until we begin to sell the inventory produced after regulatory approval was obtained, the cost of goods sold or used in clinical trials for the previously expensed inventory will be insignificant or zero. We expect that the majority of the previously expensed inventory will be sold or used in clinical trials by the first quarter of 2007.

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. A critical accounting assumption by our management is that we believe that regulatory approval of our product candidates is uncertain, and 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 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.

Stock Option Plans

We have three stock-based compensation plans. We account for those plans under APB Opinion No. 25, *Accounting for Stock Issued to Employees,* whereby generally no stock-based compensation cost is reflected in our net loss for options issued to employees and directors with exercise prices at or above the market price on the date of issuance. We recognize as an expense the fair value of options granted to persons who are neither employees nor directors. The fair value of options granted is determined using the Black-Scholes model, which requires various estimates and assumptions by management, including the expected term of the options and the expected future volatility of the value of our stock. The expected term of stock options is determined primarily based on the historical patterns for stock option exercises and cancellations. The expected future volatility is determined based on both the historical volatility as well as current and future circumstances that will affect future volatility. These estimates are sensitive to change based on external factors such as the equity markets in general and the individual circumstances of our employees, which are considered in the determination of our estimates. The adoption of FAS 123(R) in the first quarter of 2006 may result in additional changes to our estimates and assumptions because of differences between the old and new accounting pronouncements with respect to the development of certain valuation assumptions.

Recent Accounting Pronouncements

See Note 2(q) 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.

Results of Operations

All of the activities related to the manufacture, distribution and sale of Aldurazyme are reported in the results of the joint venture. Because of this presentation and the significance of the joint venture's operations compared to our total operations, we have divided our discussion of the results of operations into two sections, BioMarin in total and BioMarin/Genzyme LLC. The discussion of the joint venture's operations includes the total amounts for the joint venture, not just our 50% interest in the operations.

BioMarin Results of Operations

Net Loss

Our net loss in 2005 as compared to 2004 decreased to $74.3 million from $187.4 million. Net loss for 2005 decreased as a result of the following (in millions):

Reduction of expenses associated with Ascent Pediatrics acquisition (includes $31.5 million of non-recurring in-process research and development expense in 2004)	$ 34.7
Absence of impairment of acquired intangible assets	68.3
Increased profits from BioMarin/Genzyme LLC	14.8
Phenoptin collaborative agreement revenues	12.6
Increase in Orapred operating loss	(11.3)
Decrease in Naglazyme operating loss	11.0
Increased Phenoptin research and development expenses	(14.4)
Increased facility expenses, including depreciation	(3.3)
Absence of separation costs associated with former CEO	2.9
Increased interest expense and decrease in interest income, excluding imputed interest	(2.0)
Net decrease in other operating expenses	(0.2)
Total decrease in net loss	$113.1

The expenses associated with the Ascent Pediatrics acquisition decreased in 2005 due to the absence of a non-recurring acquired in-process research and development expense of $31.5 million incurred in 2004, $2.8 million related to amortization of acquired intangible assets and a decrease of $0.6 million related to a fair value inventory adjustment, offset by an increase of $0.2 million related to imputed interest expense. The increase in profits from BioMarin/Genzyme LLC during 2005 as compared to 2004 is primarily the result of increased Aldurazyme sales, which are recorded through the joint venture with Genzyme. The increase in Orapred operating net loss is attributable to decrease in gross profit of $10.1 million, which includes a charge for inventory write-offs of $1.1 million, increased spending on research and development for Orapred ODT of $1.5 million, offset by other net operating expenditure decreases of $0.3 million. The decrease in Naglazyme net loss is attributable to increased gross profit of $6.0 million, decreased research and development expenses of $9.3 million, partially offset by increased sales and marketing expenses for commercialization of $4.0 million and other net operating expenditure increases of $0.3 million.

Our net loss in 2004 as compared to 2003 increased to $187.4 million from $75.8 million. Net loss for 2004 increased as a result of the following (in millions):

Expenses associated with Ascent Pediatrics acquisition (includes $31.5 million of in-process research and development expense)	$ 41.3
Impairment of acquired intangible assets	68.3
Decrease in equity in loss of joint venture due to increased Aldurazyme sales	(15.7)
Lack of 2003 non-recurring milestone revenue	12.1
Orapred operating profit	(0.9)
Separation costs associated with former CEO	2.9
Absence of 2003 reversal of lease liability	2.0
Net decrease in other operating expenses	(0.5)
Increased interest expense due to convertible debt issued in June 2003	2.2
Other	(0.1)
Total increase in net loss	$111.6

Expenses associated with the Ascent Pediatrics acquisition include acquired in-process research and development of $31.5 million, amortization of acquired intangible assets of $4.0 million, imputed interest expense of $5.1 million and a fair value inventory adjustment of $0.8 million. The net decrease in other operating expenses is the result of decreased research and development expense, primarily attributable to the lack of Neutralase development costs, offset by increased Naglazyme and Phenoptin research and development expenses and corporate overhead.

Revenue and Gross Profit

Net product sales decreased $5.6 million, to $13.0 million in 2005 from $18.6 million in 2004. Net product sales in 2005 of $13.0 million included $6.1 million of net product sales of Naglazyme and $6.9 million of net product sales of Orapred. Net product sales in 2004 were exclusively related to net product sales of Orapred.

In May 2005, we received marketing approval for Naglazyme in the U.S., and began shipping product in late June 2005. Net product sales for Naglazyme for 2005 were $6.1 million. 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, all of the product sold in 2005 had a zero cost basis. We expect to report lower cost of goods sold for Naglazyme until all of the inventory manufactured prior to marketing approval is sold or used in clinical trials. We estimate that the majority of the zero balance inventory will be sold by the first quarter of 2007.

Commencing with our acquisition of the Ascent Pediatrics business on May 18, 2004, our revenues include sales of Orapred. During 2005, we recognized $6.9 million of net product sales of Orapred and approximately $4.6 million of gross profit, representing a gross margin of approximately 67%. Net sales in 2005 include a $2.0 million charge related to increases in Orapred product returns reserves, and a $2.1 million benefit related to the reversal of Medicaid and managed care rebate reserves. Cost of sales of $2.3 million includes a $1.1 million charge related to increases in inventory write-offs. Gross margin for 2005 excluding the inventory write-off was 83%. Cost of sales excludes the amortization of the developed product technology resulting from the acquisition of the Ascent Pediatrics business.

Retail demand for Orapred continued to decrease throughout 2005 due to increased generic competition. The decreased demand in conjunction with significant levels of Orapred inventory held by wholesalers has resulted in decreased Orapred net product sales. We expect the adverse impact on net product sales to continue in the future. In March 2005, we launched an authorized Orapred generic product and recognized $1.4 million of related net revenue during 2005, which is included in the $6.9 million of total Orapred net product sales during the year.

During 2004, we recognized $18.6 million of net product sales of Orapred and approximately $14.7 million of gross profit, representing a gross margin of approximately 79%. Cost of sales of $4.0 million includes a $0.8 million charge related to an inventory fair market value adjustment associated with the acquisition and a $1.6 million charge for excess Orapred raw materials. Gross margin for 2004 excluding these items was 92%. Cost of sales excludes the amortization of the developed product technology resulting from the acquisition of the Ascent Pediatrics business.

Net sales of Orapred during 2004 were lower than expected as a result of larger than anticipated levels of Orapred inventory held by distributors prior to our acquisition of the product and a new generic competitor to Orapred introduced in the fourth quarter of 2004.

Collaborative Agreement Revenues

Collaborative agreement revenues include milestone revenue under our development and commercialization agreement with Genzyme, as well as both license revenue and contract research revenue under our agreement

with Serono. Collaborative agreement revenues of $12.6 million for 2005 includes the amortization of $5.5 million of the up-front license fee received from Serono recognized as revenue during the period and $7.1 million of reimbursable Phenoptin development costs incurred during the period. The related costs are included in research and development expenses.

Collaborative agreement revenue in 2003 represents the $12.1 million milestone payment received from Genzyme related to the FDA marketing approval of Aldurazyme. We do not expect to earn additional revenue related to Aldurazyme milestones in the future.

Research and Development Expense

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

Research and development expenses increased by $6.6 million to $56.4 million in 2005 from $49.8 million in 2004. The increase is primarily attributable to increased Phenoptin costs of $14.4 million, increased Phenylase costs of $1.9 million and research and development costs of $1.5 million associated with the new Orapred ODT formulation. The increase was offset by decreased Naglazyme costs of $9.3 million and decreased costs related to other programs of $1.9 million. The increased Phenoptin costs primarily include manufacturing costs of $3.5 million and clinical development costs of $7.4 million for PKU, as well as $3.5 million in additional spending for the development of 6R-BH_4 to treat endothelial dysfunction, which includes $3.3 million for license fees paid to Daiichi Suntory Pharma Co., Ltd. related to obtaining the exclusive worldwide rights, excluding Japan, for the use of 6R-BH_4. The increase in Phenoptin development costs is primarily due to increased clinical trial expenses due to the continuation of the Phase 3 clinical trial and pre-approval manufacturing expenses. The decrease in Naglazyme development costs is primarily due to decreased clinical trial and manufacturing expenses, after marketing approval was received in May 2005. However, we expect to incur significant Naglazyme research and development costs in the foreseeable future due to long-term clinical activities related to post-approval regulatory commitments.

Research and development expenses decreased by $4.1 million to $49.8 million in 2004 from $53.9 million in 2003. The decrease is primarily attributable to $17.2 million of Neutralase development costs incurred during 2003 that were not incurred during 2004, because the program was discontinued, and decreased research and decreased development on other programs totaling $1.3 million. The decrease was offset by increased Naglazyme costs of $5.1 million, increased Phenoptin costs of $7.4 million and research and development costs associated with the new Orapred formulations of $1.9 million. The increased Naglazyme costs include $1.0 million of increased manufacturing and quality costs, $3.2 million of increased clinical costs primarily related to the Phase 3 clinical trial and $0.8 million of regulatory costs associated with the filings of the marketing authorization applications. The increased Phenoptin costs primarily include $3.6 million of manufacturing costs and $3.0 million of clinical development costs.

Selling, General and Administrative Expense

Our selling, general and administrative expenses include sales and administrative personnel, facility and external costs required to support our commercialized products and product development programs. These selling, general and administrative costs include: facility operating expenses and depreciation; sales operations in support of Naglazyme and Orapred and our product candidates; human resources; finance and support personnel expenses; and other corporate costs such as insurance, audit and legal expenses. Selling, general and administrative expenses increased by $4.0 million to $41.6 million in 2005 from $37.6 million in 2004. The components of the increase between 2004 and 2005 are as follows (in millions):

Increased sales and marketing for Naglazyme commercialization	$ 4.0
Decreased Orapred sales and marketing expenses	(4.1)
Expenses directly related to reduction of the Ascent Pediatrics sales force	0.9
Absence of former CEO separation costs	(2.9)
Increased Orapred return expense, related to product sold by the previous seller of Orapred	2.9
Decreased Orapred rebate expense, related to product sold by the previous seller of Orapred	(1.4)
Increase in facility expenses, including depreciation	3.3
Increased recruiting and relocation expenses	0.7
Net increase in corporate overhead and other administrative costs	0.6
Total increase in selling, general and administrative expenses	$ 4.0

The decrease in Orapred sales and marketing expenses is primarily attributable to the decrease in sales and marketing efforts during 2005 following the reduction in the Orapred sales force, reducing overall expenses for the period by $4.1 million. The increased Orapred return expense includes $2.9 million related to an increase in estimated product returns for sales made by Medicis prior to the acquisition. The net increase in corporate overhead and other administrative costs includes increased legal fees of $0.8 million, primarily associated with the proxy contest, and fixed asset write-offs of $0.4 million, offset by $0.6 million in other corporate decreases, related to changes in certain activities and administrative support costs.

In July 2005, we announced that we were reducing the Orapred sales force through the elimination of 52 positions. Severance and related costs and payments of approximately $0.9 million, associated with eliminating the 52 sales force positions plus six non-sales force positions, were recognized in the third quarter of 2005.

Selling, general and administrative expenses increased to $37.6 million in 2004 from $15.3 million in 2003. The components of the increase between 2003 and 2004 are as follows (in millions):

Orapred sales and marketing	$13.8
Separation costs associated with former CEO	2.9
Absence of reversal of lease liability in 2003	2.0
Preparation for commercial launch of Naglazyme	2.4
Net increase in corporate overhead and other	1.2
Total increase in selling, general and administrative expenses	22.3

The net increase in corporate overhead and other costs includes increased rent expense, audit fees and administrative personnel. During 2004, we recorded a deferred rent liability related to our occupied facilities, of which the portions attributable to prior periods were immaterial.

Amortization of Acquired Intangible Assets

Amortization of acquired 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. The acquired intangible assets are being amortized over 15 years and the amortization expense for 2005 was $1.1 million, as compared to $4.0 million during 2004. The decrease in amortization expense for 2005 is primarily attributable to the lower asset value resulting from the impairment charge recognized in the fourth quarter of 2004. We expect that the recurring annual amortization expense associated with the transaction will be approximately $1.1 million.

Acquired in-Process Research and Development

Acquired in-process research and development includes the nonrecurring charge for the portion of acquisition consideration attributable to development-stage products. Acquired in-process research and development of $31.5 million during 2004 includes the fair value of the two additional development-stage formulations of Orapred that we acquired in the Ascent Pediatrics transaction.

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

Equity in the (Loss)/Income of BioMarin/Genzyme LLC includes our 50% share of the joint venture's loss or income for the period. Equity in the Income of BioMarin/Genzyme LLC was $11.8 million in 2005 compared to a loss of $3.0 million in 2004. The income is principally due to the profits derived from $76.4 million of Aldurazyme sales in 2005 compared to $42.6 million of sales during 2004.

Equity in the Loss of BioMarin/Genzyme LLC was $3.0 million in 2004 compared to $18.7 million in 2003. The decrease was principally due to increased Aldurazyme sales of $31.1 million, to $42.6 million in 2004 from $11.5 million in 2003.

See the *"BioMarin/Genzyme LLC"* section below for further discussion of the joint venture's results of operations.

Impairment of Acquired Intangible Assets

No impairment of the Orapred acquired intangible assets was recorded for the year ended December 31, 2005. Impairment of acquired intangible assets during the year ended December 31, 2004 includes the impairment loss recorded on the Orapred product technology during the fourth quarter of 2004. In December 2004, the Company recognized an impairment loss totaling $68.3 million. The primary circumstance leading to the impairment was the introduction of a new generic competitor to Orapred during the fourth quarter of 2004 that resulted in a significant decrease in the Orapred market share. The impairment charge represents the amount by which the carrying value of the Orapred technology exceeded its fair value on December 31, 2004.

Interest Income

We invest our cash, short-term investments and restricted cash in government and other high credit quality securities in order to limit default and market risk. Interest income decreased to $1.9 million in 2005 from $2.5 million in 2004, primarily due to decreased levels of cash and investments on hand throughout the year. Interest income decreased to $2.5 million in 2004 from $2.6 million in 2003.

Interest Expense

We incur interest expense on our convertible debt issued in June 2003 and on our equipment and facility loans. Interest expense also includes imputed interest expense on the discounted obligation for the Ascent

Pediatrics transaction. Interest expense was $11.9 million and $10.5 million in 2005 and 2004, respectively, representing an increase of $1.4 million. The increase in 2005 is primarily related to increased borrowings on the equipment and facility loans during the year and higher interest rates. In 2005 and 2004, the imputed interest related to the Ascent Pediatrics transaction was $5.4 million and $5.1 million, respectively.

Interest expense was $10.5 million and $3.1 million in 2004 and 2003, respectively. The increase in 2004 was primarily due to interest expense on the convertible debt issued in June 2003 of $2.2 million and imputed interest related to the Ascent Pediatrics transaction of $5.1 million.

Discontinued Operations

In December 2001, we decided to close the carbohydrate analytical business portion of our wholly owned subsidiary, Glyko, Inc. (Glyko). As a result, the operations of Glyko are classified as discontinued operations in our consolidated financial statements. Accordingly, we have segregated its operating results in our consolidated statements of operations. Related cash flows are insignificant and have been included in the operating section of our consolidated statements of operations.

In 2003, we sold certain assets of Glyko to a third-party for a total sales price of up to $1.5 million. The sales price was comprised of cash totaling $0.2 million, a note receivable payable in quarterly installments through 2006 totaling $0.5 million and quarterly royalties based upon future sales of certain Glyko products through 2008 up to a maximum of $0.8 million. The proceeds from the sale of the Glyko assets, including the discounted note receivable of $0.4 million, were recorded as a gain from discontinued operations in 2003 totaling $0.6 million, net of transaction costs, as the net book value of the Glyko net assets was reduced to zero as of December 31, 2002. The royalties are recorded as earned.

BioMarin/Genzyme LLC Results of Operations

The discussion below gives effect to the inventory capitalization policy that we use for inventory held by the joint venture, which is different from the joint venture's inventory capitalization policy. We began capitalizing Aldurazyme inventory production costs in May 2003, after U.S. regulatory approval was obtained. The joint venture began capitalizing Aldurazyme inventory production costs in January 2002, when inventory production for commercial sale began. The difference in inventory capitalization policies results in a greater operating expense realized by us prior to regulatory approval, and lower cost of goods sold with higher gross profit realized by us as the previously expensed product is sold by the joint venture, as well as lower research and development expense when Aldurazyme is used in on-going clinical trials. These differences will be eliminated when all of the product manufactured prior to regulatory approval has been sold or has been used in clinical trials. The majority of the differences have been eliminated as of December 31, 2005. See Note 5(a) to the accompanying consolidated financial statements for further discussion of the difference in inventory cost basis between the joint venture and us.

Revenue and Gross Profit

The joint venture received marketing approval for Aldurazyme in the U.S. in April 2003 and in the E.U. in June 2003. We have subsequently received marketing approval in other countries. Aldurazyme was launched commercially in May 2003 in the U.S. and in June 2003 in the E.U. The joint venture recognized $76.4 million and $42.6 million of net revenue in 2005 and 2004, respectively. The increase in net revenue from 2004 to 2005 of $33.8 million is primarily attributable to an increase in the number of patients receiving therapy. There were approximately 370 and approximately 270 commercial patients on therapy at the end of 2005 and 2004, respectively.

Gross profit was $60.3 million and $36.8 million for 2005 and 2004, respectively, representing gross margins of approximately 79% and 86%, respectively. The decrease in gross margin during 2005 compared to 2004 is attributable to the recognition of higher cost of sales in 2005 as the joint venture sells more of the

inventory that was produced after obtaining regulatory approval, which has a higher cost basis. Excluding the effect of the difference in inventory cost basis between us and the joint venture, gross profit was $51.9 million and $27.6 million, representing gross margins of 68% and 65%, for 2005 and 2004, respectively.

Operating Expenses

Operating expenses of the joint venture include the costs associated with the development and commercial support of Aldurazyme and totaled $36.7 million for 2005 as compared to $42.9 million for 2004. Operating expenses in 2005 included $22.0 million of selling, general and administrative expenses associated with the commercial support of Aldurazyme and $14.9 million of research and development costs, primarily long-term clinical trial costs. Operating expenses in 2004 included $26.9 million of selling, general and administrative expenses associated with the commercial launch of Aldurazyme and $16.0 million of research and development expenses. Selling, general and administrative expenses decreased in 2005 due to normalization of sales and marketing efforts for the product following post-launch commercialization.

Operating expenses in 2003 totaled $87.9 million and included $17.2 million of selling, general and administrative expenses related to the commercial launch of Aldurazyme and $23.2 million of research and development expenses. Research and development decreased in 2004 compared to 2003 due to capitalization of a full year of production costs into inventory in 2004 as compared to 2003, as well as decreased clinical trial and research and development costs during 2004. Selling, general and administrative expenses increased in 2004 due to increased post launch commercialization activities.

Liquidity and Capital Resources

Cash and Cash Flow

We have financed our operations by the issuance of common stock, convertible debt, equipment and other commercial financing, collaborative agreements and the related interest income earned on cash, cash equivalents and short-term investments. During 2005, we received $56.3 million of net proceeds from a public offering of common stock and $25.0 million from Serono as consideration for execution of our Development, License and Commercialization Agreement. During 2004, we received $20.0 million of proceeds from our equipment and facility loan.

As of December 31, 2005, our combined cash, cash equivalents, short-term investments, restricted cash and cash balances related to long-term debt totaled $64.8 million, a decrease of $25.7 million from $90.4 million at December 31, 2004. Cash balances related to long-term debt represent an amount totaling $17.0 million that is a portion of the $25.0 million that we are required to keep on deposit with Comerica Bank pursuant to the terms of the equipment and facility loan that we entered into in May 2004. This amount is equal to the long-term portion of the outstanding balance under this facility. The maintenance of a deposit equal to the outstanding amount under the facility, or $10.0 million, whichever is greater, is a covenant of the facility and the failure to satisfy this covenant would constitute a breach under the facility. However, we have the ability to access this amount at our discretion and therefore it is not restricted cash.

The $25.7 million decrease in cash, cash equivalents, short-term investments, restricted cash and cash balances related to long-term debt during 2005 includes net proceeds from the public offering of common stock of $56.3 million. Excluding the offering proceeds, the decrease in cash, cash equivalents, short-term investments, restricted cash and cash balances related to long-term debt was $82.0 million, which was $33.9 million less than the net decrease in cash, cash equivalents, short-term investments and restricted cash during 2004 of $115.9 million. The primary items contributing to the decrease in net cash outflow in 2005 were as follows (in millions):

Receipt of the up-front collaboration payment from Serono	$ 25.0
Decreased capital expenditures	21.1
Increased net paydowns and decreases in accruals of accounts payable and accrued liabilities	(18.8)
Decreased investments in the joint venture	16.3
Decrease in net proceeds from equipment and facility loans	(15.9)
Decreased cash payment for the acquisition of the Ascent Pediatrics business	10.6
Increased program development, commercialization and support activities	(9.1)
Receipt of cash proceeds from the ESPP and exercise of stock options	6.9
Reimbursement from Medicis for Orapred returns	6.0
Increased investment in accounts receivable, inventory and other assets	(8.2)
Total decrease in net cash outflow	$ 33.9

The increased program development, commercialization and support activities relate to 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. Increases in net payments for working capital primarily include items such as Naglazyme and Orapred inventory and accounts receivable.

The primary uses of cash during 2004 were to finance operations, which primarily included the manufacturing and clinical trials of Naglazyme and the related supporting functions, the Ascent Pediatrics transaction and the manufacturing and clinical development of Phenoptin. Uses of cash during 2004 include payments related to the Ascent Pediatrics transaction totaling $44.8 million, an increase in capital expenditures primarily related to the development of our facilities of $18.1 million, and the lack of the $12.1 million milestone revenue received in 2003. These uses of cash were partially offset by equipment and facility loan proceeds of $20.0 million, net Orapred operating cash inflow, a decrease in the cash investment in the joint venture and other working capital changes.

Pursuant to our settlement of a dispute with Medicis in January 2005, Medicis made available to us a convertible note of up to $25.0 million beginning July 1, 2005, based on certain terms and conditions and provided that the Company does not experience a change of control. Advances under the convertible note are convertible into our common stock, at Medicis' option, according to the terms of the convertible note. Medicis may only exercise the conversion right at the maturity or earlier repayment of the loan. As of December 31, 2005, we have not made any draws on the note. We anticipate that we will only draw funds from this note to the extent necessary to fund operations or to maintain financial covenants. Medicis also agreed to pay us $6.0 million for Orapred returns, all of which was received by July 2005.

We do not expect to generate net positive cash flow from operations for the foreseeable future because we expect to continue to incur operational expenses and continue our research and development activities, including:

- preclinical studies and clinical trials;
- process development, including quality systems for product manufacture;
- regulatory processes in the U.S. and international jurisdictions;

- clinical and commercial scale manufacturing capabilities and contract manufacturing; and
- expansion of sales and marketing activities, including commercial launch activities for Naglazyme and the support of the Ascent Pediatrics business.

As a result of the Ascent Pediatrics transaction and the January 2005 amendments to the transaction agreements, we expect to pay Medicis $86.2 million in specified cash payments through 2009, of which $7.7 million is payable in 2006.

Funding Commitments

We expect to fund our operations with our cash, cash equivalents, short-term investments and currently restricted cash, supplemented by proceeds from equity or debt financings, loans or collaborative agreements with corporate partners. We expect our current cash, short-term investments, currently restricted cash and cash balances related to long-term debt and funds contractually committed to us will meet our operating and capital requirements into the first quarter of 2007.

Our investment in our product development programs has a major impact on our operating performance. Our research and development expenses for the years 2003, 2004 and 2005, and for the period since inception (March 1997) represent the following (in millions):

	2003	2004	2005	Since Program Inception
Naglazyme	$24.5	$29.8	$20.6	$ 94.5
Phenoptin	0.7	8.3	22.7	31.7
Orapred	—	1.9	3.9	5.8
Vibrilase	0.7	0.4	0.3	8.4
Not allocated to specific major projects	28.0	9.4	8.9	110.5
	$53.9	$49.8	$56.4	$250.9

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*" for a discussion of the reasons that we are unable to estimate such information, and in particular *"—If we fail to maintain regulatory approval to commercially market or 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 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 expect that the proceeds from equity or debt financing, loans or collaborative agreements will be used to fund future operating costs, capital expenditures and working capital requirements, which may include: costs associated with the commercialization of our products; additional clinical trials and the manufacturing of Aldurazyme, Naglazyme, Orapred and Phenoptin; 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 in the U.S. and E.U.;
- our joint venture partner's ability to successfully commercialize Aldurazyme;
- our ability to successfully regain market share of Orapred;
- the progress, timing, scope and results of our preclinical studies and clinical trials;
- the time and cost necessary to obtain regulatory approvals;
- 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.

Borrowings and Contractual Obligations

Our $125 million of 3.5% convertible notes will impact our liquidity due to the semi-annual cash interest payments and the scheduled repayment of the notes in 2008. Should we redeem the notes after June 2006, at our option according to the terms of the notes, we will be subject to premiums upon redemption ranging from 0.7% to 1.4%, depending on the time the notes are redeemed. We also must repay the debt if there is a qualifying change in control or termination of trading of our common stock.

We have entered into a $25.0 million credit facility with Comerica Bank executed in May 2004 to finance our equipment purchases and facility improvements. The outstanding loan balance totaled $20.9 million at December 31, 2005. The loan bears interest at LIBOR plus 1.25% (5.78% as of December 31, 2005), and is secured by liens on certain assets. Payments of principal and interest are due through maturity of the credit facility in 2011. During 2005, the agreement with Comerica Bank was amended to require that we maintain a total unrestricted cash balance of at least $25.0 million and that we maintain a deposit with Comerica Bank equal to the outstanding principal balance, or $10.0 million, whichever is greater. Our unrestricted cash, as defined in the loan agreement, totaled $64.8 million as of December 31, 2005.

As a result of the Ascent Pediatrics transaction, we expect to pay Medicis $94.8 million in specified payments through 2009, of which $7.7 million is payable in 2006. At our option, we may elect to pay Medicis $8.6 million of the amounts due in 2009 through the issuance of our common stock.

We will need to obtain additional financing to fund our future operations, including the commercialization of our drug product candidates currently under development. We cannot provide assurance that additional financing will be obtained or, if obtained, will be available on reasonable terms or in a timely manner.

We have contractual and commercial obligations under our debt, operating leases and other obligations related to research and development activities, licenses and sales royalties with annual minimums. Information about these obligations as of December 31, 2005 is presented in the table below (in thousands).

	Payments Due by Period				
	Total	2006	2007-2008	2009-2010	2011 and Thereafter
Medicis obligations	$ 94,800	$ 7,700	$ 13,500	$73,600	$ —
Convertible debt and related interest	136,023	4,375	131,648	—	—
Operating leases	25,552	3,875	7,809	7,546	6,322
Equipment and facility loans	20,909	3,860	7,720	7,720	1,609
Research and development and license commitments	5,996	5,703	293	—	—
Total	$283,280	$25,513	$160,970	$88,866	$7,931

We have also licensed technology, for which we are required to pay royalties upon future sales, subject to certain annual minimums totaling $0.5 million.

We are also subject to contingent payments totaling approximately $45.2 million upon achievement of certain regulatory and licensing milestones if they occur before certain dates in the future. Included in the total amount is $8.9 million of contingent payments related to Neutralase, for which we terminated development during 2003 and, accordingly, we do not expect they will ever be payable.

Related Party Transactions

Our Chief Medical Officer, Emil D. Kakkis, M.D., Ph.D. holds an adjunct faculty position with Harbor-UCLA Research Educational Institute (REI) for purposes of conducting research. REI licenses certain intellectual property and provides other research services to us. We are also obligated to pay REI royalties on future sales of products covered by the license agreement. Minimum annual royalties payable to REI are $25,000. We paid REI approximately $0.3 million and $0.1 million in 2004 and 2005, respectively, primarily for research and certain related license fees. Our joint venture with Genzyme is subject to a second agreement with REI that requires the joint venture to pay REI a royalty on sales of products covered by the license agreement through November 2019, of which Dr. Kakkis is entitled to certain portions, based on net sales of Aldurazyme per the terms of the agreement. The license agreement was effective before Dr. Kakkis was an officer of our company. Pursuant to these agreements, Dr. Kakkis was entitled to approximately $498,000 and $888,000 during 2004 and 2005, 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 have no investments denominated in foreign country currencies and, therefore, our investment portfolio is not subject to foreign exchange 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.

Based on our investment portfolio and interest rates at December 31, 2005, we believe that a 100 basis point increase or decrease in interest rates would result in a decrease or increase of approximately $0.5 million and

$0.8 million, respectively, in the fair value of our investment portfolio. 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.

The table below presents the carrying value of our cash and investment portfolio, which approximates fair value at December 31, 2005 (in thousands):

	Carrying Value
Cash and cash equivalents	$38,092*
Short-term investments	9,700**
Total	$47,792

* 95% of cash and cash equivalents invested in money market funds and 5% of uninvested cash.
** 100% of short-term investments invested in U.S. agency securities.

Our debt obligations consist of our convertible debt and our equipment and facility loans. Our convertible debt carries a fixed interest rate and, as a result, we are not exposed to interest rate market risk on our convertible debt. The interest rates for certain of our equipment and facility loans are based on the London Inter-Bank Offer Rate (LIBOR) and we are therefore exposed to fluctuations in the LIBOR market. The outstanding principal balance on our equipment and facility loans that carry LIBOR-based rates was $20.9 million as of December 31, 2005. The carrying value of our convertible debt and equipment loans approximates their fair value at December 31, 2005.

Foreign currency exchange rate market risk

A significant portion of Aldurazyme sales by BioMarin/Genzyme LLC are earned outside of the U.S. and, therefore, our Equity in the (Loss)/Income of BioMarin/Genzyme LLC is subject to risk of foreign currency rate fluctuations. The policies and procedures related to the management of foreign currency risk of Aldurazyme sales are maintained and performed by our joint venture partner, Genzyme, which may include foreign currency forward contracts.

Based on our overall currency rate exposures at December 31, 2005, we do not expect that a near-term 10% appreciation or depreciation of the U.S. dollar would have a material effect on our financial position, results of operations and cash flows over the next fiscal year.

A significant portion of Naglazyme sales are earned outside of the U.S. and our related revenues and account receivables are subject to risk of foreign currency rate fluctuations. These risks may be managed with selective use of derivatives. We may use derivatives to mitigate or eliminate certain financial and market risks because we conduct business in diverse markets around the world and local funding is not always efficient.

We periodically enter into foreign currency forward contracts, which have a maturity of less than one year. These contracts have not been designated as hedges and, accordingly, unrealized gains or losses on these contracts are reported in current earnings. The notional settlement value of foreign currency forward contracts outstanding at December 31, 2005 is $0.3 million. At December 31, 2005, these contracts had a fair value of $33,000, representing an unrealized loss. The amount has been recorded in our consolidated statement of operations for the year ended December 31, 2005 and in accrued expenses in our consolidated balance sheet as of December 31, 2005.

Item 8. Financial Statements and Supplementary Data

The information required to be filed in this item appears on pages F-1 to F-35 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) 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 sufficiently effective to ensure that the information required to be disclosed by us in this Form 10-K 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, 2005. 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, 2005 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 management's assessment of our internal control over financial reporting as well as on the effectiveness of our internal control over financial reporting. The attestation reports of KPMG on management's assessment of internal control over financial reporting and on the audit of the financial statements are 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 period covered by this Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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 the 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.

Part III

Item 10. Directors and Executive Officers of the Registrant

We incorporate information regarding our directors and executive officers into this section by reference from sections captioned "Election of Directors" and "Executive Officers" in the proxy statement for our 2006 annual meeting of stockholders.

Item 11. Executive Compensation

We incorporate information regarding our directors and executive officers into this section by reference from the section captioned "Executive Compensation" in the proxy statement for our 2006 annual meeting of stockholders.

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

We incorporate information regarding our directors and executive officers into this section by reference from the section captioned "Security Ownership of Certain Beneficial Owners" in the proxy statement for our 2006 annual meeting of stockholders.

Item 13. Certain Relationships and Related Transactions

We incorporate information regarding our directors and executive officers into this section by reference from the section captioned "Interest of Insiders in Material Transactions" in the proxy statement for our 2006 annual meeting of stockholders.

Item 14. Principal Accountant 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 2006 annual meeting of stockholders.

Part IV

Item 15. Exhibits and Financial Statement Schedules

Financial Statements

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 Bylaws of BioMarin Pharmaceutical Inc., previously filed with the Commission on April 4, 2005 as Exhibit 3.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.
4.1	Rights Agreement, dated as of September 11, 2002, between BioMarin Pharmaceutical Inc. and Mellon Investor Services LLC, as Rights Agent, previously filed with the Commission on September 13, 2002 as Exhibit 4.1 to the Company's Form 8-A, which is incorporated herein by reference.
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	3.50% Convertible Subordinated Note due 2003, in the principal amount of $125,000,000, dated June 23, 2003, previously filed with the Commission on August 12, 2003 as Exhibit 4.2 to the Company's Quarterly report on Form 10-Q, which is incorporated herein by reference.

4.4	Registration Rights Agreement dated June 23, 2003 by and among, UBS Securities LLC and CIBC World Markets Corp., as Initial Purchasers, and BioMarin Pharmaceutical Inc., previously filed with the Commission on August 12, 2003 as Exhibit 4.3 to the Company's Quarterly report on Form 10-Q, 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 27,2 004 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	1997 Stock Plan, as amended on December 22, 1998, and forms of agreements, previously filed with the Commission on May 4, 1999 as Exhibit 10.2 to the Company's Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.
10.4	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.
10.5	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.
10.6	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 amended, 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	1998 Employee Stock Purchase Plan and forms of agreements thereunder, previously filed with the Commission on May 4, 1999 as Exhibit 10.4 to the Company's Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.
10.11	BioMarin Pharmaceutical Inc. Nonqualified Deferred Compensation Plan, as adopted December 1, 2005, previously filed with the Commission on December 2, 2005 as Exhibit 10.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.
10.12	Separation Agreement and Release of All Claims, dated August 12, 2004, by and between the BioMarin Pharmaceutical Inc. and Fredric D. Price, previously filed with the Commission on November 9, 2004 as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.13	Employment Agreement with Stuart J. Swiedler, M.D., Ph.D., dated May 29, 1998, as amended, previously filed with the Commission on May 4, 1999 as Exhibit 10.12 to the Company's Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.

10.14 Employment Agreement with Emil Kakkis, M.D., Ph.D., dated June 30, 1998, as amended, previously filed with the Commission on May 4, 1999 as Exhibit 10.13 to the Company's Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.

10.15 Employment Agreement with Robert Baffi dated April 20, 2000, previously filed with the Commission on March 20, 2001 as Exhibit 10.29 to the Company's Annual Report on Form 10-K, which is incorporated herein by reference.

10.16 Employment Agreement with Jean-Jacques Bienaimé, dated May 11, 2005, previously filed with the Commission on May 12, 2005, as Exhibit 10.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.

10.17 Amendment No. 1 to Employment Agreement dated December 15, 2005 by and among BioMarin Pharmaceutical Inc. and Jean-Jacques Bienaimé, previously filed with the Commission on December 13, 2005 as Exhibit 10.2 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.

10.18 Severance Agreement and Release of All Claims dated January 4, 2005 between BioMarin Pharmaceutical Inc. and Jeffrey I. Landau, previously filed with the Commission on March 16, 2005 as Exhibit 10.18 to the Company's Annual Report on Form 10-K, which is incorporated herein by reference.

10.19 Severance Agreement and Release of All Claims dated August 23, 2005 by and between BioMarin Pharmaceutical Inc. and Louis Drapeau, previously filed with the Commission on August 23, 2005 as Exhibit 10.1 to the Company's Current Report on Form 8-K, 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 between BioMarin Pharmaceutical Inc., and Children's Hospital, Adelaide, Australia dated August 14, 1998, previously filed with the Commission July 21, 1999 as Exhibit 10.18 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.

10.22 Development and Initial Supply Agreement dated November 19, 2003, between BioMarin Pharmaceutical Inc. and Merck Eprova AG, previously filed with the Commission on February 27, 2004 as Exhibit 10.20 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.

10.23 License Agreement dated October 15, 2004, between BioMarin Pharmaceutical Inc. and Merck Eprova AG, as amended by Amendment No. 1 to License Agreement dated January 25, 2005, previously filed with the Commission on March 16, 2005 as Exhibit 10.24 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.

10.24 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.

10.26 Supply Agreement dated July 30, 2004, among BioMarin Pharmaceutical Inc., Daiichi Suntory Pharma Co., Ltd. and Shiratori Pharmaceutical Co., Ltd., previously filed with the Commission on March 16, 2005 as Exhibit 10.26 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.

10.27 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.

10.28 Standard Industrial Commercial Single-Tenant Lease dated May 29, 1998 for 95 Digital Drive (formerly referred to as 110 Digital Drive), as amended, previously filed with the Commission on May 4, 1999 as Exhibit 10.21 to the Company's Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.

10.29 Third Amendment to Lease for 95 Digital Drive dated May 27, 2004, by and among Digital Drive, LLC, Eastman Family LLC, Basalacchi Family LLC, Atkinson Family LLC and BioMarin Pharmaceutical Inc., previously filed with the Commission on August 9, 2004 as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q, which is incorporated herein by reference.

10.30 Agreement of Sublease dated July 27, 2001 for 79 Digital Drive, previously filed with the Commission on April 1, 2002 as Exhibit 10.22 to the Company's Annual Report on Form 10-K, which is incorporated herein by reference.

10.31 Bayview Business Park Standard Lease for 90 and 105 Digital Drive, dated June 16, 2003 by and between BioMarin Pharmaceutical Inc. and Bayview Ignacio, LLC, previously filed with the Commission on August 12, 2003 as Exhibit 10.2 to the Company's Quarterly report on Form 10-Q, which is incorporated herein by reference.

10.32 Collaboration Agreement with Genzyme Corporation dated September 4, 1998, previously filed with the Commission on July 21, 1999 as Exhibit 10.24 to the Company's Amendment No. 3 to Registration Statement on Form S-1 (Registration No. 333-77701), which is incorporated herein by reference.

10.33 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.

10.34 Note Purchase Agreement dated June 18, 2003 by and among UBS Securities LLC and CIBC World Markets Corp., as Initial Purchasers, and BioMarin Pharmaceutical Inc., previously filed with the Commission on August 12, 2003 as Exhibit 10.3 to the Company's Quarterly report on Form 10-Q, which is incorporated herein by reference.

10.35 Purchase Agreement dated July 14, 2005, by and between BioMarin Pharmaceutical Inc. and Merrill Lynch & Co., Merrill Lynch, Pierce, Fenner & Smith Incorporated, previously file with the Commission on July 14, 2005 as Exhibit 1.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.

10.36 Fourth Amendment to Loan and Security Agreement dated June 29, 2005, between BioMarin Pharmaceutical Inc. and Comerica Bank, previously filed with the Commission on July 5, 2005 as Exhibit 10.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.

10.37 Fifth Amendment to Loan and Security Agreement dated October 31, 2005, between BioMarin Pharmaceutical Inc. and Comerica Bank, previously filed with the Commission on December 13, 2005 as Exhibit 10.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.

10.38	Loan and Security Agreement dated May 14, 2004, by and between Comerica Bank and BioMarin Pharmaceutical Inc., previously filed with the Commission on August 9, 2004 as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.39	First Amendment to Loan and Security Agreement dated November 3, 2004, by and between BioMarin Pharmaceutical Inc. and Comerica Bank, previously filed with the Commission on November 9, 2004 as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, which is incorporated herein by reference.
10.40	Second Amendment To Loan And Security Agreement dated February 15, 2005, by and between BioMarin Pharmaceutical Inc. and Comerica Bank, previously filed with the Commission on March 16, 2005 as Exhibit 10.37 to the Company's Annual Report on Form 10-K, which is incorporated herein by reference.
10.41	Agreement dated May 27, 2005, between BioMarin Pharmaceutical Inc. and the Caduceus Group, previously filed with the Commission on May 27, 2005 as Exhibit 10.1 to the Company's Current Report on Form 8-K, which is incorporated herein by reference.
10.42	Convertible Promissory Note dated January 12, 2005, executed by BioMarin Pharmaceutical Inc. in favor of Medicis Pharmaceutical Corporation as Holder, previously filed with the Commission on March 16, 2005 as Exhibit 10.38 to the Company's Annual Report on Form 10-K, which is incorporated herein by reference.
10.43	CRO Services Agreement dated September 15, 2004 by and between BioMarin Pharmaceutical Inc. and Kendle International Inc. as amended by the First Amendment to the CRO Services Agreement dated February 10, 2005, previously file with the Commission on March 16, 2005 as Exhibit 10.39 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.
10.44*	Services Agreement dated December 15, 2005 by and between BioMarin Pharmaceutical Inc. and Groupe Novasep SAS. Portions of this document have been redacted pursuant to a Request for Confidential Treatment filed pursuant to the Freedom of Information Act.
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 Auditors for BioMarin/Genzyme LLC.
24.1*	Power of Attorney (Included in Signature Page)
31.1*	Certification of CEO pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of CFO pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of CEO and CFO 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, 2005 and 2004, and for the years ended December 31, 2005, 2004 and 2003.

* Filed herewith.

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: March 7, 2006

By: /s/ JEFFREY H. COOPER
Jeffrey H. Cooper
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)	March 7, 2006
/s/ JEFFREY H. COOPER **Jeffrey H. Cooper**	Vice President, Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 7, 2006
/s/ PIERRE LAPALME **Pierre Lapalme**	Chairman and Director	March 7, 2006
/s/ FRANZ L. CRISTIANI **Franz L. Cristiani**	Director	March 7, 2006
/s/ ELAINE HERON **Elaine Heron**	Director	March 7, 2006
/s/ JOSEPH KLEIN, III **Joseph Klein, III**	Director	March 7, 2006
/s/ ALAN J. LEWIS **Alan J. Lewis**	Director	March 7, 2006
/s/ MICHAEL G. GREY **Michael G. Grey**	Director	March 7, 2006

INDEX TO BIOMARIN PHARMACEUTICAL INC.

CONSOLIDATED FINANCIAL STATEMENTS

REPORTS OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
BioMarin Pharmaceutical Inc.:

We have audited the accompanying consolidated balance sheets of BioMarin Pharmaceutical Inc. and subsidiaries (the Company) as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for the each of the years in the three-year period ended December 31, 2005. In connection with our audits of the consolidated financial statements, we also have audited financial statement schedule II. These consolidated financial statements and financial statement schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements and financial statement schedule based on our audits. We did not audit the financial statements of BioMarin/Genzyme LLC (a 50 percent owned joint venture) for the years 2005 and 2003. The Company's investment in BioMarin/Genzyme LLC (in thousands) at December 31, 2005 and 2003, was $31,983 and $12,007, respectively, and its equity in income (loss) of BioMarin/Genzyme (in thousands) was $11,838 and ($18,693) for the years ended December 31, 2005 and 2003, respectively. The financial statements of BioMarin/Genzyme LLC for the years 2005 and 2003 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 the years 2005 and 2003, 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 audits 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, and evaluating the overall financial statement presentation. We believe that our audits and the report of the other auditors provide a reasonable basis for our opinion.

In our opinion, based on our audits and the report of the other auditors, 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, 2005 and 2004, and the results of their operations and their cash flows for each of the years in the three-year period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the related financial statement schedule, when considered in relation to the basic consolidated financial statements taken as a whole, present fairly, in all material respects, the information set forth therein.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of BioMarin Pharmaceutical Inc.'s internal control over financial reporting as of December 31, 2005, 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 March 7, 2006 expressed an unqualified opinion on management's unqualified opinion on management's assessment of, and the effective operation of, internal control over financial reporting.

/s/ KPMG LLP

San Francisco, California
March 7, 2006

The Board of Directors and Stockholders of
BioMarin Pharmaceutical Inc.:

We have audited management's assessment, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting, that BioMarin Pharmaceutical Inc. maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). BioMarin Pharmaceutical Inc.'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. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of 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, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and 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, management's assessment that BioMarin Pharmaceutical Inc. maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Also, in our opinion, BioMarin Pharmaceutical Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

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, 2005 and 2004, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for the each of the years in the three-year period ended December 31, 2005. In connection with our audits of the consolidated financial statements, we also have audited financial statement schedule II. Our report dated March 7, 2006 expressed an unqualified opinion on those consolidated financial statements and related financial statement schedule. Our report was based on our audits and the report of other auditors.

/s/ KPMG LLP

San Francisco, California
March 7, 2006

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED BALANCE SHEETS
December 31, 2004 and 2005
(In thousands, except for share and per share data)

	2004	2005
ASSETS		
Current assets:		
Cash and cash equivalents	$ 13,081	$ 38,092
Short-term investments	35,734	9,700
Restricted cash	25,180	—
Accounts receivable, net	4,047	5,860
Advances to BioMarin/Genzyme LLC	2,160	1,071
Inventory	2,316	10,898
Other current assets	2,641	3,320
Total current assets	85,159	68,941
Cash balances related to long-term debt	16,406	17,049
Investment in BioMarin/Genzyme LLC	23,129	31,983
Property and equipment, net	42,501	37,321
Acquired intangible assets, net	16,451	15,306
Goodwill	45,053	21,262
Other assets	4,267	3,441
Total assets	$ 232,966	$ 195,303
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable and accrued liabilities	$ 27,249	$ 20,934
Current portion of acquisition obligation, net of discount	39,122	7,477
Current portion of deferred revenue	—	8,096
Current portion of equipment and facility loans	3,683	3,860
Total current liabilities	70,054	40,367
Convertible debt	125,000	125,000
Long-term portion of acquisition obligation, net of discount	86,632	70,873
Deferred revenue, net of current portion	—	11,825
Equipment and facility loan, net of current portion	16,406	17,049
Other long-term liabilities	2,852	7,651
Total liabilities	300,944	272,765
Stockholders' equity (deficit):		
Common stock, $0.001 par value: 150,000,000 shares authorized; 64,501,159 and 74,301,610 shares issued and outstanding at December 31, 2004 and 2005, respectively	65	75
Additional paid-in capital	421,141	485,570
Accumulated other comprehensive loss	(363)	(16)
Accumulated deficit	(488,821)	(563,091)
Total stockholders' equity (deficit)	(67,978)	(77,462)
Total liabilities and stockholders' equity (deficit)	$ 232,966	$ 195,303

See accompanying notes to consolidated financial statements.

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF OPERATIONS
Years ended December 31, 2003, 2004 and 2005
(In thousands, except for per share data)

	December 31,		
	2003	2004	2005
Net product sales	$ —	$ 18,641	$ 13,039
Collaborative agreement revenue	12,100	—	12,630
Total revenues	12,100	18,641	25,669
Operating expenses:			
Cost of sales (excludes amortization of developed product technology)	—	3,953	2,629
Research and development	53,932	49,784	56,391
Selling, general and administrative	15,278	37,606	41,556
Amortization of acquired intangible assets	—	3,987	1,144
Acquired in-process research and development	—	31,453	—
Impairment of acquired intangible assets	—	68,251	—
Total operating expenses	69,210	195,034	101,720
Equity in the (loss)/income of BioMarin/Genzyme LLC	(18,693)	(2,972)	11,838
Loss from operations	(75,803)	(179,365)	(64,213)
Interest income	2,559	2,466	1,861
Interest expense	(3,131)	(10,544)	(11,918)
Net loss from continuing operations	(76,375)	(187,443)	(74,270)
Gain on disposal of discontinued operations	577	—	—
Net loss	$(75,798)	$(187,443)	$ (74,270)
Net loss per share, basic and diluted:			
Net loss from continuing operations	$ (1.23)	$ (2.91)	$ (1.08)
Gain on disposal of discontinued operations	0.01	—	—
Net loss per share, basic and diluted	$ (1.22)	$ (2.91)	$ (1.08)
Weighted average common shares outstanding, basic and diluted	62,125	64,354	68,830

See accompanying notes to consolidated financial statements.

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
For the Years ended December 31, 2003, 2004 and 2005 (in thousands)

	Common stock		Additional paid-in capital	Warrants		Deferred compensation	Notes receivable from stockholder	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount		Shares	Amount					
Balance at January 1, 2003	53,782	$ 54	$319,038	780	$5,219	$ (47)	$(468)	$ 327	$(225,580)	$ 98,543
Issuance of common stock under ESPP	135	—	712	—	—	—	—	—	—	712
Issuance of common stock to Acqua Wellington, net of issuance costs	766	1	7,949	—	—	—	—	—	—	7,950
Issuance of common stock in a public offering, net of issuance costs	8,625	8	80,522	—	—	—	—	—	—	80,530
Deferred compensation related to restricted common stock issuance	39	—	275	—	—	(145)	—	—	—	130
Exercise of common stock options	800	1	5,368	—	—	—	—	—	—	5,369
Interest accrued on notes receivable from stockholders	—	—	17	—	—	—	(17)	—	—	—
Repayment of notes receivable from stockholders	—	—	—	—	—	—	485	—	—	485
Foreign currency translation	—	—	—	—	—	—	—	49	—	49
Fair market value adjustments of available-for-sale investments	—	—	—	—	—	—	—	(393)	—	(393)
Amortization of deferred compensation	—	—	—	—	—	47	—	—	—	47
Issuance of restricted stock to non-employees	9	—	98	—	—	—	—	—	—	98
Other	—	—	131	—	—	—	—	—	—	131
Net loss	—	—	—	—	—	—	—	—	(75,798)	(75,798)
Balance at December 31, 2003	64,156	$ 64	$414,110	780	$5,219	$(145)	$ —	$ (17)	$(301,378)	$117,853

See accompanying notes to consolidated financial statements.

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)—(Continued)
For the Years ended December 31, 2003, 2004 and 2005 (in thousands)

	Common stock		Additional paid-in capital	Warrants		Deferred compensation	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount		Shares	Amount				
Balance at January 1, 2004	64,156	$ 64	$414,110	780	$ 5,219	$(145)	$ (17)	$(301,378)	$ 117,853
Amortization of deferred compensation	—	—	—	—	—	145	—	—	145
Issuance of common stock under ESPP	187	—	785	—	—	—	—	—	785
Exercise of common stock options	158	1	1,016	—	—	—	—	—	1,017
Fair market value adjustments of available-for-sale investments	—	—	—	—	—	—	(346)	—	(346)
Expiration of warrants	—	—	5,219	(780)	(5,219)	—	—	—	—
Other	—	—	11	—	—	—	—	—	11
Net loss	—	—	—	—	—	—	—	(187,443)	(187,443)
Balance at December 31, 2004	64,501	$ 65	$421,141	—	$ —	$ —	$(363)	$(488,821)	$ (67,978)

See accompanying notes to consolidated financial statements.

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)—(Continued)
For the Years ended December 31, 2003, 2004 and 2005 (in thousands)

	Common stock		Additional paid-in capital	Warrants		Deferred compensation	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount		Shares	Amount				
Balance at January 1, 2005	64,501	$ 65	$421,141	—	$—	$—	$(363)	$(488,821)	$(67,978)
Issuance of common stock in a public offering, net of issuance costs	8,500	8	56,320	—	—	—	—	—	56,328
Issuance of common stock under ESPP	251	—	889	—	—	—	—	—	889
Exercise of common stock options	1,050	2	6,893	—	—	—	—	—	6,895
Fair market value adjustments of available-for-sale investments	—	—	—	—	—	—	346	—	346
Stock compensation expense related to modification of awards	—	—	327	—	—	—	—	—	327
Foreign currency translation adjustment	—	—	—	—	—	—	1	—	1
Net loss	—	—	—	—	—	—	—	(74,270)	(74,270)
Balance at December 31, 2005	74,302	$ 75	$485,570	—	$—	$—	$ (16)	$(563,091)	$(77,462)

See accompanying notes to consolidated financial statements.

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES

CONSOLIDATED STATEMENTS OF CASH FLOWS
Years ended December 31, 2003, 2004 and 2005
(In thousands)

	December 31,		
	2003	2004	2005
Cash flows from operating activities			
Net loss from continuing operations	$ (76,375)	$(187,443)	$(74,270)
Adjustments to reconcile net loss from continuing operations to net cash used in operating activities:			
Depreciation and amortization	9,747	13,279	10,075
Acquired in-process research and development	—	31,453	—
Impairment of acquired intangible assets	—	68,251	—
Imputed interest on acquisition obligation	—	5,160	5,444
Lease liability reversal	(2,002)	—	—
Gain on disposals and impairments of property and equipment	—	(104)	404
Equity in the loss/(income) of BioMarin/Genzyme LLC	18,693	2,972	(11,838)
Changes in operating assets and liabilities:			
Accounts receivable	—	(4,047)	(1,813)
Advances to BioMarin/Genzyme LLC	(1,914)	1,891	1,089
Inventory	—	—	(8,582)
Other current assets	(575)	197	(679)
Notes receivable from officer	—	1,040	—
Other assets	(410)	(101)	(59)
Accounts payable and accrued liabilities	6,168	14,907	(7,173)
Other liabilities	(248)	1,497	4,799
Deferred revenue	—	—	19,921
Net cash used in operating activities	(43,088)	(51,048)	(62,680)
Cash flows from investing activities			
Purchase of property and equipment	(5,975)	(24,075)	(2,957)
Proceeds from sale of equipment	28	—	—
Acquisition of Ascent Pediatrics	—	(14,788)	—
(Increase) Decrease in restricted cash	—	(25,298)	25,180
Sale of short-term investments	80,072	86,306	26,380
Purchase of short-term investments	(125,076)	(37,435)	—
Investment in BioMarin/Genzyme LLC	(31,710)	(14,093)	—
Distributions from BioMarin/Genzyme LLC	—	—	3,000
Settlement of dispute with Medicis	—	—	6,000
Net cash provided by (used in) investing activities	(82,661)	(29,383)	57,603
Cash flows from financing activities			
Proceeds from equipment and facility loans	—	19,957	17,543
Proceeds from exercise of stock options	5,369	1,017	6,893
Increase in cash balances related to long-term debt	—	(16,406)	(643)
Repayment of equipment and facility loans	(2,504)	(3,258)	(16,723)
Repayment of acquisition obligation	—	(30,000)	(34,200)
Proceeds from public offering of common stock, net	80,530	—	56,328
Proceeds from sale of common stock to Acqua Wellington, net	7,950	—	—
Proceeds from convertible debt offering, net	120,900	—	—
Receipts from notes receivable from stockholders	485	—	—
Issuance of common stock for ESPP, and other	738	796	889
Net cash provided by (used in) financing activities	213,468	(27,894)	30,087
Effect of foreign currency translation on cash	49	—	1
Net increase (decrease) in cash	87,768	(108,325)	25,011
Cash and cash equivalents:			
Beginning of year	33,638	121,406	13,081
End of year	$ 121,406	$ 13,081	$ 38,092

See accompanying notes to consolidated financial statements.

(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. The Company and its joint venture partner, Genzyme Corporation (Genzyme), received marketing approval for Aldurazyme® (laronidase) in the United States (U.S.) in April 2003 and in the European Union (E.U.) in June 2003. BioMarin received marketing approval for Naglazyme™ (galsulfase) in the U.S. in May 2005, and in the E.U. in January 2006. In May 2004, BioMarin completed the transaction to acquire the Ascent Pediatrics business. The transaction included: the exclusive marketing and development rights to Orapred® (prednisolone sodium phosphate oral solution), a drug primarily used to treat asthma exacerbations in children; two additional proprietary formulations of Orapred in development; and a U.S.-based sales force. See Note 3 for further discussion of the transaction. The Company is incorporated in the state of Delaware.

Through December 31, 2005, the Company had accumulated losses of approximately $563.1 million. Management expects to incur further losses for the foreseeable future. Management believes that the Company's cash, cash equivalents, short-term investments, currently restricted cash and cash balances related to long-term debt at December 31, 2005, plus funds contractually committed to the Company, will be sufficient to meet the Company's obligations into the first quarter of 2007. Until the Company can generate sufficient levels of cash from its operations, the Company expects to continue to finance future cash needs primarily through proceeds from equity or debt financings, loans and collaborative agreements with corporate partners.

The Company is subject to a number of risks, including: the need for additional financings; the financial performance of Orapred, Naglazyme and the Aldurazyme joint venture; significant competition from larger organizations and generic competition with respect to Orapred; 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; 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.

In 2001, the Company decided to close the business of Glyko, Inc. (Glyko), a wholly owned subsidiary. Glyko's operations ceased on July 31, 2002. In January 2003, the Company sold certain assets of Glyko to a third-party for total consideration of up to $1.5 million (Note 19).

(2) SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Basis of Presentation

These consolidated financial statements have been prepared in accordance with generally accepted accounting principles (GAAP) in the United States 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 United States 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.

(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) Short-Term Investments

The Company records its investments 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). Short-term investments are comprised mainly of corporate bonds, federal agency investments and taxable municipal debt securities. As of December 31, 2005, the Company had no available-for-sale investments. See Note 17 for further information.

(e) Inventory

The Company values inventories at the lower of cost or fair market 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 in excess of expected requirements. Expired inventory is disposed of and the related costs are written off. During 2005, increased generic competition to Orapred has resulted in continued decreases in end-user demand. As a result, the Company revised its estimates of expected inventory requirements and recognized Orapred inventory write-offs of $1.5 million during 2005. The inventory write-off included $1.1 million of commercial inventory, which increased cost of goods sold, and $0.4 million of sample inventory, which increased sales and marketing expense. See Note 9 for details of the Company's inventory balances as of December 31, 2004 and 2005.

Regulatory approval for Naglazyme was not received until May 2005, and costs related to the manufacturing of Naglazyme 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 related manufacturing costs for Naglazyme were not capitalized as inventory. When regulatory approval was obtained in May 2005, the Company began capitalizing inventory at the lower of cost or fair value. Naglazyme inventory as of December 31, 2005 includes a portion of the zero cost basis quantities. Until the Company begins to sell the inventory produced after regulatory approval was obtained, the cost of goods sold or used in clinical trials for the previously expensed inventory will be insignificant or zero. The Company expects that the majority of the previously expensed inventory will be sold or used in clinical trials by the first quarter of 2007.

(f) Cash Balances Related to Long-term Debt

Cash balances related to long-term debt represent an amount that the Company is required to keep on deposit with Comerica Bank pursuant to the terms of the equipment and facility loan that the Company executed in May 2004.

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

Under the Aldurazyme joint venture agreement with Genzyme, the Company and Genzyme each provide 50% of the funding for the joint venture. All manufacturing, research and development, sales and marketing, and

other services performed by Genzyme and the Company on behalf of the joint venture are billed to the joint venture at cost. Any profits or losses of the joint venture are shared equally by the two parties.

The Company accounts for its 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. Equity in the (Loss)/Income 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 during the most recent month, and the investment in BioMarin/Genzyme LLC includes the Company's share of the net equity of the joint venture.

(h) Goodwill, Acquired 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. Currently, the Company has identified the Orapred business as a separate reporting unit, which includes all of the Company's intangible assets and goodwill, and is a component of the Company's single operating segment. 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 units using a combination of discounted cash flow models, quoted market prices when available and independent appraisals. See Note 4 for further discussion of the Company's goodwill impairment analysis.

The recoverability of the carrying value of leasehold improvements for the Company's administrative 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.

(i) Property and Equipment

Property 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 research and development projects with no alternative uses are expensed as incurred.

(j) Revenue Recognition

The Company recognizes revenue in accordance with the provisions of SEC Staff Accounting Bulletin No. 104, *Revenue Recognition*, and Emerging Issues Task Force Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*.

The Company's revenues consist of Naglazyme and Orapred product sales and revenues from its collaborative agreements with Serono and Genzyme (see Note 7). All Aldurazyme sales are reported by BioMarin/Genzyme LLC and are included in the results of the joint venture (see Note 5).

Naglazyme product sales—The Company recognizes revenue from Naglazyme 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. Naglazyme product sales transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents.

Naglazyme is generally sold to specialty pharmacies or end-users, such as hospitals, which act as retailers. Because of the pricing of Naglazyme, the limited number of patients and the customers' limited return rights, the specialty pharmacies generally carry a very limited inventory. Accordingly, the Company expects that sales related to Naglazyme in the U.S. 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 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 of Naglazyme is required, including its patient population, the customers' limited return rights and the Company's joint venture's experience of returns for Aldurazyme, which is a similar 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 Naglazyme customers to make required payments. The Company first recorded sales of Naglazyme during the second quarter of 2005 and as of December 31, 2005, the Company had experienced no bad debts and had no allowance for doubtful accounts.

Orapred product sales—The Company recognizes revenue from Orapred product sales when persuasive evidence of an arrangement exists, the product has been shipped, 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. Orapred product sales transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents.

The timing of customer purchases and the resulting product shipments have a significant impact on the amount of revenue from Orapred product sales that the Company recognizes in a particular period. Also, 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 Company's principal customers for Orapred, and inventory held by retailers. The Company's revenue from Orapred sales in a particular period is impacted by increases or decreases in wholesaler inventory levels. If wholesaler inventories continue to substantially exceed the retail demand, the Company could experience reduced revenue from sales in subsequent periods, or product returns from the distribution channel due to overstocking, low end-user demand or product expiration.

The Company establishes and maintains rebate reserves for amounts payable to managed care organizations and state Medicaid programs for the reimbursement of a portion of the retail price of prescriptions filled that are covered by the respective plans. The amounts estimated to be paid relating to products sold are recognized as revenue reductions and as additions to accrued expenses at the time of the original sale. The rebate reserves are based on the Company's best estimate of the expected prescription fill rate to these managed care organizations and state Medicaid patients. The estimates are developed using the product's rebate history adjusted to reflect known and forecasted changes in the factors that impact such reserves. During 2005, the Company reduced its Orapred rebate reserves by $2.8 million, which increased net revenues by $2.1 million for rebates related to product sold by the Company and decreased operating expenses by $0.7 million for rebates related to product sold by the previous seller. The reduction was due to a lower-than-expected number of rebate contracts executed by the Company.

Provisions for sales discounts and estimates for chargebacks and product returns are established as a reduction of product sales at the time such revenues are recognized. These revenue reductions are established by the Company's management as its best estimate at the time of the original sale based on the product's historical experience adjusted to reflect known and forecasted changes in the factors that impact such reserves. These revenue reductions are generally reflected either as a direct reduction to gross sales and accounts receivable through an allowance or as an addition to accrued expenses. The Company generally permits product returns only if the product is damaged or if it is returned near or after expiration. During 2005, the Company increased its reserves for Orapred product returns by $4.9 million, which decreased net revenues by $2.0 million for returns related to product sold by the Company and increased operating expenses by $2.9 million for returns related to product sold by the previous seller. The reduction was due to increased generic competition in conjunction with high levels of wholesaler inventories of Orapred.

A reconciliation of the Company's gross and net product sales for the years ended December 31, 2004 and 2005 is as follows (in thousands):

	2004		2005	
	Dollars	Percentage	Dollars	Percentage
Gross product sales	$22,341	100%	$15,776	100%
(Allowances) Reversals for:				
Returns	(790)	(4)%	(2,565)	(16)%
Rebates	(2,240)	(10)%	900	6%
Discounts	(670)	(3)%	(1,072)	(7)%
Total allowances	(3,700)	(17)%	(2,737)	(17)%
Net product sales	$18,641	83%	$13,039	83%

The Company maintains allowances for doubtful accounts for estimated losses resulting from the inability of its customers to make required payments. As of December 31, 2005, the Company's allowance for doubtful accounts was insignificant.

Collaborative agreement revenues—Collaborative agreement revenues from 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 license revenue over the estimated period for which the Company continues to have a performance obligation. 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 Serono's share of Phenoptin™ (sapropterin dihydrochloride) development costs under the agreement. Collaborative agreement revenues include $5.5 million of the up-front license fee received from Serono recognized as revenue during 2005, and $7.1 million of reimbursable Phenoptin development costs incurred during 2005. The up-front license fee received from Serono is being amortized as revenue on a straight-line basis over approximately 3.25 years, which represents the best estimate of the time from inception of the agreement until European regulatory approval of Phenoptin for the treatment of phenylketonuria (PKU), at which point the Company's performance obligations for developing Phenoptin for the treatment of PKU will end. The estimate was revised during 2005, from 2.75 years to 3.25 years, based on updated information regarding the estimated timing of European regulatory approval. The change in estimate did not have a significant impact on revenues during 2005, but is expected to have a material impact in future periods.

Collaborative agreement revenue from Genzyme includes $12.1 million received in 2003, related to the FDA marketing approval for Aldurazyme. 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.

(k) 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. The Company believes that regulatory approval of our 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, at which time inventory is capitalized at the lower of cost or fair value.

(l) Net 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 income per share is calculated by dividing net income by the weighted 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 options, warrants and contingent issuances of common stock related to our convertible debt and acquisition payable. For all periods presented, 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 include (in thousands):

	December 31,		
	2003	2004	2005
Options to purchase common stock	9,682	10,008	6,969
Common stock issuable under convertible debt	8,920	8,920	8,920
Portion of acquisition payable in common stock	—	3,130	798
Warrants to purchase common stock	780	—	—
Total	19,382	22,058	16,687

(m) Stock Option Plans

The Company has three stock-based compensation plans. The Company accounts for those plans under APB Opinion No. 25, *Accounting for Stock Issued to Employees,* whereby generally no stock-based compensation cost is reflected in net loss for options issued to employees and directors with exercise prices at or above the market price on the date of issuance. The following table (in thousands, except per share data) illustrates the effect on net loss and net loss per share as if the Company had applied the fair value recognition provisions of SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123), as amended by SFAS No. 148, *Accounting for Stock Based Compensation—Transition and Disclosure,* to stock-based compensation recognized on a straight-line basis.

	Years ended December 31,		
	2003	2004	2005
Net loss as reported	$(75,798)	$(187,443)	$(74,270)
Add: Total stock based compensation expense determined under intrinsic value based method recognized in net loss as reported	—	—	327
Deduct: Total stock-based compensation expense determined under fair value based method for all awards	(15,615)	(14,382)	(10,184)
Pro forma net loss	$(91,413)	$(201,825)	$(84,127)
Net loss per common share as reported, basic and diluted	$ (1.22)	$ (2.91)	$ (1.08)
Pro forma net loss per common share, basic and diluted	(1.47)	(3.14)	(1.22)

The Company recognizes as an expense the fair value of options granted to persons who are neither employees nor directors.

The following summarizes the weighted average assumptions used to determine the fair value of each option using the Black-Scholes option-pricing model:

Dates of grant	Interest rate	Expected dividend yield	Expected life	Expected volatility
January 1, 2003 to December 31, 2003	4.1%	0.00%	6 years	79%
January 1, 2004 to December 31, 2004	4.1%	0.00%	6 years	56%
January 1, 2005 to December 31, 2005	4.4%	0.00%	6 years	54%

(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 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 $261.2 million at December 31, 2005. 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. See Note 16 for further discussion of the Company's income taxes.

(o) Discontinued Operations

The operations of Glyko have been classified as discontinued operations in the accompanying consolidated financial statements for all years presented. In addition, the Company has segregated the Glyko operating results in the accompanying consolidated statements of operations and changes in stockholders' equity (deficit) for all years presented. The related cash flows were insignificant and have been included within the operating section of our consolidated statements of cash flows. The notes to the accompanying consolidated financial statements also reflect the classification of Glyko operations as discontinued operations for all years presented.

(p) Accumulated Other Comprehensive Loss

Accumulated Other Comprehensive Loss includes unrealized gains and losses on short-term investments and foreign currency translation adjustments.

(q) Recent Accounting Pronouncements

In May 2005, the FASB issued Statement of Financial Accounting Standards (SFAS) No. 154, *Accounting Changes and Error Corrections—A Replacement of APB Opinion No. 20 and FASB Statement No. 3 (SFAS 154)*. SFAS 154 requires retrospective application to prior periods' financial statements for changes in accounting principle, unless it is impracticable to determine either the period-specific effects or the cumulative effect of the change. SFAS 154 also requires that a change in depreciation, amortization, or depletion method for long-lived non-financial assets be accounted for as a change in accounting estimate affected by a change in accounting principle. The Company is required to adopt the provisions of SFAS 154, as applicable, beginning in the first quarter of 2006.

In December 2004, the Financial Accounting Standards Board (FASB) issued Statement No. 123(R), *Share-Based Payment* (SFAS 123(R)), which requires companies to measure and recognize compensation expense for all stock-based payments at fair value. In April 2005, the SEC postponed the effective date of SFAS 123(R) until the fiscal year beginning after June 15, 2005. In March 2005, the SEC staff issued guidance on SFAS 123(R). Staff Accounting Bulletin No. 107 ("SAB 107") was issued to assist preparers by simplifying some of the implementation challenges of SFAS 123(R) while enhancing the information that investors receive. The Company will apply the principles of SAB 107 in conjunction with its adoption of SFAS 123(R). The Company will adopt SFAS 123R in the first quarter of 2006. Management estimates that the Company's net loss for 2006 will increase by approximately $7.5 million due to non-cash stock compensation in accordance with SFAS 123(R), which excludes approximately $1.7 million of estimated stock compensation to be capitalized into inventory during 2006. However, management expects that actual results may differ due to differences and

changes in components of the calculation during the 2006 fiscal year. See Note 2(m) for information related to the pro forma effects on the Company's reported net loss and net loss per common share of applying the fair value recognition provisions of the previous SFAS 123, *Accounting for Stock-Based Compensation*, to stock-based employee compensation.

In November 2004, the FASB issued SFAS No. 151, *Inventory Costs—An Amendment of ARB No. 43, Chapter 4* (SFAS 151). FAS 151 clarifies that abnormal amounts of idle facility expense, freight, handling costs and spoilage should be expensed as incurred and not included in overhead. Further, SFAS 151 requires that allocation of fixed and production facilities overheads to conversion costs should be based on normal capacity of the production facilities. The provisions in SFAS 151 are effective for inventory costs incurred during fiscal years beginning after June 15, 2005. Management does not believe that the adoption of SFAS 151 will have a significant effect on the Company's financial position and results of operations.

(r) Reclassifications

Certain items in the prior years consolidated financial statements have been reclassified to conform to the 2005 presentation.

(3) ASCENT PEDIATRICS TRANSACTION

On May 18, 2004, the Company acquired the Ascent Pediatrics business from Medicis Pharmaceutical Corporation (Medicis). The transaction included: The exclusive marketing and development rights to Orapred, a patent-protected drug to treat asthma in children; two additional proprietary formulations of Orapred in development; and a U.S.-based sales force. In connection with the transaction, the Company also acquired certain tangible assets, including inventory and equipment. The transaction provided the Company with financial and strategic benefits, primarily the addition of a commercial product and a commercial infrastructure. In January 2005, the agreements related to the transaction were amended due to a settlement of a dispute with Medicis and the acquisition obligation was reduced. The effect of these amendments totaled $21.0 million and was recorded in the first quarter of 2005 as a reduction of the acquisition obligation and goodwill.

Medicis agreed to make available to the Company a convertible note of up to $25.0 million beginning July 1, 2005, based on certain terms and conditions, including a change of control provision. Advances under the convertible note are convertible into shares of the Company's common stock at a conversion price equal to the average closing price of the stock for the 20 trading days prior to such advance. The convertible note, once drawn, matures in August 2009, but may be repaid by the Company, at the Company's option, at any time prior to the maturity date. At the time of repayment, Medicis may elect to receive cash or convert the amount due into shares of the Company's common stock. As of December 31, 2005, the Company has not made any draws on the note.

The amended transaction agreements provided for total acquisition payments of $169.0 million payable to Medicis in specified amounts through 2009, of which $94.8 million remains payable as of December 31, 2005. The remaining payments to Medicis include a payment due in 2009 of $8.6 million that 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 total acquisition cost as amended, including transaction costs totaling approximately $3.5 million, acquired tangible assets and operating liabilities, and the $6.0 million reimbursement for product returns discussed above, was $168.0 million. The remaining payments to Medicis are payable as follows (in thousands):

	As of December 31, 2005
2006	$ 7,700
2007	7,000
2008	6,500
2009	73,600
Total	$94,800

Pursuant to the acquisition, the Company was required to deposit $25.0 million of BioMarin common stock and $25.0 million of cash in escrow until the last of the first four quarterly payments to Medicis were made. The $25.0 million of BioMarin common stock was released in 2004 and the $25.0 million of cash was released in the first six months of 2005.

The acquisition has been 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 Company's consolidated financial statements for the period subsequent to the acquisition date reflect these values and the results of operations of the Ascent Pediatrics business. The total consideration has been allocated based on an estimate of the fair value of assets acquired and liabilities assumed.

The fair value of the transaction was allocated as follows (in thousands):

Product technology	$ 88,689
In-process research and development	31,453
Imputed discount on purchase price	27,054
Inventory	2,301
Equipment	131
Goodwill	21,262
Liabilities assumed	(2,901)
Total	$167,989

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 15 years using the straight-line method of amortization and includes no estimated residual value. See Note 4 for further discussion of the Company's acquired intangible assets.

In-process research and development represents the fair value of the two additional proprietary formulations of Orapred that were currently under development but not yet completed.

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.

The allocation to inventory at the purchase date included an adjustment of $0.9 million in addition to the cost basis of the finished inventory to reflect the fair value of the finished inventory, less the cost of disposal and a reasonable profit for the selling effort.

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 attributed to the premium that the Company was willing to pay to obtain the value of the Orapred business and the synergies created with the integration of key components of a commercial infrastructure. The entire amount of goodwill is expected to be deductible for tax purposes. The purchase price allocation also included $2.9 million of estimated liabilities assumed for product returns and unclaimed rebates.

(4) ACQUIRED INTANGIBLE ASSETS AND GOODWILL

(a) Acquired Intangible Assets

Acquired intangible assets relate to the Ascent Pediatrics transaction completed during May 2004 (see Note 3) and consist of the Orapred product technology as of December 31, 2005. The gross and net carrying values of the Orapred product technology as of December 31, 2005 were as follows (in thousands):

	December 31,	
	2004	2005
Gross value	$20,437	$20,437
Accumulated amortization	(3,986)	(5,131)
Net carrying value	$16,451	$15,306

In December 2004, the Company recognized an impairment loss totaling approximately $68.3 million, which was recorded as impairment of acquired intangible assets in the consolidated statement of operations for the year ended December 31, 2004. The primary circumstance leading to the impairment was the introduction of a new generic competitor to Orapred during the fourth quarter of 2004 that resulted in a significant decrease in the Orapred market share. As a result of this change in circumstance, the Company tested the recoverability of the related acquired intangible assets by first comparing the assets' carrying amount to the undiscounted future cash flows that the assets are expected to generate. The Company determined that the carrying value of the assets was not recoverable and an impairment loss was recorded for the amount by which the carrying value of the Orapred product technology exceeded its fair value. The fair value of the Orapred product technology was estimated using the present value of the expected future cash flows from the technology. The Company completed its 2005 annual impairment test during the fourth quarter of 2005 and determined that no impairment of the acquired intangible assets existed as of December 31, 2005.

The Orapred product technology is being amortized on a straight-line basis over its useful life of 15 years. Prior to the 2004 impairment charge, amortization expense was approximately $4.0 million during 2004. Amortization expense recognized during 2005 was approximately $1.1 million. The estimated amortization expense associated with the revised cost basis of the Orapred product technology for each of the succeeding five years is approximately $1.1 million per year.

(b) Goodwill

Goodwill as of December 31, 2005 relates to the Ascent Pediatrics transaction completed during May 2004 (see Note 3). The aggregate amount of goodwill acquired in the transaction was approximately $21.3 million, which reflects the reduction for the settlement of the dispute with Medicis during the first quarter of 2005 of $23.8 million, net, from $45.1 million as of December 31, 2004. Using the reporting unit basis required by SFAS No. 142, *Goodwill and Other Intangible Assets*, the Company completed its 2005 annual impairment test during the fourth quarter of 2005, and determined that no impairment of goodwill existed as of December 31, 2005. Whether or not goodwill will be impaired in the future is dependent upon the future sales of Orapred and the successful development and sales of the new formulations of Orapred.

(5) JOINT VENTURE

(a) Joint Venture Financial Data

The results of the joint venture's operations for the years ended December 31, 2003, 2004 and 2005, are presented in the table below (in thousands). Equity in the (Loss)/Income of BioMarin/Genzyme LLC represents the Company's 50% share of the joint venture's loss/income. The joint venture's results and summarized assets and liabilities as presented below give effect to the difference in inventory cost basis between the Company and the joint venture. The difference in basis primarily represents the difference in inventory capitalization policies between the joint venture and the Company. The Company began capitalizing Aldurazyme inventory costs in May 2003 after regulatory approval was obtained. The joint venture began capitalizing Aldurazyme inventory costs in January 2002 when inventory production for commercial sale began. The difference in inventory capitalization policies resulted in greater operating expense recognized by the Company prior to regulatory approval compared to the joint venture. Correspondingly, this results in less cost of goods sold recognized by the Company when the previously expensed product is sold by the joint venture and less operating expenses when this previously expensed product is used in clinical trials. The adjustment will be eliminated when all of the product produced prior to obtaining regulatory approval has been sold or used in clinical trials. The majority of the difference has been eliminated as of December 31, 2005.

	Year ended December 31,		
	2003	2004	2005
Revenue	$ 11,540	$42,583	$76,417
Cost of goods sold	3,090	5,787	16,089
Gross profit	8,450	36,796	60,328
Operating expenses	45,907	42,890	36,906
(Loss)/Income from operations	(37,457)	(6,094)	23,422
Other income	71	151	254
Net (loss)/income	$(37,386)	$ (5,943)	$23,676
Equity in the (loss)/income of BioMarin/Genzyme LLC	$(18,693)	$ (2,972)	$11,838

At December 31, 2004 and 2005, 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,	
	2004	2005
Assets	$ 58,009	$70,436
Liabilities	(11,751)	(6,470)
Net equity	$ 46,258	$63,966
Investment in BioMarin/Genzyme LLC (50% share of net equity)	$ 23,129	$31,983

(b) Joint Venture Critical Accounting Policies

Revenue recognition—BioMarin/Genzyme LLC recognizes revenue from 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. Revenue transactions are evidenced by customer purchase orders, customer contracts in certain instances, invoices and the related shipping documents.

The timing of product shipment and receipts can have a significant impact on the amount of revenue that BioMarin/Genzyme LLC recognizes in a particular period. Also, Aldurazyme is sold in part through distributors. Inventory in the distribution channel consists of inventory held by distributors, who are BioMarin/Genzyme LLC's customers, and inventory held by retailers, such as pharmacies and hospitals. BioMarin/Genzyme LLC's revenue in a particular period can be impacted by increases or decreases in distributor inventories. If distributor inventories increased to excessive levels, BioMarin/Genzyme LLC could experience reduced purchases in subsequent periods. To determine the amount of Aldurazyme inventory in the joint venture's U.S. distribution channel, BioMarin/Genzyme LLC receives data on sales and inventory levels directly from its primary distributors for the product.

BioMarin/Genzyme LLC records reserves for rebates payable under Medicaid and third-party payer contracts, such as managed care organizations, as a reduction of revenue at the time product sales are recorded.

Certain components of the BioMarin/Genzyme LLC rebate reserves are calculated based on the amount of inventory in the distribution channel, and are impacted by BioMarin/Genzyme LLC's assessment of distribution channel inventory. BioMarin/Genzyme LLC's calculation also requires other estimates, including estimates of sales mix, to determine which sales will be subject to rebates and the amount of such rebates. BioMarin/Genzyme LLC updates its estimates and assumptions each period, and records any necessary adjustments to its reserves.

BioMarin/Genzyme LLC 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 the nature of Aldurazyme and its patient population, the customers' limited return rights, Genzyme's experience of returns for similar products and BioMarin/Genzyme LLC's estimate of distribution channel inventory, based on sales and inventory level information provided by the primary distributors for Aldurazyme, as described above. Based on these factors, BioMarin/Genzyme LLC 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.

Inventory—BioMarin/Genzyme LLC values inventories at the lower of cost or fair value. BioMarin/Genzyme LLC determines the cost of raw materials using the average cost method and the cost of work in process and finished goods using the specific identification method. BioMarin/Genzyme LLC analyzes its inventory levels quarterly and writes down to its net realizable value inventory that has expired, become obsolete, has a cost basis in excess of its expected net realizable value, or is in excess of expected requirements. If actual market conditions are less favorable than those projected by the joint venture, additional inventory write-offs may be required.

BioMarin/Genzyme LLC capitalizes inventory produced for commercial sale. Refer to Note 5(a) above for discussion of the difference in inventory cost basis between the Company and BioMarin/Genzyme LLC.

(6) PROPERTY AND EQUIPMENT

Property and equipment at December 31, 2004 and 2005 consisted of (in thousands):

Category	December 31, 2004	December 31, 2005	Estimated useful lives
Leasehold improvements	$ 57,481	$ 57,809	Shorter of life of asset or lease term
Manufacturing and laboratory equipment	15,086	13,938	5 years
Computer hardware and software	4,512	5,055	3 years
Office furniture and equipment	3,123	3,269	5 years
Construction-in-progress	240	759	
	80,442	80,830	
Less: Accumulated depreciation	(37,941)	(43,509)	
Total property and equipment, net	$ 42,501	$ 37,321	

Depreciation expense for the years ended December 31, 2003, 2004, and 2005 was, $9.0 million, $8.2 million and $7.7 million, respectively.

(7) COLLABORATIVE AGREEMENTS

(a) Genzyme

In 1998, the Company entered into an agreement with Genzyme to establish a joint venture (BioMarin/Genzyme LLC) for the worldwide development and commercialization of Aldurazyme to treat mucopolysaccharidosis I (MPS I). Under the agreement, Genzyme purchased 1,333,333 shares of the Company's common stock for $8.0 million and, concurrent with the Company's IPO in 1999, purchased an additional 769,230 shares of the Company's common stock for an additional $10.0 million. During May 2003, the Company received $12.1 million from Genzyme for the one-time milestone payment related to the marketing approval of Aldurazyme. The milestone payment is included as collaborative agreement revenue in the accompanying consolidated statements of operations.

(b) Serono

In May 2005, the Company entered into an agreement with Serono S.A. (Serono) for the further development and commercialization of two BioMarin product candidates, Phenoptin and Phenylase (phenylalanine ammonia lyase). Through the agreement, Serono acquired exclusive rights to market these

products in all territories outside the U.S. and Japan, and BioMarin retained exclusive rights to market these products in the U.S. The Company and Serono will generally share equally all development costs following successful completion of Phase 2 trials for each product candidate in each indication. BioMarin and Serono are individually responsible for the costs of commercializing the products within their respective territories. Serono will also pay BioMarin royalties on its net sales of these products.

Pursuant to the agreement, Serono paid BioMarin $25.0 million as consideration for executing the agreement, and will 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 with Phenoptin for the treatment of PKU. 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 2005, deferred revenue included $19.9 million related to the remaining unamortized up-front license fee and accounts receivable included $3.3 million due from Serono for reimbursable Phenoptin development costs.

(c) 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.

(8) DAIICHI SUNTORY PHARMA LICENSE

In May 2005, the Company entered into a license agreement with Daiichi Suntory Pharma Co., Ltd. (Daiichi Suntory Pharma) whereby the Company obtained the exclusive worldwide rights, excluding Japan, for the use of tetrahydrobiopterin (6R- BH_4) to treat the endothelial dysfunction that causes vascular complications in diabetes, cardiovascular and other diseases. 6R- BH_4 is the active pharmaceutical ingredient in Phenoptin. BioMarin paid Daiichi Suntory Pharma $3.3 million in connection with the license, which was included in research and development expense during 2005.

(9) SUPPLEMENTAL BALANCE SHEET INFORMATION

As of December 31, 2004 and 2005, accounts payable and accrued liabilities consisted of the following (in thousands):

	December 31,	
	2004	2005
Accounts payable	$ 946	$ 484
Accrued accounts payable	13,662	10,019
Accrued vacation	1,357	1,581
Accrued compensation	3,319	4,219
Accrued other	2,484	707
Accrued rebates	3,578	1,751
Acquired rebate reserve	1,020	1,546
Short-term returns reserves	726	430
Current portion of deferred rent	157	198
Total accounts payable and accrued liabilities	$27,249	$20,934

As of December 31, 2004 and 2005, other long-term liabilities consisted of the following (in thousands):

	December 31, 2004	December 31, 2005
Long-term portion of returns reserve	$ 790	$5,684
Long-term portion of deferred rent	2,062	1,967
Total other long term liabilities	$2,852	$7,651

As of December 31, 2004 and 2005, inventory consisted of the following (in thousands):

	December 31, 2004	December 31, 2005
Orapred finished goods	$2,316	$ 821
Naglazyme raw materials	—	1,717
Naglazyme work in process	—	8,032
Naglazyme finished goods	—	328
Total inventory	$2,316	$10,898

A rollforward of our significant estimated revenue dilution reserves is as follows (in thousands):

	Balance at beginning of period	Provision for current period sales	Provision/ (reversals) for prior period sales	Actual charges related to current period sales	Actual charges related to prior period sales	Balance at end of period
Year ended December 31, 2004:						
Returns reserve	$ —	$ 790	$ —	$ —	$ —	$ 790
Accrued rebates	—	2,240	1,338	—	—	3,578
Reserve for cash discounts	—	670	—	(581)	—	89
Year ended December 31, 2005:						
Returns reserve	$ 790	$ 279	$ 5,129	$ —	$(184)	$6,014
Accrued rebates	3,578	1,019	(2,497)	(349)	—	1,751
Reserve for cash discounts	89	212	—	(197)	(80)	24

(10) CONVERTIBLE DEBT

In June 2003, the Company sold $125 million of convertible debt due on June 15, 2008. The debt was issued at face value and bears interest at the rate of 3.5% 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 $14.01 per share, subject to adjustment in certain circumstances. On or after June 20, 2006, the Company may, at its option, redeem the notes, in whole or in part, at predetermined prices, plus any accrued and unpaid interest to the redemption date. 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 debt, the Company paid approximately $4.1 million in offering costs, which have been deferred and are included in other assets. They are being amortized as interest expense over the life of the debt, and the Company recognized $0.8 million of amortization expense during both 2004 and 2005.

(11) EQUIPMENT AND FACILITY LOANS

The Company entered into several agreements for secured loans totaling $2.6 million during 2002. The loans bore interest at rates ranging from 7.88% to 9.33% and were secured by certain manufacturing and laboratory equipment. Additionally, the agreements had covenants that required the Company to maintain a minimum unrestricted cash balance of $35 million, and the loans were repaid in full during 2005.

In May 2004, the Company executed a $25 million credit facility to finance the Company's equipment purchases and facility improvements. As of December 31, 2005, $20.9 million was outstanding on the facility. Payments of principal and interest of LIBOR plus 1.25% (5.78 % as of December 31, 2005) are due through maturity in 2011. The facility requires an all-asset first priority lien, excluding certain assets such as intellectual property and assets related to the Ascent Pediatrics transaction. The lender requires that the Company maintain a total unrestricted cash balance, including short-term investments, of at least $25 million and that the Company maintain a deposit with the lender equal to the outstanding balance, or $10.0 million, whichever is greater. As of December 31, 2005, $17.0 million of the total minimum unrestricted cash balance is required to be maintained in an account with the lender as an unrestricted compensating balance. The facility also contains additional customary non-financial covenants. Principal payments due on equipment and facility loans range from approximately $5,000 to $119,000 per month and are payable as follows (in thousands):

2006	$ 3,860
2007	3,860
2008	3,860
2009	3,860
2010 and thereafter	5,469
Total	$20,909

(12) REDUCTION OF ORAPRED SALES FORCE

In July 2005, the Company reduced the Orapred sales force through the elimination of 52 positions. The severance and related costs associated with eliminating the 52 sales force positions, plus six non-sales force positions, totaling approximately $0.9 million, were recorded as selling, general and administrative expense in the third quarter of 2005. The Company will continue to market Orapred through non-personal promotion activities.

(13) DERIVATIVE FINANCIAL INSTRUMENTS

The Company periodically enters into foreign currency forward contracts, which have a maturity of less than one year. These contracts have not been designated as hedges and, accordingly, unrealized gains or losses on these contracts are reported in current earnings. The notional settlement value of foreign currency forward contracts outstanding at December 31, 2005 was $0.3 million. At December 31, 2005, these contracts had a fair value of $33,000, representing an unrealized loss. The amount has been recorded in the Company's consolidated statement of operations for the year ended December 31, 2005 and in accrued expenses in the Company's consolidated balance sheet as of December 31, 2005.

(14) STOCKHOLDERS' EQUITY

(a) Common Stock

In July 2005, the Company completed a public offering of its common stock. In the offering, the Company sold 8,500,000 shares at a price to the public of $7.05 per share, or a total offering price of $59.9 million. The net proceeds were approximately $56.3 million.

During 2004, certain warrants expired resulting in a reclassification of $5.2 million from warrants to additional paid-in capital.

The Company had an agreement with Acqua Wellington for an equity investment facility with the Company. The Company voluntarily terminated the agreement with Acqua Wellington in September 2003. During 2003, Acqua Wellington purchased 765,816 shares of BioMarin common stock for $8.0 million, net of issuance costs.

In February 2003, the Company completed a public offering of its common stock. In the offering, the Company sold 8,625,000 shares, and the net proceeds were approximately $80.5 million. The offering was pursuant to the Company's shelf registration statement filed in December 2002, which allows the Company to sell shares of its common stock in one or more offerings, up to a total dollar amount of $150.0 million.

In June 2003, the Company amended its articles of incorporation to increase the number of authorized shares of common stock from 75 million shares to 150 million shares.

(b) Notes Receivable from Stockholders

In 1997, the Company issued 2.5 million shares of Founders' Stock to three officers in exchange for notes receivable from the officers. The notes and associated interest were repaid during 2003. The notes carried an interest rate of 6% and were secured by the underlying stock.

(c) Deferred Compensation

In connection with certain stock option and stock grants to employees from 1998 to 2000, the Company recorded deferred compensation totaling $4.2 million, which has been amortized over the estimated vesting periods of the grantees. Amortization expense recognized for these grants during the years ended December 31, 2003, 2004 and 2005 was $47,000, $0 and $0, respectively.

(d) Stockholders' Rights Plan

In 2002, the Board of Directors authorized a stockholders' rights plan. 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 Series B Junior Participating Preferred Stock of the Company that have significantly superior dividend, liquidation, and voting rights to the 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 Plan expires in 2012.

(15) STOCK-BASED COMPENSATION PLANS

The Company has three stock-based compensation plans:

- The 1997 Stock Plan (the 1997 Plan) provides for the grant of stock options and the issuance of common stock to employees, officers, directors, and consultants. As of December 31, 2005, 17,172,422 shares were reserved for issuance of options under the 1997 Plan, of which 6,348,569 options were outstanding.
- The 1998 Director Option Plan (the Director Plan) provides for the grant of stock options and the issuance of common stock to non-employee directors. As of December 31, 2005, 1,489,650 shares were reserved for issuance of options under the Director Plan, of which 620,000 options were outstanding.

Options currently outstanding under the 1997 Plan and the Director Plan generally vest in four years or less. Options generally terminate from 5 to 10 years from the date of grant or 90 days after termination of employment.

- The 1998 Employee Stock Purchase Plan (1998 Purchase Plan) provides for the purchase by eligible employees of Company common stock at semi-annual intervals through periodic payroll deductions. Purchases are limited to 5% of the total combined voting power or value of the Company. Individual employee contributions are limited to 10% of the employee's salary and a maximum value of $25,000 per calendar year. Shares are purchased on April 30 and October 31 of each year. As of December 31, 2005, 719,350 shares have been issued under the 1998 Purchase Plan and 230,650 shares are reserved for future issuances.

A summary of the activity in the 1997 Plan and the Director Plan is as follows:

	Option shares	Weighted average exercise price	Exercisable at end of year	Weighted average fair value of options granted
Outstanding at December 31, 2002	7,077,509	11.21	4,524,655	
Granted	3,662,775	7.89		5.69
Exercised	(799,757)	6.68		
Canceled	(258,821)	9.74		
Outstanding at December 31, 2003	9,681,706	10.37	5,369,082	
Granted	1,795,800	6.19		3.66
Exercised	(157,879)	6.44		
Canceled	(1,311,602)	8.25		
Outstanding at December 31, 2004	10,008,025	9.96	7,285,031	
Granted	2,712,471	7.02		3.92
Exercised	(1,049,639)	6.56		
Canceled	(4,702,288)	11.04		
Outstanding at December 31, 2005	6,968,569	8.60	4,156,056	

There were 3,082,391 and 7,666,119 options available for grant under the 1997 Plan and the Director Plan at December 31, 2004 and 2005, respectively.

As of December 31, 2005, the options outstanding consisted of the following:

	Options outstanding			Options exercisable	
Range of exercise prices	Number of options outstanding	Weighted average remaining contractual life	Weighted average exercise price	Weighted average number of options exercisable	Weighted average exercise price
$ 3.50 to 7.00	2,808,952	7.0	$ 5.82	1,316,955	$ 5.43
7.01 to 10.50	3,021,927	7.0	8.71	1,752,007	8.78
10.51 to 14.00	707,967	5.6	12.39	657,371	12.44
14.01 to 17.50	141,930	4.1	16.68	141,930	16.68
17.51 to 21.00	77,793	4.4	19.66	77,793	19.66
21.01 to 24.50	210,000	4.4	22.00	210,000	22.00
	6,968,569			4,156,056	

(16) INCOME TAXES

As of December 31, 2005, the Company had federal net operating loss carryforwards of approximately $301.8 million and state net operating loss carryforwards of approximately $111.4 million. The Company also had federal research and development and orphan drug credit carryforwards of approximately $61.1 million as of December 31, 2005, and state research credit carryovers of approximately $12.8 million. The federal net operating loss and credit carryforwards expire at various dates beginning in the year 2006 through 2025, if not utilized. The state net operating loss carryforwards begin to expire in 2006 and will completely expire in 2015 if not utilized. Certain state research credit carryovers will begin to expire in 2015 if not utilized with others carrying over indefinitely.

Utilization of the Company's net operating loss carryforwards and credits may be subject to limitations due to the "change in ownership" provisions of the Internal Revenue Code of 1986 and similar state provisions. The annual limitations may result in the expiration of net operating losses and credits before utilization.

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 deferred tax assets for federal and state income taxes are as follows (in thousands):

	December 31,	
	2004	2005
Deferred tax assets:		
Net operating loss carryforwards	$ 104,577	$ 115,487
Research and other credits	60,685	73,919
Capitalized research expenses	12,261	14,225
Depreciation and amortization	9,587	8,675
Accrued expenses and reserves	3,382	7,103
Goodwill and intangible assets	44,501	29,941
Deferred revenue	—	8,734
Other	6,611	3,146
Total deferred tax assets	241,604	261,230
Valuation allowance	(241,604)	(261,230)
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. The net valuation allowance increased $93.7 million and $19.6 million during the years ended December 31, 2004 and 2005.

The Company had no current federal income tax expense and minimal current state income tax expense for the years ended December 31, 2003, 2004 and 2005. The reconciliations between the U.S. federal statutory tax rates to the Company's effective tax rates are as follows:

	December 31,		
	2003	2004	2005
Federal tax	(35.0)%	(35.0)%	(35.0)%
Other permanent items	3.4%	2.1%	6.4%
General business credits	(12.0)%	(6.0)%	(13.6)%
Prior year tax return true-up	(0.3)%	—	—
Valuation allowance	43.9%	38.9%	42.2%
Effective tax rate	—	—	—

(17) SHORT-TERM INVESTMENTS

At December 31, 2005, 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 held-to-maturity at December 31, 2005 and were previously classified as available-for-sale as of December 31, 2004. The decision to classify the short-term investments as held-to-maturity during 2005 was based on changes to the Company's liquidity needs.

	Contractual Maturity Date For the Years Ending December 31,		December 31, 2005		
	2006	2007	Total Book Value	Unrealized Losses	Aggregate Fair Value
U.S. Government agencies	$9,700	$—	$9,700	$(71)	$9,629

At December 31, 2004, 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, 2004.

	Contractual Maturity Date For the Years Ending December 31,		December 31, 2004		
	2005	2006	Total Book Value	Unrealized Losses	Aggregate Fair Value
U.S. Government agencies	$ 8,628	$18,700	$27,328	$(260)	$27,068
Corporate notes	3,570	5,182	8,752	(86)	8,666
Total	$12,198	$23,882	$36,080	$(346)	$35,734

At December 31, 2005, the aggregate amount of unrealized losses and related fair value of investments with unrealized losses were as follows (in thousands):

	Less Than 12 Months		12 Months or More		Total	
	Aggregate Fair Value	Unrealized Losses	Aggregate Fair Value	Unrealized Losses	Aggregate Fair Value	Unrealized Losses
U.S. Government Agencies . . .	$9,629	$(71)	$—	$—	$9,629	$(71)

Management determined that there were no other-than-temporary impairments of the Company's investments at December 31, 2005 and believes that the unrealized losses incurred are the result of decreases in the related interest rate markets since the purchase of the investments. Because the investments are placed in financial institutions with strong credit ratings, management expects full recovery of the amortized cost.

At December 31, 2004, the aggregate amount of unrealized losses and related fair value of investments with unrealized losses were as follows (in thousands):

	Less Than 12 Months		12 Months or More		Total	
	Aggregate Fair Value	Unrealized Losses	Aggregate Fair Value	Unrealized Losses	Aggregate Fair Value	Unrealized Losses
U.S. Government Agencies . . .	$21,084	$(216)	$ 5,984	$(44)	$27,068	$(260)
Corporate notes	3,098	(38)	5,568	(48)	8,666	(86)
Total	$24,182	$(254)	$11,552	$(92)	$35,734	$(346)

(18) 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 2014. 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):

2006	$ 3,875
2007	3,858
2008	3,951
2009	3,901
2010	3,645
Thereafter	6,322
	$25,552

Rent expense for the years ended December 31, 2003, 2004, and 2005 was $2.6 million, $4.4 million and $3.7 million, respectively. Deferred rent accruals were $2.2 million, of which $0.2 million was current, at both December 31, 2004 and 2005.

(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.

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, 2005, such minimum annual commitments are approximately $0.5 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 $45.2 million upon achievement of certain regulatory and licensing milestones if they occur before certain dates in the future, which includes $8.9 million of contingent payments related to Neutralase, for which the Company terminated development during 2003 and, accordingly, management does not expect they will ever be payable.

(19) SALE OF GLYKO, INC. ASSETS

On January 2, 2003, the Company sold certain Glyko assets including intellectual property, inventory and customer lists, to a third-party for a total sales price of up to $1.5 million. The sales price was comprised of cash totaling $0.2 million, a note receivable payable in installments through 2006 totaling $0.5 million, without interest, and quarterly royalties based upon the future sales of certain Glyko products up to a maximum of $0.8 million. The note receivable was collected in full as of December 31, 2005. The related cash flows are insignificant and have been included in the operating section of our consolidated statements of cash flows. The future royalties are based upon the terms of the related license agreement, which terminates in January 2008. As the net book value of the Glyko assets was reduced to zero as of December 31, 2002, the Company recognized a gain on disposal of discontinued operations totaling $0.6 million in 2003. The gain represents the cash and note receivable received offset by the discount on the note receivable and related transaction fees incurred during 2003.

(20) RELATED-PARTY TRANSACTIONS

In 2001, the Company loaned its former Chief Executive Officer $860,000 to purchase a property and received a promissory note secured by the property. The note and interest accrued to date totaling $983,000, were repaid in full in August 2004. The original maturity date of the note was October 31, 2006, and the interest rate on the note was the Federal mid-term rate. In August 2004, the Company incurred $2.9 million of expenses associated with the separation agreement between the Company and its former Chief Executive Officer.

In March 2002, we entered into an employment agreement with a former officer that entitled him to loans from the Company of up to $100,000 to be applied to the purchase of a home or up to $36,000 annually if a purchase of a home was not completed. In January 2005, the officer retired and the Company entered into a severance agreement, and the officer was paid the severance payments required under his employment agreement, including forgiveness of the loans discussed above. Additionally, the exercise date of the officer's vested stock options was extended to December 31, 2005.

During 2002, certain consulting services were rendered by one of our directors. The director was paid $56,000 in 2002, and $52,300 in January 2003, for services.

An officer of the Company holds an adjunct faculty position with Harbor-UCLA Research Educational Institute (REI) for purposes of conducting research. REI licenses certain intellectual property and provides other research services to the Company. The Company is also obligated to pay REI royalties on future sales of products covered by the license agreement. Minimum annual royalties payable to REI are $25,000. The Company paid REI approximately $0.3 million and $0.1 million in 2004 and 2005, respectively, primarily for research. The Company's joint venture with Genzyme is subject to a second agreement with REI that requires the joint venture to pay REI a royalty on sales of products covered by the license agreement through November 2019, of which the officer is entitled to certain portions, based on the sales level per the terms of the agreement. The license agreement was effective before the officer was a BioMarin employee. Pursuant to these agreements, the officer was entitled to approximately $498,000 and $888,000 during 2004 and 2005, respectively.

(21) COMPENSATION 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 six months prior notice, or by the officer upon three months 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 compensation or $4,000 per year. The Company's matching contribution vests over four years from employment commencement and was approximately $292,000, $452,000 and $534,000 for the years ended December 31, 2003, 2004 and 2005, respectively. Employer contributions not vested upon employee termination are forfeited.

(c) Deferred Compensation Plan

On December 1, 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 and annual cash bonus. 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 invested based on participant direction as allowed by the Deferred Compensation Plan. The recorded cost of any investments will approximate fair value. No investments or deferred compensation were recorded as of December 31, 2005.

(22) SUPPLEMENTAL CASH FLOW INFORMATION

The following non-cash transactions took place in the periods presented (in thousands):

	Years ended December 31,		
	2003	2004	2005
Fair value of restricted stock grant issued pursuant to an employment contract	$275	$ —	$ —
Acquisition obligation, net of discount	—	151,702	—
Settlement of dispute with Medicis, net of discount	—	—	22,648

The Company's cash payments for interest on debt were $2.5 million, $4.7 million and $5.6 million for the years ended 2003, 2004, and 2005 respectively.

(23) FINANCIAL INSTRUMENTS—CONCENTRATIONS OF CREDIT RISK

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist principally of cash, cash equivalents, short-term investments and accounts receivable. All cash, cash equivalents, and short-term investments are placed in financial institutions with strong credit ratings, which minimizes the risk of loss due to nonpayment. Accounts receivable as of December 31, 2005 relates to net product sales of both Naglazyme and Orapred. With respect to Naglazyme accounts receivable, a significant portion of net product sales are made to a limited number of financially viable specialty pharmacies. The Company's three largest customers accounted for 20%, 13% and 11% of net revenues, respectively, or 44% of the Company's total net product sales of Naglazyme in aggregate for the year ended December 31, 2005.

With respect to Orapred accounts receivable, a significant portion of Orapred sales is made to a limited number of financially viable distributors. The Company sold $5.5 million of the Orapred liquid formulation, of which the Company's three largest customers accounted for 32%, 30% and 20% of net revenues, respectively, or 82% of the Company's total net product sales of the Orapred liquid formulation in aggregate for the year ended December 31, 2005. The Company also recorded $1.4 million of net product sales through the Orapred authorized generic brand, which were sold to our exclusive wholesaler of the generic product.

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. The Company has not experienced any significant losses related to its financial instruments and management does not believe a significant credit risk existed at December 31, 2005.

(24) QUARTERLY CONSOLIDATED FINANCIAL DATA (UNAUDITED)

The Company's 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 completion of development projects and variations in levels of production.

During the fourth quarter of 2005, the Company recognized additional Orapred return reserves of $4.9 million, Orapred rebate reserve reversals of $2.8 million and Orapred inventory write-offs of $1.3 million.

The Company's common stock has been traded on the Nasdaq National Market since July 22, 1999. There were 93 common stockholders of record at December 31, 2005. No dividends have ever been paid by the Company.

	Quarter ended			
	March 31	June 30	September 30	December 31
	(In thousands, except per share data)			
2005:				
Total revenue	$ 4,989	$ 3,626	$ 7,579	$ 9,475
Net loss from continuing operations	(22,458)	(21,340)	(15,476)	(14,996)
Net loss	(22,458)	(21,340)	(15,476)	(14,996)
Net loss per share, basic and diluted	(0.35)	(0.33)	(0.21)	(0.20)
Common stock price per share:				
High	6.41	7.77	9.47	11.70
Low	4.40	4.75	7.02	6.94
2004:				
Total revenue	$ —	$ 4,563	$ 181	$ 13,897
Net loss from continuing operations	(19,945)	(55,598)	(29,478)	(82,422)
Net loss	(19,945)	(55,598)	(29,478)	(82,422)
Net loss per share, basic and diluted	(0.31)	(0.86)	(0.46)	(1.28)
Common stock price per share:				
High	8.87	8.12	6.66	6.49
Low	7.09	5.53	4.50	3.87

SCHEDULE II

BIOMARIN PHARMACEUTICAL INC. AND SUBSIDIARIES VALUATION ACCOUNTS
Years ended December 31, 2004 and 2005
(in thousands)

	Balance at beginning of period	Additions (Deductions) charged to costs and expenses	Additions charged to other accounts(1)	Deductions	Balance at end of period
Year ended December 31, 2004:					
Returns reserve	$ —	$ 790	$ —	$ —	$ 790
Accrued rebates	—	3,578	—	—	3,578
Reserve for cash discounts	—	670	—	(581)	89
Acquired returns reserve	—	—	883	(157)	726
Acquired rebates reserve	—	—	1,161	(141)	1,020
Year ended December 31, 2005:					
Returns reserve	$ 790	$ 5,408	$ —	$ (184)	$6,014
Accrued rebates	3,578	(1,478)	—	(349)	1,751
Reserve for cash discounts	89	212	—	(277)	24
Acquired returns reserve	726	—	466	(1,092)	100
Acquired rebates reserve	1,020	538	392	(404)	1,546

(1) Amounts relate to changes in estimates of business acquisition-related liabilities originally accounted for as components of purchase consideration and are included as components of goodwill.

Exhibit 10.44

CONFIDENTIAL TREATMENT REQUESTED
Redacted Portions are indicated by [****]

SERVICES AGREEMENT

This SERVICES AGREEMENT (the "**Agreement**"), dated December 15, 2005 (the "**Effective Date**"), is entered into by and among **Groupe Novasep SAS**, a French corporation having its registered place of business at Site Eiffel, Boulevard de la Moselle, 54340 Pompey, France, acting in its own name as well as on behalf of its Affiliates: **Dynamit Nobel GmbH, Explosivstoff- und Systemtechnik**, Kalkstr. 218, 51377 Leverkusen, Germany; **Finorga S.A.S**., Route de Givors, 38670 Chasse-sur-Rhône, France; **Seripharm S.A.S.**, 1 rue Démocrite, 72000 Le Mans, France; **Novasep Inc**., 23 Creek Circle, Boothwyn, PA 19061, USA; and **Rohner AG**, Gempenstr. 6, 4133 Pratteln, Switzerland ("**Novasep**"), on the one hand, and BioMarin Pharmaceutical Inc., a Delaware corporation having its principal office at 105 Digital Drive, Novato, CA 94949, USA ("**BioMarin**"), on the other hand (the "**Agreement**"). Each of Novasep and BioMarin are referred to herein individually as a "**Party**" and collectively as the "**Parties**".

WHEREAS, Novasep is engaged in the business of supplying chemistry services to synthesize, improve synthetic processes, manufacture, and the like, chemical compounds for the pharmaceutical industry; and

WHEREAS, BioMarin is engaged in developing and commercialisation of innovative biopharmaceuticals for serious diseases and medical conditions and desires to utilize the services of Novasep to synthesize, improve synthetic processes, manufacture and provide BioMarin with a commercial supply of Product, as defined below, which is the active pharmaceutical ingredient for one of BioMarin's product candidates; and

WHEREAS, BioMarin has requested that Novasep supply it with Product and Novasep is willing to supply Product on the terms and conditions set forth below.

NOW THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Agreement, the Parties agree as follows:

1. **Definitions**. In addition to the capitalized terms defined elsewhere in this Agreement, the following terms shall have the meanings set forth below.

   1.1. "**Applicable Laws**" means all laws, ordinances, rules and regulations of any governmental or quasi-governmental body applicable to the performance by each Party of its obligations hereunder, or any aspect thereof, as the context requires under this Agreement, including, without limitation: (a) all applicable federal, state and local laws and regulations; (b) the U.S. Federal Food, Drug and Cosmetic Act; (c) cGMP requirements; and (d) regulations for shipment of the Product into or out of the European Union and Switzerland.

   1.2. "**BioMarin Supplied Raw Materials**" means the [****] required for the production of the Product to be supplied pursuant to the terms of this Agreement.

1.3. "**cGMP**" means current good manufacturing practices and general biological products standards as promulgated under ICH Q7A - Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, US Federal Food Drug and Cosmetic Act at 21 CFR and the EEC Guide to Good Manufacturing Practices for Medical Products (Vol. IV - rules governing medical products in the European Community 1989) in the most recent version.

1.4. "**Certificate of Analysis**" means a certificate in a form reasonably acceptable to BioMarin certifying that a batch of Product meets the Specifications and such other specific requirements as contained in the Quality Agreement.

1.5. "**EMEA**" means the European Medicines Agency.

1.6. "**FDA**" means the United States Food and Drug Administration, and any successor agency thereto.

1.7. "**Novasep Supplied Raw Materials**" means all raw materials used in the production of the Product other than the BioMarin Supplied Raw Materials.

1.8. "**Regulatory Agency**" means the EMEA, the FDA and any other governmental regulatory authority or agency involved in regulating any aspect of the development, manufacture, market approval, sale, distribution, packaging or use of the Product.

2. **Supply of Product.**

2.1. Obligation to Supply. Pursuant to the terms of this Agreement, Novasep shall supply BioMarin with Sapropterin Hydrochloride [****], as more fully described in **Exhibit A**, (the "**Product**") for use as the active pharmaceutical ingredient in a human drug product in such quantities as BioMarin may order pursuant to the provisions of **Section 3**.

2.2. Specification of Product. The Product shall be produced in accordance with all Applicable Laws and utilizing the synthetic pathway previously transferred to Novasep by BioMarin and as summarized in **Exhibit B** (the "**Synthetic Pathway**"). All Product supplied hereunder shall be tested by Novasep to ensure that it meets the release specifications set forth in **Exhibit C** (the "**Specifications**"). During the term of this Agreement, the Parties may modify the Synthetic Pathway or the Specifications by mutual written agreement. A material change to the Synthetic Pathway or the Specifications may be subject to a corresponding change in the price of the Product, as agreed to by the Parties in writing.

2.3. Exclusive Supply Obligation. [****]

2.4. Limited Right to Use Contractors. Without limiting Novasep's responsibility under this Agreement, and subject to obtaining BioMarin's prior written consent, which may be granted or withheld in BioMarin's sole discretion, Novasep may

satisfy its supply obligations to BioMarin hereunder, either in whole or in part, through arrangements with contractors engaged to perform services or supply facilities or goods in connection with the manufacture, testing, and/or packaging of Product. Novasep shall ensure that all facilities processes and procedures of such contractors comply with Applicable Laws, including cGMP standards. To the extent that the use of contractors requires preparing and making any requisite filings with Regulatory Agencies for any pharmaceutical product incorporating the Product, BioMarin shall have sole responsibility for such filings.

2.5. Priority Supplier. Novasep acknowledges that BioMarin has an existing obligation to purchase the first [****] of Product required annually from Shiratori Pharmaceutical Co., Ltd., subject to certain conditions. Subject to such obligation, BioMarin agrees that, during the term of this Agreement, subject to the conditions below, Novasep shall be BioMarin's primary supplier of Product, which shall include purchasing no less than [****] Such obligation shall be conditioned on Novasep being able to supply sufficient quantities of Product, meeting all then applicable requirements of any Regulatory Agency to allow the Product to be used in a pharmaceutical product, and otherwise satisfying all of the terms and conditions of this Agreement. Annually, upon request by Novasep, BioMarin will provide Novasep with information regarding the aggregate quantities of Product from entities other than Novasep and Shiratori Pharmaceutical Co., Ltd., provided that BioMarin shall not be obligated to identify the other entities.

3. **Order Process.**

3.1. Forecasts. [****]

3.2. Purchase Orders. Together with the delivery of each Rolling Forecast, BioMarin shall issue a binding purchase order (a "**Purchase Order**") for the supply of Product [****]. Such Purchase Order shall specify reasonable delivery dates and instructions for shipping and packaging the Product. If there is any inconsistency between any of the terms and conditions of a Purchase Order and the terms and conditions of this Agreement, the terms and conditions of this Agreement shall prevail.

3.3. Acceptance Procedures. Within [****] after receiving a Purchase Order from BioMarin, Novasep shall give written notice to BioMarin specifying whether or not Novasep has accepted such Purchase Order; provided that Novasep shall be obligated to accept the Purchase Order if the amount to be purchased does not exceed the amount included for such period in the most recent previous Rolling Forecast provided to Novasep. Subject to the foregoing, in the event that Novasep does not accept a Purchase Order, Novasep shall give written notice to BioMarin explaining the reason(s) for non-acceptance. The Parties shall promptly consult with each other to resolve the issues as promptly as feasible and such Purchase Order will be modified accordingly by written agreement signed by both Parties.

3.4. Supply in excess of Rolling Forecast. Should, at any future time during the Term, BioMarin's requirements for Product to be included in the next Purchase Order exceed the amount specified for such period in the prior Rolling Forecast, BioMarin shall provide Novasep, as soon as reasonably practicable, with written notice to this effect with a good faith indication of the total amount of such excess requirements. [****]

3.5. Changes to Purchase Orders. If BioMarin requests a change to a Purchase Order (a "**Change Order**") after such Purchase Order is accepted by Novasep, BioMarin shall inform Novasep about such Change Order as soon as possible. Novasep shall use commercially reasonable efforts to accommodate such Change Order. Notwithstanding the foregoing, and provided a [****] is respected by BioMarin, BioMarin, by providing written notice to Novasep, may cancel or modify any of its outstanding Purchase Orders for Product in the event of a recall of Product (unless such recall does not result from an act or omission of Novasep) and BioMarin may then modify the related Rolling Forecast accordingly. Unless such recall is due to Novasep's breach of this Agreement, in the event BioMarin cancels or reduces any Purchase Order as permitted under this **Section 3.5**, BioMarin shall pay Novasep all non-cancelable costs relating to any unused materials that have been purchased by Novasep or Novasep's contractors in connection with such Purchase Order that have been rendered unusable by BioMarin's termination or change, provided that Novasep will use commercially reasonable efforts to mitigate such costs. Within [****] after cancellation or of any of the aforementioned changes, Novasep shall furnish BioMarin with a statement of all such unusable materials in inventory, and shall ship such materials and the applicable invoice therefore to BioMarin or to such location as BioMarin shall designate and per BioMarin's instructions. BioMarin shall pay for such unused materials and for any related storage and/or transportation or shipment costs within [****]after receipt of such invoice.

4. **Supply Price.**

4.1. Price Generally. BioMarin shall purchase the Product at the price set forth on **Exhibit D** (the "**Price**") as the price may be adjusted pursuant to the terms of this **Section 4** or pursuant to **Section 5.5**. The Parties acknowledge that, subject to any amounts payable pursuant to **Section 4.2**, such Price is the total compensation payable for the performance of all of Novasep's obligations under this Agreement, including, without limitation, the cost of labor, facilities, the Novasep Supplied Raw Materials including those listed in **Exhibit E**, reagents, solvents, analysis, packaging materials, incoming inspection and testing of all raw material and components, waste disposal, reports, packaging of product, preparation of finished Product for shipment, testing of final product and shipping of final Product and Novasep's reasonable profit margin. The Price does not include the purchase of the BioMarin Supplied Raw Materials. BioMarin shall be responsible for providing Novasep with the BioMarin Supplied Raw Materials at BioMarin's expense.

4.2. Payment of Taxes. BioMarin shall reimburse Novasep or its affiliates for any federal, state or local excise or other tax, assessment, license fee or other charge or increase thereof, which Novasep or its affiliates may be required to pay based on the sale, transportation or use of the Product. In no event shall BioMarin be required to reimburse Novasep or its affiliates for taxes based on Novasep or its affiliates' income or franchise fees.

4.3. Payment Procedures. BioMarin shall pay to Novasep for the Product supplied hereunder in United States currency by wire transfer to a bank account designated by Novasep no later than [****] after the date of the invoice for such Product. Novasep shall invoice BioMarin for each delivery of Product according to the following schedule: [****]

4.4. Reduction of Price for Process Improvements. [****]

4.5. Periodic Increase to Price. On an annual basis on January 1st of each year commencing on January 1, 2007, the Price may be increased by Novasep by the lesser of: [****]

5. **Manufacture.**

5.1. Quality Agreement. Within four (4) months after the Effective Date of this Agreement, Novasep and BioMarin will enter into a Quality Agreement (the "**Quality Agreement**"), which will further define the specific, task level, responsibilities of each Party, consistent with the terms of this Agreement. In the event of a conflict between the Quality Agreement and this Agreement, this Agreement shall govern and control.

5.2. Manufacture Obligations. Novasep shall be responsible for the manufacture of the Product to be supplied pursuant to this Agreement and shall cause the Product to be manufactured and supplied in accordance with the Applicable Laws, the Specifications and the Quality Agreement, and pursuant to the Synthetic Pathway. Novasep shall be responsible for the procurement, proper quality and documentation of the quality of all materials (other than the BioMarin Supplied Raw Materials,) equipment and facilities used for the preparation and analysis of the Product.

5.3. Supply of BioMarin Supplied Raw Materials. BioMarin shall be responsible to provide, at its expense, the BioMarin Supplied Raw Materials in sufficient quantity and with sufficient lead time to allow Novasep to manufacture Product as requested in a Purchase Order. Novasep shall be solely responsible for risk of loss of BioMarin Supplied Raw Materials after they are delivered to Novasep's facility.

5.4. Validation Processes. Novasep shall be responsible for the performance of all process validation associated with the manufacturing process and as required by the Quality Agreement or to generate the Certificate of Analysis. All costs and expenses relating to all process validation associated with the manufacturing

process and as required by the Quality Agreement or to generate the Certificate of Analysis are included in the Price. Prior to releasing the Product, Novasep shall have performed or shall have had performed quality control testing on samples of each batch of Product to determine whether it meets the Specifications and other warranties set forth in **Section 15** hereof. In the event that BioMarin wishes to perform additional validation testing, at its expense, to confirm the validation performed by Novasep, for no additional consideration, Novasep shall provide BioMarin with reasonable assistance in such efforts, such as responding to inquiries or investigation questions.

5.5. Manufacturing Changes.

(a) Manufacturing process and control changes that affect the Product, regardless of whether they are reportable to the FDA, will be reported by Novasep to BioMarin prior to implementation by Novasep. Any such changes shall require BioMarin's prior written approval, provided that, if such changes are not reportable to the FDA or EMEA, such approval will not be unreasonably withheld and if such changes do require notice to, or any filing with, the FDA or EMEA, such approval may be granted or withheld in BioMarin's sole discretion.

(b) BioMarin shall promptly advise Novasep in writing of any new standards, procedures or specifications related to the Product or the manufacturing process required by the applicable Regulatory Agencies and Novasep will use its best efforts to implement such requirements. [****]

6. **Compliance with Forecasts; Shipping Dates and Delivery**.

6.1. Delivery. Each shipment of Product to be supplied hereunder shall be delivered to BioMarin [****]. Product will be packaged in accordance with the specifications reasonably required by BioMarin. Title and risk of loss shall pass to BioMarin upon delivery, as defined above, provided Novasep shall provide reasonable cooperation to ensure that delivery is coordinated with the pick-up of such Product by the common carrier designated by BioMarin. Product shall be delivered free and clear of any security interest, lien, or other encumbrance.

6.2. Delivery Date. Novasep shall use commercially reasonable efforts to deliver to BioMarin the Product identified in each Purchase Order by the delivery date specified in the Purchase Order, subject to the coordination with the common carrier as described in **Section 6.1**. If Novasep anticipates any delay to the scheduled delivery date as included in a Purchase Order, Novasep will notify BioMarin as soon as possible, shall use commercially reasonable efforts (best efforts if such delay is due to circumstances within Novasep's control) to deliver Product not later than the scheduled delivery date or as soon as possible thereafter. All expenses for efforts to deliver Product in as timely a manner as possible shall be included within the Price.

6.3. Excess Delivery. [****]

7. **Documentation Associated with Shipments.**

7.1. Five (5) days prior to each delivery of Product, Novasep shall send to BioMarin by facsimile a copy of the detailed packing list indicating gross and net weights, invoice, airway bill number and flight details.

7.2. Novasep shall send with each shipment of Product a pro forma invoice or comparable document to be agreed upon with BioMarin containing at least BioMarin's material description and code, BioMarin's purchase order number, Product batch number, manufacturing date, unit of measure and total quantity delivered. Each delivery of Product shall also be accompanied by a batch identifier and a Certificate of Analysis verifying that the Product meets the Specifications.

7.3. Novasep shall prepare a comprehensive batch record for the production of each lot of Product under this Agreement, in accordance with the Quality Agreement, cGMP and the Specifications and will retain such documentation pursuant to an appropriate document retention schedule that complies with FDA and EMEA requirements. The batch documentation will be available to BioMarin for inspection and review. Upon BioMarin's request, Novasep will supply BioMarin with copies of such batch record, and if any batch record is not provided in English, Novasep shall provide to BioMarin copies of such batch documentation translated into English.

8. **Rejection**.

8.1. Promptly upon receipt of each delivery of Product, and no later than [****] after receipt of each delivery of Product, BioMarin shall perform appropriate inspection procedures designed to determine whether such Product conforms at the time of delivery to the applicable Specifications. If the Product supplied to BioMarin under this Agreement fails to conform to the Specifications, BioMarin shall so notify Novasep promptly after its discovery of such non-conformity, and BioMarin shall concurrently present reasonable evidence to Novasep of such non-conformity. If BioMarin notifies Novasep that Product is non-conforming and Novasep does not dispute such determination, Novasep shall promptly supply BioMarin with replacement Product or, at Novasep's election, have the non-conforming batch of the Product reprocessed, so long as such reprocessing has been previously approved by the FDA and EMEA, at Novasep's cost and expense. [****]

8.2. [****]

8.3. [****]

8.4. In the event that it is determined, based on the above procedures, that the allegedly non-conforming Product was conforming, then BioMarin shall pay Novasep the

applicable Price for any such Product. In the event that it is determined, based on the above procedures, that any Product delivered to BioMarin does not meet the Specifications, Novasep shall replace promptly, at no additional expense to BioMarin, such non-conforming Product with new Product that does conform with the Specifications thereof, and shall bear all costs of shipment of such new Product. Novasep shall give BioMarin written instructions as to how BioMarin should, at Novasep's expense, handle any non-conforming Product, and such instructions shall comply with all Applicable Laws.

9. **Audit**.

9.1. BioMarin will have the right to be present when Novasep is conducting an audit of any contractor facility where Product is manufactured, packaged and/or stored; provided, however such right to be present shall be limited to once per calendar year. During normal business hours and upon reasonable advance notice, BioMarin will have the right to audit the facilities of Novasep where Product is manufactured, packaged, and/or stored, for purposes of monitoring the conditions and processes under which Product is manufactured, packaged and stored, provided, however, that any such audits of Novasep may be performed only once per calendar year with respect to a given facility.

9.2. During normal business hours and upon reasonable advance notice, BioMarin will have the right to give power to an independent auditing company accepted by both parties to audit Novasep's books and records for the sole and exclusive purpose of verifying Novasep's commercially reasonable efforts to reduce costs associated with the manufacture of the Product and proper notification to BioMarin regarding such reduction in costs pursuant to **Section 4.4** or increases in the Price pursuant to **Section 4.5**; provided, however, that any such audit of Novasep may be performed only once every two years. Should the independent auditing company make a determination that any amounts to be paid or reimbursed hereunder have been incorrectly reported by Novasep, Novasep shall have a [****] period to demonstrate that the alleged reimbursements/adjustments are not due to BioMarin. If Novasep accepts the findings of the independent auditing company, then Novasep shall, within [****] of its receipt of the audit report, make a payment to BioMarin such that all amounts paid hereunder shall conform to the amounts so determined to be payable. If the Parties are unable to reach a resolution within an additional [****] period following Novasep's response to the independent auditing company's alleged reimbursements/adjustments, the Parties shall agree to submit their dispute to an independent expert accepted by both Parties that shall be charged with determining whether or not the calculations required pursuant to **Section 4.4** or **4.5** have been properly made and if not, determining the proper calculations. Such expert's findings shall be final and binding on the Parties, and the Parties will therefore make such adjustments/reimbursements, and make such payment as is necessary such that all amounts paid hereunder shall conform to the amounts so determined to be payable within [****] following the communication to both Parties of the expert's findings. If the expert determines that Novasep's

calculations were correct (or incorrect in favor of Novasep), BioMarin shall pay for such expert's costs and expenses, and if the expert determines that Novasep's calculations were incorrect in favor of Novasep, Novasep shall pay for such costs and expenses. Any audit under this **Section 9.2** will be at BioMarin's expense unless the audit, as supported by the expert analysis is such analysis is undertaken as provided above, determines that a calculation made by Novasep is inaccurate in favor of Novasep by more than [****], in which case Novasep shall reimburse BioMarin for the cost of the Audit.

10. **Ownership and Licenses**.

10.1. All information received from BioMarin or obtained as a result of Novasep's performance hereunder, including, but not limited to, batch records, results, data, reports, final reports, laboratory work sheets, methods, Product information, process information, improvements and the like ("**BioMarin Information**"), shall be the sole property of BioMarin and BioMarin shall be free to disclose and use BioMarin Information, regardless of origin, for any purpose, including, but not limited to, the preparation, use, sale and the like of the Product or anything produced using the Product.

10.2. Until the expiration of Novasep's obligations of confidentiality and non-use under **Section 2.3 and 11** hereof, Novasep covenants to promptly disclose to BioMarin all discoveries, inventions, improvements, innovations technologies, processes, and the like made by Novasep hereunder or otherwise using BioMarin Information or the Product or any process directly related to the manufacture of the Product ("**BioMarin Discoveries**").

10.3. Novasep hereby agrees to assign to BioMarin any and all rights, title and interest of Novasep to BioMarin Discoveries. All BioMarin Discoveries shall be deemed owned solely by BioMarin. Novasep shall take such action as BioMarin may reasonably request to vest title to any BioMarin Discoveries to BioMarin. BioMarin shall have the sole right to file, prosecute and maintain patent applications and patents with respect to new technology or process, directly related to the Product, developed by Novasep under this Agreement or any Purchase Order hereunder. BioMarin grants Novasep a fully-paid royalty-free, non-exclusive, worldwide, perpetual, irrevocable license, with the right to sublicense, to practice this technology for use in the manufacture of the Product.

10.4. Any new technology or process, not directly relating to the Product, developed by Novasep under this Agreement, remains the property of Novasep ("**Novasep Discoveries**"). Novasep shall have the sole right to file, prosecute and maintain patent applications and patents with respect to new technology or process, not directly relating to the Product, developed by Novasep under this Agreement or any Purchase Order hereunder. Novasep grants BioMarin a fully-paid royalty-free, non-exclusive, worldwide, perpetual, irrevocable license, with the right to sublicense solely to a subcontractor producing the Product, to practice this technology solely for use and manufacture of the Product.

10.5. Except for the Novasep Discoveries, BioMarin shall have the sole right to file, prosecute and maintain patent applications and patents with respect to BioMarin Information and BioMarin Discoveries. Novasep hereby undertakes and agrees to execute and have its employees execute such assignments and other documents which are necessary at any time to permit the filing and prosecution of applications for patents claiming BioMarin Information and BioMarin Discoveries. Novasep hereby further agrees that, at BioMarin's request and expense, Novasep may accept to assist BioMarin in the preparation, filing and prosecution of such patent applications and patents.

10.6. All intellectual property, including notably any discovery or invention (whether or not patentable or otherwise susceptible to intellectual property protection), improvements, modifications, know-how, substances, compounds, data, test results, techniques, processes, formulations or designs related to synthesis, purification, separation, and filtration technologies and processes developed by Novasep prior to this Agreement as evidenced by competent written records shall remain the sole and exclusive property of Novasep.

11. **Confidentiality.** Each Party shall abide by the terms and conditions of that certain Non-Disclosure Agreement effective December 31, 2004 (the "**NDA**"), attached hereto as **Exhibit F** and incorporated herein by this reference, provided that the purpose stated under the NDA shall include the performance of each Party's obligations under this Agreement.

12. **Term And Termination**.

12.1. Term. This Agreement shall be effective on the Effective Date and shall continue for five (5) years thereafter. BioMarin may, at its election, extend the term of this agreement for an additional five (5) year period by providing at least six (6) months prior notice of such extension to Novasep. Thereafter, unless either Party notifies the other of its election not to renew this Agreement at least twelve (12) months prior to the expiration of the term, this Agreement shall automatically, without further action of the Parties, renew for successive two (2) year periods.

12.2. Termination for Convenience. Following the initial five year term, or upon BioMarin's termination of the development program related to the Product, if sooner, upon six (6) months advanced notice to Novasep, BioMarin may terminate this Agreement, provided that such termination shall not apply to any Purchase Order made prior to the date of such notice.

12.3. Termination for Cause. Either Party may terminate this Agreement at any time if the other Party:

(a) fails to perform any material obligation, covenant, condition, or limitation herein, provided such other Party shall not have remedied its failure within sixty (60) days after receipt of written notice from the terminating Party of such failure; or

(b) the other party files a petition in bankruptcy, or enters into an agreement with its creditors, or applies for or consents to the appointment of a receiver or trustee, or makes an assignment for the benefit of creditors, or suffers or permits the entry of any order adjudicating it to be bankrupt or insolvent and such order is not discharged within thirty (30) days.

12.4. Survival. **Sections 2.3**, **7.3**, **8**, **9.2**, **10**, **11**, **13**, **14**, **15**, **16**, **18, 19** and **23-31** and all then-outstanding payment and reimbursement obligations shall survive any termination or expiration of this Agreement.

12.5. Technology Transfer. Should this Agreement terminate due to: (a) BioMarin's rights under **Section 12.3**; or (b) any event that has prevented Novasep or Novasep's contractor(s) from shipping Products in accordance with BioMarin orders for [****], except if such event is an event of Force Majeure as described in Section 21, BioMarin shall have the right to require Novasep, at is sole expense, to effect a transfer of manufacturing know-how sufficient to enable BioMarin, or a third Party designated by BioMarin, to manufacture the Product in accordance with the Specifications. The Parties acknowledge that a breach of such obligation would cause BioMarin irreparable damage and, accordingly, BioMarin shall be entitled to obtain specific performance of such obligation in any court of competent jurisdiction.

13. **Indemnification**.

13.1. BioMarin shall indemnify and hold harmless Novasep, its directors, officers and employees (collectively, the "**Novasep Indemnitees**"), from and against any and all liability, damage, loss, cost (including reasonable attorneys' fees) and expense resulting from claims of any kind and character by any third Party (including, without limitation, employees or agents of BioMarin) with respect to the manufacture, storage, or use of Product supplied by Novasep to BioMarin pursuant to this Agreement and/or the BioMarin Supplied Raw Materials supplied to Novasep so long as such BioMarin Supplied Raw Materials are processed, stored and used in accordance with the instructions provided by BioMarin, as required by law and in accordance with good business practices. Notwithstanding the foregoing, Novasep shall not be entitled to indemnification under this **Section 13.1** for any claim based in whole or in part on Novasep's negligence, wilful misconduct or breach of its obligations hereunder.

13.2. Novasep shall indemnify and hold harmless, BioMarin, its directors, officers and employees (collectively, the "**BioMarin Indemnitees**"), from and against any and all liability, damage, loss, cost (including reasonable attorneys' fees) and expense resulting from claims of any kind and character by any third Party (including, without limitation, employees or agents of Novasep) arising out of or in connection with Novasep's negligence, wilful misconduct or breach of its obligations hereunder. Notwithstanding the foregoing, BioMarin shall not be entitled to indemnification under this **Section 13.2** for any claim based in whole or in part on BioMarin's negligence, wilful misconduct or breach of its obligations hereunder.

13.3. Each Party, on behalf of itself and its respective BioMarin Indemnitees or Novasep Indemnitees (each such Person, an "**Indemnitee**"), agrees to provide the indemnifying Party prompt written notice of any action, claim, demand, discovery of fact, proceeding or suit (collectively, a "**Claim**") for which such Indemnitee intends to assert a right to indemnification under this Agreement; provided, however, that failure to give such notification shall not affect each applicable Indemnitee's entitlement to indemnification (or the corresponding indemnifying Party's indemnification obligations) hereunder except to the extent that the indemnifying Party shall have been prejudiced as a result of such failure. The indemnifying Party shall have the initial right (but not obligation) to defend, settle or otherwise dispose of any Claim for which an Indemnitee intends to assert a right to indemnification under this Agreement as contemplated in the preceding sentence if, and for so long as, the indemnifying Party has recognized in a written notice to the Indemnitee provided within thirty (30) days of such written notice its obligation to indemnify the Indemnitee for any losses relating to such Claim; provided, however, that if the indemnifying Party assumes control of the defense, settlement or disposition of a Claim, the indemnifying Party shall obtain the written consent of each applicable Indemnitee prior to ceasing to defend, settling or otherwise disposing of the Claim. If the indemnifying Party fails to state in a written notice during such thirty (30) day period its willingness to assume the defense of such a Claim, the BioMarin Indemnitee(s) or Novasep Indemnitee(s), as the case may be, shall have the right to defend, settle or otherwise dispose of such Claim, subject to the applicable provides of Sections 13.1 and 13.2.

14. **Limitation of Liability.** NOTWITHSTANDING ANYTHING TO THE CONTRARY HEREIN, NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES ARISING OUT OF ANY TERMS OR CONDITIONS IN THIS AGREEMENT OR WITH RESPECT TO THE PERFORMANCE THERETO.

15. **Representations, Warranties and Covenants**.

15.1. General. Each Party represents and warrants to the other Party that:

(a) it has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof; and

(b) the execution, delivery and performance of this Agreement by such Party does not conflict with any agreement, instrument or understanding, oral or written, to which it is a Party or by which it may be bound, nor does it violate any material law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

15.2. Regarding the Product. Novasep further warrants and represents that the Products delivered to BioMarin under this Agreement shall, at the time of delivery:

(a) meet the Specifications;

(b) be in good, usable and merchantable condition; and

(c) have been manufactured in compliance with all Applicable Laws

15.3. No Conflict. Each Party covenants that it will not grant any right to any third Party that would conflict with the rights granted to the other Party or its obligations hereunder.

16. **Successors and Assigns; Parties in Interest.**

16.1. This Agreement shall be binding upon and shall inure to the benefit of the respective permitted successors and assigns of each of the Parties hereto (if any). No person who is not a Party shall have any rights hereunder as a third-party beneficiary or otherwise.

16.2. Neither this Agreement nor the rights and obligations of either Party shall be assigned without the prior written consent of the other Party, which consent may be given or withheld in such party's sole and absolute discretion, except to a successor by merger or sale of substantially all of its business to which this Agreement relates.

17. **Waiver.** No provision of this Agreement shall be waived by any act, omission or knowledge of a Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party.

18. **Insurance.**

18.1. From and after the commencement of Phase III Clinical Trials for the Product with respect to item (a) and from and after the first commercial sale with respect to item (b), each of BioMarin and Novasep shall obtain and maintain in effect, in a form and with insurers reasonably acceptable to the other Party (or if self-insured, to the other Party's reasonable satisfaction with such self insurance), and which shall name the other Party as an additional insured:

(a) commercial general liability insurance with a minimum limit of indemnity of Ten Million U.S. Dollars (US$10,000,000) per occurrence and in the aggregate; and

(b) product liability insurance with a minimum limit of liability of Twenty Million U.S. Dollars (US$20,000,000) per occurrence and in the aggregate. It is understood that such insurance shall not be construed to limit a Party's liability with respect to such indemnification obligations.

18.2. Each Party shall provide to the other Party upon request a certificate evidencing the insurance such Party is required to obtain and keep in force under this **Section 18**. Such certificate shall provide that such insurance shall not expire or be cancelled or modified without at least thirty (30) days' prior written notice to the other Party.

19. **Severability.** In the event that any provision of this Agreement is held by a court of competent jurisdiction to be unenforceable because it is invalid or in conflict with any law of any relevant jurisdiction, the validity of the remaining provision shall be not affected, and the Parties shall negotiate a substitute provision that, to the extent possible, accomplishes the original business purpose.

20. **Independent Contractors.** Each Party shall act as an independent contractor and shall not bind nor attempt to bind the other Party to any contract, or any performance of obligations outside of this Agreement. Nothing contained or done under this Agreement shall be interpreted as constituting either Party the agent of the other in any sense of the term whatsoever unless expressly so stated. Each Party shall be responsible for all taxes and payments concerning such Party, its employees or its sales representatives. This Agreement does not create or evidence any joint venture or partnership of the Parties.

21. **Force Majeure.** Neither Party shall be liable for its failure to perform hereunder as a result of any event of force majeure beyond the Party's reasonable control including, but not limited to, acts of God, fire, floods, wars, sabotage, terrorism, demonstrations, accidents, strikes, lockouts or other labor disputes, shortages, government actions or regulations, inability to obtain transportation, or changes to Applicable Laws. If either Party's performance is prevented in whole or part by any such event, such Party shall be excused of any of its obligations hereunder during the period of delay of performance resulting from such event, and the time for performance of such obligations shall be automatically extended for a period of time equal to the duration of such events; provided, however, that the Party claiming force majeure shall promptly notify the other Party of the existence of such force majeure, shall use commercially reasonable efforts to avoid or remedy such force majeure and shall continue performance hereunder with the utmost dispatch whenever such force majeure is avoided or remedied. When such circumstances arise, the Parties shall discuss what, if any, modification of the terms of this Agreement may be required in order to arrive at an equitable solution.

22. **Amendment.** No modification of this Agreement shall be effective unless made in writing and signed by a duly authorized representative of each Party. This Agreement may not be amended by a Purchase Order. No waiver of any right or remedy hereunder shall be effective unless in a writing signed by the Party to be bound, nor shall any waiver in once instance constitute a waiver of the same or any other right or remedy in any other instance.

23. **Governing Law.** This Agreement shall be governed by the laws of the State of New York, U.S.A. without giving effect to principles of conflicts of laws provisions thereof, and any legal action or other legal proceeding relating to this Agreement or the enforcement of any provision of this Agreement may be brought or otherwise commenced solely and exclusively in the state or federal court located in New York, New York. Consistent with the foregoing, each party to this Agreement:

23.1. expressly and irrevocably consents and submits to the jurisdiction of each state and federal court located in New York, New York (and each appellate court located in the State of New York) in connection with any such legal proceeding;

23.2. agrees that each state and federal court located in New York, New York shall be deemed to be a convenient forum; and

23.3. agrees not to assert (by way of motion, as a defense or otherwise), in any such legal proceeding commenced in any state or federal court located in New York, New York any claim that such Party is not subject personally to the jurisdiction of such court, that such legal proceeding has been brought in an inconvenient forum, that the venue of such proceeding is improper or that this Agreement or the subject matter of this Agreement may not be enforced in or by such court.

The Parties agree that, if any proceeding is commenced against any Indemnified Party by any person in or before any court or other tribunal anywhere in the world, then such Indemnified Party may proceed against the Indemnifying Party in or before such court or other tribunal with respect to any indemnification claim or other claim arising directly or indirectly from or relating directly or indirectly to such proceeding or any of the matters alleged therein or any of the circumstances giving rise thereto. The application of the UN Convention on Contracts for the International Sale of Goods (1980) is excluded.

24. **Arbitration**.

24.1. Any dispute, controversy or claim arising out of or relating to this Agreement or to a breach hereof, including its interpretation, performance or termination, shall be finally resolved by arbitration. The arbitration shall be conducted by three (3) arbitrators, one to be appointed by BioMarin, one to be appointed by Novasep, and the third to be nominated by the two arbitrators so selected or, if they cannot agree on the third arbitrator, by the President of the American Arbitration Association. In the event any such dispute, controversy or claim involves a claim of damages for fifty-thousand United States dollars ($50,000 U.S.) or less, the arbitration shall be conducted by one (1) arbitrator appointed by BioMarin and Novasep, or if they cannot agree on an arbitrator, by the President of the American Arbitration Association.

24.2. The arbitration shall be conducted in the English language and in accordance with the rules of the American Arbitration Association, which shall administer the arbitration and act as appointing authority. The arbitration, including the rendering of the award, shall take place in New York, New York in the United

States of America, and shall be the exclusive forum for resolving such dispute, controversy or claim. For the purposes of this arbitration, the provisions of this Agreement and all rights and obligations hereunder shall be governed and construed in accordance with the laws of the State of New York in the United States of America. The decision of the arbitrators shall be final and binding upon the Parties hereto. The decision of the arbitrators shall be executory, and judgment thereon may be entered by any court of competent jurisdiction.

24.3. Notwithstanding anything contained in this **Section 24** to the contrary, each Party shall have the right to institute judicial proceedings against the other Party or anyone acting by, through or under such other Party, in order to enforce the instituting Party's rights hereunder through reformation of contract, specific performance, injunction or similar equitable relief.

25. **Attorneys' Fees.** If any legal action or other legal proceeding relating to this Agreement, the transactions contemplated hereby or the enforcement of any provision of this Agreement is brought by one Party against the other Party, the prevailing Party shall be entitled to recover reasonable attorneys' fees, costs and disbursements (in addition to any other relief to which the prevailing Party may be entitled).

26. **Use of Names.** Both Parties agree that they will not use the name, trademark, trade name or other designation of the other Party or any of its personnel in any public announcements, publicity, promotional literature or advertising without the prior written approval of the other Party, such approval to be given or withheld in such Party's sole and absolute discretion; provided that, each Party may make such disclosure as is required by Applicable Laws, including, without limitation, the disclosure obligations under the Securities Act of 1933.

27. **Headings.** The descriptive headings of this Agreement are for convenience of reference only and shall be of no force or effect in construing or interpreting any of the provisions of this Agreement.

28. **Entire Agreement.** This Agreement is the entire agreement between BioMarin and Novasep regarding the subject matter hereof and shall supersede any prior agreements between the Parties hereto with the exception of the NDA. This Agreement becomes effective and binding on both Parties only when signed by each Party below. Each Party acknowledges that there are no other understandings that relate to the matters covered herein or which are inconsistent with any provisions of this Agreement.

29. **Conflict of Terms.** In the event of any inconsistency between this Agreement and any Exhibit, Purchase Order, or the Quality Agreement, the terms of this Agreement shall control.

30. **Notices.** Any notice required, contemplated or permitted to be given herein shall be deemed to have been sufficiently given to either Party for all of the purposes hereof if given by telephone, confirmed facsimile transmission, telex or cable and confirmed by

registered mail, or dispatched by a major national express courier service, postage prepaid and return receipt requested addressed as follows:

If to BioMarin:

BioMarin Pharmaceutical Inc.
105 Digital Drive
Novato, California 94949
Attention: Corporate Counsel
Facsimile No.: (415) 506-6425

If to Novasep:

Groupe Novase SAS Site Eiffel
Boulevard de la Moselle
Attention: Chief Legal Officer
Facsimile No.: + 33 (0)3 83 49 71 40

or to such other address as either of the Parties shall designate by notice given as herein required. Any such notice, instruction or communication shall be deemed to have been delivered upon receipt if delivered by hand, three business days after it is sent by registered or certified mail, return receipt requested, postage prepaid, one business day after it is sent via a reputable nationwide overnight courier service, or when transmitted with electronic confirmation of receipt, if transmitted by facsimile (if such transmission is on a business day; otherwise, on the next day following such transmission).

31. **Exhibits.** Exhibits to this Agreement shall be deemed to be an integral part hereof, and schedules or exhibits to such Exhibits shall be deemed to be an integral part thereof.

32. **Counterparts.** This Agreement may be executed in one or more counterparts, each of which shall be deemed an original but all of which together shall constitute one and the same instrument. Any photocopy, facsimile or electronic reproduction of the executed Agreement shall constitute an original.

33. **Approvals.** Unless expressly required not to be withheld unreasonably, it is understood that when approval of either Party is required, such approval may be given or withheld in such Party's sole and absolute discretion, without regard to the reason or basis for granting or withholding such consent.

34. **Construction**.

34.1 The English language of this Agreement shall govern any interpretation of or dispute regarding this Agreement

34.2 For purposes of this Agreement whenever the context requires: the singular number shall include the plural, and vice versa; the masculine gender shall include the feminine and neuter genders; the feminine gender shall include the masculine and neuter genders; and the neuter gender shall include the masculine and feminine genders.

34.3 The Parties hereto agree that any rule of construction to the effect that ambiguities are to be resolved against the drafting Party shall not be applied in the construction or interpretation of this Agreement.

34.4 As used in this Agreement, the words "include" and "including," and variations thereof, shall not be deemed to be terms of limitation, but rather shall be deemed to be followed by the words "without limitation."

34.5 Except as otherwise indicated, all references in this Agreement to "Sections" and "Exhibits" are intended to refer to Sections of this Agreement and Exhibits to this Agreement. Any reference to a Section shall be deemed to include a reference to any subsidiary Sections.

35. **Further Assurances.** From and after the Effective Date, each Party shall execute and deliver such documents and take such other actions, as such other Party may reasonably request, for the purpose of carrying out or evidencing any of the transactions contemplated hereby.

ACCEPTED AND AGREED TO:

GROUPE NOVASEP	BIOMARIN PHARMACEUTICAL INC.
/S/ ROGER-MARC NICOUD	/S/ ROBERT BAFFI
BY: MR. ROGER-MARC NICOUD	BY: ROBERT BAFFI
Its: CEO	Its: SVP TECHNICAL OPS

Attachments:

ExhibitA: Description of Drug substance

ExhibitB: Synthesis

ExhibitC: Product Specifications

ExhibitD: Price

ExhibitE: Novasep Supplied Raw Materials

ExhibitF: Non-Disclosure Agreement dated December 31, 2004

EXHIBIT A
DESCRIPTION OF DRUG SUBSTANCE

[****]

Exhibit B: Synthetic Pathway

[****]

EXHIBIT C
PRODUCT SPECIFICATIONS

[****]

21

EXHIBIT D
PRICE

[****]

22

EXHIBIT E

NOVASEP SUPPLIED RAW MATERIALS

[****]

EXHIBIT F

NON-DISCLOSURE AGREEMENT
DATED DECEMBER 31, 2004

[****]

Exhibit 21.1

Subsidiaries of BioMarin Pharmaceutical Inc.

Name	Jurisdiction of Incorporation
Glyko, Inc.	Delaware
BioMarin Acquisition (Nova Scotia) Company	Nova Scotia, Canada
Glyko Biomedical Ltd.	British Columbia
BioMarin Pharmaceutical Nova Scotia Company	Nova Scotia, Canada
BioMarin Genetics, Inc.	Delaware
BioMarin/Genzyme LLC	Delaware
BioMarin Holdings (Nova Scotia) Company	Nova Scotia, Canada
BioMarin Delivery Canada Inc.	Canada
BioMarin Pharmaceutical Delivery Nova Scotia Company	Nova Scotia, Canada
BioMarin Pharmaceutical (Canada) Inc.	Canada
BioMarin Holding (Lux) S.a.r.l.	Luxembourg
BioMarin Holding Ltd.	Ireland
BioMarin Europe Ltd.	Ireland
BioMarin Clinical Ltd.	United Kingdom

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
BioMarin Pharmaceutical Inc.:

We consent to the incorporation by reference in (i) the registration statements (Nos. 333-84787 and 333-85368) on Form S-8 and (ii) the registration statements (Nos. 333-116575, 333-102066 and 333-108972) on Form S-3 of BioMarin Pharmaceutical Inc. of our reports dated March 7, 2006, with respect to the consolidated balance sheets of BioMarin Pharmaceutical Inc. as of December 31, 2005 and 2004, and the related consolidated statements of operations, changes in stockholders' equity (deficit), and cash flows for each of the years in the three-year period ended December 31, 2005, and the related financial statement schedule, management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2005, and the effectiveness of internal control over financial reporting as of December 31, 2005, which reports appear in the December 31, 2005, annual report on Form 10-K of BioMarin Pharmaceutical Inc.

Our reports were based on our audits and the report of other auditors.

/s/ KPMG LLP

San Francisco, California
March 7, 2006

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-116575, 333-108972, 333-102066) and Form S-8 (No. 333-85368, 333-84787) of BioMarin Pharmaceutical Inc. of our report dated March 6, 2006 relating to the financial statements of BioMarin/Genzyme LLC, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 6, 2006

Exhibit 31.1

CERTIFICATION

I, Jean-Jacques Bienaimé, Chief Executive Officer, certify that:

1. I have reviewed this Annual Report on Form 10-K of BioMarin Pharmaceutical Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2006

/s/ JEAN-JACQUES BIENAIMÉ
Jean-Jacques Bienaimé
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Jeffrey H. Cooper, Chief Financial Officer, certify that:

1. I have reviewed this Annual Report on Form 10-K of BioMarin Pharmaceutical Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2006

/s/ JEFFREY H. COOPER
Jeffrey H. Cooper
Chief Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of BioMarin Pharmaceutical Inc. (the "Company") for the year ended December 31, 2005, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we, Jean-Jacques Bienaimé, as Chief Executive Officer of the Company, and Jeffrey H. Cooper, as Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ JEAN-JACQUES BIENAIMÉ
Jean-Jacques Bienaimé
Chief Executive Officer
March 7, 2006

/s/ JEFFREY H. COOPER
Jeffrey H. Cooper
Chief Financial Officer
March 7, 2006

Exhibit 99.1

BioMarin/Genzyme LLC
Consolidated Financial Statements

As of December 31, 2005 and 2004 (Unaudited)
and For the Years Ended December 31, 2005, 2004 (Unaudited) and 2003

BioMarin/Genzyme LLC
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Steering Committee of BioMarin/Genzyme LLC:

In our opinion, the accompanying consolidated balance sheet as of December 31, 2005, and the related consolidated statements of operations, of cash flows and of changes in Venturers' capital present fairly, in all material respects, the financial position of BioMarin/Genzyme LLC (the "LLC") at December 31, 2005, and the results of its operations and its cash flows for the years ended December 31, 2005 and 2003 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the LLC's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements 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, assessing the accounting principles used and significant estimates made by the LLC's management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 6, 2006

BioMarin/Genzyme LLC
Consolidated Balance Sheets
(Amounts in thousands)

	December 31,	
	2005	2004
		(Unaudited)
ASSETS		
Current assets:		
Cash and cash equivalents	$ 8,127	$ 14,351
Accounts receivable, net	20,725	16,710
Due from Genzyme Corporation	12,746	—
Inventories	30,286	38,626
Prepaid expenses and other current assets	220	—
Total current assets	72,104	69,687
Technology license fees, net	285	—
Total assets	$72,389	$ 69,687
LIABILITIES AND VENTURERS' CAPITAL		
Current liabilities:		
Due to BioMarin Companies	$ 1,070	$ 2,160
Due to Genzyme Corporation	—	6,212
Accrued expenses	4,827	2,921
Deferred revenue	573	458
Total liabilities	6,470	11,751
Commitments and contingencies (Note I)	—	—
Venturers' capital:		
Venturers' capital – BioMarin Companies	32,960	28,968
Venturers' capital – Genzyme Corporation	32,959	28,968
Total Venturers' capital	65,919	57,936
Total liabilities and Venturers' capital	$72,389	$ 69,687

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

BioMarin/Genzyme LLC
Consolidated Statements of Operations
(Amounts in thousands)

	For the Years Ended December 31,		
	2005	2004	2003
		(Unaudited)	
Revenues:			
Net product sales	$76,417	$ 42,583	$ 11,540
Operating costs and expenses:			
Cost of products sold	24,513	14,954	4,723
Selling, general and administrative	22,019	26,872	21,829
Research and development	16,156	20,191	14,738
Total operating costs and expenses	62,688	62,017	41,290
Income (loss) from operations	13,729	(19,434)	(29,750)
Interest income	254	151	71
Net income (loss)	$13,983	$(19,283)	$(29,679)
Net income (loss) attributable to each Venturer:			
BioMarin Companies	$ 6,992	$ (9,641)	$(14,840)
Genzyme Corporation	$ 6,991	$ (9,642)	$(14,839)

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

BioMarin/Genzyme LLC
Consolidated Statements of Cash Flows
(Amounts in thousands)

	For the Years Ended December 31,		
	2005	2004	2003
		(Unaudited)	
Cash Flows from Operating Activities:			
Net income (loss)	$ 13,983	$ (19,283)	$(29,679)
Reconciliation of net income (loss) to net cash provided by (used in) operating activities:			
Amortization expense	73	—	—
Noncash charge for inventory write down	—	—	2,800
Increase (decrease) in cash from working capital changes:			
Accounts receivable	(4,015)	(11,287)	(5,423)
Inventories	8,340	(1,349)	(22,792)
Prepaid expenses and other current assets	(220)	—	—
Due from (to) BioMarin Companies	(1,090)	(1,891)	1,914
Due from (to) Genzyme Corporation	(18,958)	(652)	4,094
Accrued expenses	1,906	1,745	1,076
Deferred revenue	115	391	67
Cash flows from operating activities	134	(32,326)	(47,943)
Cash Flows from Investing Activities:			
Purchase of technology licenses	(358)	—	—
Cash flows from investing activities	(358)	—	—
Cash Flows from Financing Activities:			
Capital distribution to BioMarin Companies	(3,000)	—	—
Capital distribution to Genzyme Corporation	(3,000)	—	—
Capital contributed by BioMarin Companies	—	16,045	25,943
Capital contributed by Genzyme Corporation	—	16,046	25,942
Cash flows from financing activities	(6,000)	32,091	51,885
(Decrease) increase in cash and cash equivalents	(6,224)	(235)	3,942
Cash and cash equivalents at beginning of period	14,351	14,586	10,644
Cash and cash equivalents at end of period	$ 8,127	$ 14,351	$ 14,586

Supplemental disclosure of noncash transaction:
Funding Receivable – Note D.

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

BioMarin/Genzyme LLC
Consolidated Statements of Changes in Venturers' Capital
(Amounts in thousands)

	Venturers' Capital		
	BioMarin Companies	Genzyme Corporation	Total Venturers' Capital
Balance at December 31, 2002	$ 11,461	$ 11,461	$ 22,922
2003 capital contributions	27,881	27,880	55,761
2003 net loss	(14,840)	(14,839)	(29,679)
Balance at December 31, 2003	24,502	24,502	49,004
2004 capital contributions (unaudited)	14,107	14,108	28,215
2004 net loss (unaudited)	(9,641)	(9,642)	(19,283)
Balance at December 31, 2004 (unaudited)	28,968	28,968	57,936
2005 capital distributions	(3,000)	(3,000)	(6,000)
2005 net income	6,992	6,991	13,983
Balance at December 31, 2005	$ 32,960	$ 32,959	$ 65,919

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

BioMarin/Genzyme LLC
Notes to Consolidated Financial Statements

A. Nature of Business and Organization

BioMarin/Genzyme LLC, or the Joint Venture, is a limited liability company organized under the laws of the State of Delaware. The Joint Venture is owned:

- 50% by BioMarin Pharmaceutical Inc., which is referred to as BioMarin, and BioMarin Genetics, Inc., a wholly-owned subsidiary of BioMarin. BioMarin and its subsidiary are referred to as the BioMarin Companies; and
- 50% by Genzyme Corporation, which is referred to as Genzyme.

The BioMarin Companies and Genzyme are collectively referred to as the Venturers and individually as a Venturer. The Joint Venture was organized in September 1998 to develop and commercialize Aldurazyme®, a recombinant form of the human enzyme alpha-L-iduronidase, used to treat a lysosomal storage disorder known as mucopolysaccharidosis I, or MPS I. The Joint Venture commenced operations as of September 4, 1998.

The Joint Venture, BioMarin Companies and Genzyme entered into a Collaboration Agreement dated as of September 4, 1998. Under the terms of the Collaboration Agreement, Genzyme and the BioMarin Companies granted to the Joint Venture a world-wide, exclusive, irrevocable, royalty-free right and license or sublicense to develop, manufacture and market Aldurazyme for the treatment of MPS I and other alpha-L-iduronidase deficiencies. All program-related costs are equally funded by BioMarin, on behalf of the BioMarin Companies, and Genzyme. BioMarin and Genzyme are required to make monthly capital contributions to the Joint Venture to fund budgeted operating costs. If either BioMarin or Genzyme fails to make all or two or more of the monthly capital contribution, and the other party does not exercise its right to terminate the Collaboration Agreement or compel performance of the funding obligation, the defaulting party's (or, in the case of default by BioMarin, the BioMarin Companies') percentage interest in the Joint Venture and future funding responsibility will be adjusted proportionately. No contributions were made in 2005 because the Joint Venture was profitable.

The Steering Committee of the Joint Venture serves as the governing body of the Joint Venture and is responsible for determining the overall strategy for the program, coordinating activities of the Venturers as well as performing other such functions as appropriate. The Steering Committee is comprised of an equal number of representatives of each Venturer.

On April 30, 2003, the United States Food and Drug Administration, commonly referred to as the FDA, granted marketing approval for Aldurazyme as an enzyme replacement therapy for patients with the Hurler and Hurler-Scheie forms of MPS I, and Scheie patients with moderate to severe symptoms. Aldurazyme has been granted orphan drug status in the United States, which generally provides seven years of market exclusivity. On June 11, 2003, the European Commission granted marketing approval for Aldurazyme to treat the non-neurological manifestations of MPS I in patients with a confirmed diagnosis of the disease. Aldurazyme has been granted orphan drug status in the European Union, which generally provides ten years of market exclusivity.

On behalf of the Joint Venture, Genzyme is commercializing Aldurazyme in the United States, Canada, the European Union, Latin America and the Asia Pacific regions. Genzyme continues to launch Aldurazyme in additional countries in the European Union, Latin America and the Asia Pacific regions on a country-by-country basis as pricing and reimbursement approvals are obtained. Aldurazyme is manufactured at BioMarin's facility in Novato, California and is sent to either Genzyme's manufacturing facility in Allston, Massachusetts or to a third-party facility for the final fill-finish process.

B. Summary of Significant Accounting Policies

Basis of Presentation

The Joint Venture is considered a partnership for federal and state income tax purposes. As such, items of income, loss, deductions and credits flow through to the Venturers. The Venturers have responsibility for the payment of any income taxes on their proportionate share of the taxable income of the Joint Venture. The Joint Venture has reclassified certain 2004 data to conform to its 2005 presentation.

For the year ended December 31, 2003, the Joint Venture qualified as a significant subsidiary to both BioMarin and Genzyme and, as a result, audited consolidated financial statements are presented for that period. As of December 31, 2004 and for the year ended December 31, 2004, the Joint Venture does not meet the criteria of a significant subsidiary to either BioMarin or Genzyme and, as a result, the consolidated financial statements for those periods have not been audited. As of December 31, 2005 and for the year ended December 31, 2005, the Joint Venture does not meet the criteria of a significant subsidiary to either BioMarin or Genzyme. However, the books and records for the Joint Venture are maintained by Genzyme and because KPMG LLP, as auditors to BioMarin, will rely on the opinion of PricewaterhouseCoopers LLP, as auditors to the Joint Venture and Genzyme, the consolidated financial statements for those periods have been audited.

B. Summary of Significant Accounting Policies (Continued)

Accounting Method

The financial statements have been prepared under the accrual method of accounting in conformity with accounting principles generally accepted in the United States of America.

Fiscal Year End

The Venturers have determined that the fiscal year end of the Joint Venture is December 31.

Uncertainties

The Joint Venture is subject to risks common to companies in the biotechnology industry, including:

- the ability of the Joint Venture to manufacture sufficient amounts of its products for development and commercialization activities;
- the accuracy of the Joint Venture's estimates of the size and characteristics of markets to be addressed by the Joint Venture's products;
- market acceptance of the Joint Venture's products;
- the Joint Venture's ability to obtain reimbursement for its products from third-party payors, where appropriate;
- the accuracy of the Joint Venture's information concerning the products and resources of competitors and potential competitors;
- the Joint Venture's ability to successfully obtain timely additional regulatory approvals and adequate patent and other proprietary rights protection for its products; and
- the content and timing of decisions made by the FDA and other regulatory agencies regarding the Joint Venture's products and manufacturing facilities.

Use of Estimates

Under accounting principles generally accepted in the United States of America, the Joint Venture is required to make certain estimates and assumptions that affect reported amounts of assets, liabilities, revenues, expenses, and disclosure of contingent assets and liabilities in its financial statements. The Joint Venture's actual results could differ from these estimates.

Cash and Cash Equivalents

Cash and cash equivalents, consisting principally of money market funds with initial maturities of three months or less, are valued at cost plus accrued interest, which approximates fair market value. All of the Joint Venture's cash is held on deposit at one financial institution.

Inventories

Inventories are valued at cost or, if lower, fair value. The Venturers determine the cost of raw materials using the average cost method and the cost of work in process and finished goods using the specific identification method. The Venturers analyze the Joint Venture's inventory levels quarterly and write down to its net realizable value:

- inventory that has become obsolete;
- inventory that has a cost basis in excess of its expected net realizable value;
- inventory in excess of expected requirements; and
- expired inventory.

B. Summary of Significant Accounting Policies (Continued)

Inventories (continued)

The Joint Venture capitalizes inventory produced for commercial sale, which may result in the capitalization of inventory that has not yet been approved for sale. If a product is not approved for sale, it would likely result in the write off of the inventory and a charge to earnings. At December 31, 2005 and 2004 (unaudited), all of the Joint Venture's inventories are related to Aldurazyme, a product approved for sale.

Comprehensive Loss

The Joint Venture reports comprehensive income (loss) in accordance with Financial Accounting Standards Board, or FASB, Statement of Financial Accounting Standards, or SFAS, No. 130, "Reporting Comprehensive Income." The Comprehensive income (loss) for the years ended December 31, 2005, 2004 (unaudited) and 2003 does not differ from the reported net income (loss).

Transactions with Affiliates

Genzyme is commercializing Aldurazyme in the United States, Canada, the European Union, Latin America and the Asia Pacific regions and, as a result, conducts sales and collects cash from product sales in those territories on behalf of the Joint Venture. The majority of the Joint Venture's operating expenses consist of project expenses incurred by the Venturers, either for internal operating costs or for third-party obligations incurred by the Venturers on behalf of the Joint Venture which are then charged to the Joint Venture. All charges to the Joint Venture are subject to approval by the Steering Committee. The determination of the amount of internal operating costs incurred by each Venturer on behalf of the Joint Venture requires significant judgment by each Venturer. As a result, the financial statements for the Joint Venture may not be indicative of the results that would have occurred had the Joint Venture obtained all of its manufacturing, commercialization and research and development services from third-party entities. Genzyme Corporation owed the Joint Venture $12.7 million at December 31, 2005 consisting of cash received on behalf of the Joint Venture for net product sales, net of project expenses incurred on behalf of the Joint Venture. The Joint Venture owed BioMarin Companies a total of $1.1 million at December 31, 2005 for project expenses incurred on behalf of the Joint Venture. The Joint Venture owed a total of $8.4 million at December 31, 2004 (unaudited) to the Venturers primarily for project expenses incurred on behalf of the Joint Venture.

Translation of Foreign Currencies

The Joint Venture translates the financial transactions performed by Genzyme's foreign subsidiaries on behalf of the Joint Venture from local currency into U.S. dollars using the average exchange rate prevailing during each period. The Joint Venture includes any gains and losses on these transactions in selling, general and administrative expenses in its results of operations. Selling, general and administrative expenses includes foreign currency transaction net losses of approximately $2.5 million in 2005 and net gains of approximately $341,000 in 2004 (unaudited) and $16,500 in 2003.

Revenue Recognition

The Joint Venture recognizes revenue from 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. Revenue transactions are evidenced by customer purchase orders, customer contracts in certain instances, invoices and related shipping documents.

The timing of product shipments and receipts can have a significant impact on the amount of revenue that the Joint Venture recognizes in a particular period. Also, Aldurazyme is sold in part through distributors. Inventory in the distribution channel consists of inventory held by distributors, who are the Joint Venture's customers, and inventory held by retailers, such as pharmacies and hospitals. The Joint Venture's revenue in a particular period can be impacted by increases or decreases in distributor inventories. If distributor inventories increased to excessive levels, the Joint Venture could experience reduced purchases in subsequent periods. To determine the amount of Aldurazyme inventory in the Joint Venture's U.S. distribution channel, the Joint Venture receives data on sales and inventory levels directly from its primary distributors for the product. As of December 31, 2005, the Joint Venture believes the amount of Aldurazyme inventory held by U.S. distributors is sufficient to meet the current forecast of demand for the product in the United States.

The Joint Venture records reserves for rebates payable under Medicaid and payor contracts, such as managed care organizations, as a reduction of revenue at the time product sales are recorded. The Joint Venture's Medicaid and payor rebate reserves have two components:

- an estimate of outstanding claims for end-user sales that have occurred, but for which related claim submissions have not been received; and
- an estimate of future claims that will be made when inventory in the distribution channel is sold to end-users.

B. Summary of Significant Accounting Policies (Continued)

Revenue Recognition (Continued)

Because the second component is calculated based on the amount of inventory in the distribution channel, the Joint Venture's assessment of distribution channel inventory levels impacts its estimated reserve requirements. The Joint Venture's calculation also requires other estimates, including estimates of sales mix, to determine which sales will be subject to rebates and the amount of such rebates. The Joint Venture updates its estimates and assumptions each period and records any necessary adjustments to its reserves. Accrued expenses for the Joint Venture includes a reserve for Medicaid and payor rebates payable of $1.6 million at December 31, 2005 and $0.5 million at December 31, 2004 (unaudited).

The Joint Venture 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:

- the nature of Aldurazyme. Aldurazyme serves as a treatment, rather than a cure, for MPS I and, therefore, must be administered/infused to the patient on a weekly basis. Aldurazyme treats a small patient population, and the Joint Venture has insight into the patients receiving treatment. In addition, Aldurazyme has been granted Orphan Drug status in the United States and European Union. As a result, Aldurazyme is not currently subject to significant external risk factors such as technological obsolescence or competition;
- the customers' limited return rights. Due to the nature, purpose and means of use of Aldurazyme, customers do not have the right to return the product in the ordinary course of business, other than for defects. Aldurazyme, like all biotechnology products, must meet stringent FDA regulations and therefore is subjected to strict quality testing before it is sold. As a result, the Joint Venture expects the incidence of defects to be de minimus. Coupled with the inability to return the product, there is a high cost to the product which deters Aldurazyme customers from carrying significant amounts of inventory;
- the Joint Venture and Genzyme's experience of returns for similar products. Genzyme has extensive experience with other lysosomal storage disorder products in the market, similar to Aldurazyme. These products are marketed and distributed through similar means and to similar customers. Genzyme's experience with these products is directly applicable to Aldurazyme and supports the Joint Venture's conclusions related to returns; and
- the Joint Venture's estimate of distribution channel inventory, based on sales and inventory level information provided by the primary distributors for Aldurazyme, as described above.

Based on these factors, the Joint Venture has concluded that product returns will be minimal and therefore, an allowance for product returns for Aldurazyme is not necessary at December 31, 2005 or 2004 (unaudited). In the future, if any of these factors and/or the history of product returns changes, an allowance for product returns may be required.

Emerging Issues Task Force Issue No. 01-09, "Accounting for Consideration Given by a Vendor to a Customer or a Reseller of the Vendor's Products," specifies that cash consideration (including a sales incentive) given by a vendor to a customer is presumed to be a reduction of the selling prices of the vendor's products or services and, therefore, should be characterized as a reduction of revenue. That presumption is overcome and the consideration should be characterized as a cost incurred if, and to the extent that, both of the following conditions are met:

- the vendor receives, or will receive, an identifiable benefit (goods or services) in exchange for the consideration; and
- the vendor can reasonably estimate the fair value of the benefit received.

The Joint Venture records fees paid to its distributors for services as operating expense where the criteria set forth above are met. The fees incurred for these services were approximately $822,000 in 2005, $960,000 in 2004 (unaudited) and $497,000 in 2003.

Research and development

Research and development costs are expensed in the period incurred. These costs are primarily comprised of development efforts performed by the Venturers or payments to third parties made by the Venturers, both on behalf of the Joint Venture, during the respective periods.

Income Taxes

The Joint Venture is organized as a pass-through entity and accordingly, the consolidated financial statements do not include a provision for income taxes. Taxes, if any, are the liability of the BioMarin Companies and Genzyme, as Venturers.

B. Summary of Significant Accounting Policies (Continued)

Recent Accounting Pronouncements

In October 2005, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards, or SFAS, No. 151, "Inventory Costs, and Amendment of ARB No. 43, Chapter 4." SFAS No. 151 which clarifies that abnormal amounts of idle facility expense, freight, handling costs, and wasted material (spoilage) should be recognized as current period charges in all circumstances. SFAS No. 151 is effective for inventory costs incurred during fiscal years beginning after June 15, 2005. The Joint Venture adopted SFAS No. 151 effective January 1, 2006, and does not believe the adoption of SFAS No. 151 will have a material impact on its financial position or results of operations.

In May 2005, the FASB issued SFAS No. 154, "Accounting Changes and Error Corrections, a replacement of APB Opinion No. 20 and FASB Statement No. 3." SFAS No. 154 applies to all voluntary changes in accounting for and reporting of changes in accounting principles and requires retrospective application to prior periods' financial statements of a voluntary change in accounting principles unless it is not practical to do so. Accounting Principles Board, or APB, Opinion No. 20, "Accounting Changes," previously required that most voluntary changes in accounting principles be recognized by including in net income (loss) of the period of the change, the cumulative effect of changing to the new accounting principle. SFAS No. 154 also requires that a change in depreciation, amortization, or depletion method for long-lived non-financial assets be accounted for as a change in accounting estimate affected by a change in accounting principle. SFAS No. 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. The Joint Venture does not expect the adoption of SFAS No. 154 to have a material impact on its financial position or results of operations.

C. Accounts Receivable

The Joint Venture's trade receivables primarily represent amounts due from distributors and healthcare service providers. The Joint Venture states accounts receivable at fair value, after reflecting an allowance for doubtful accounts for estimated losses resulting from the inability of its customers to make payments. The Joint Venture believes that its credit risk associated with trade receivables is mitigated by the following factors:

- the product is sold to a number of customers over a broad geographic range;
- the Joint Venture performs credit evaluations of its customers on an ongoing basis; and
- the Joint Venture performs a detailed, monthly review of the receivable aging and specific customer balances.

The Joint Venture did not record an allowance for doubtful accounts at either December 31, 2005 or 2004 (unaudited). To-date, due to the customers' credit worthiness, the monthly review of the receivable balances and the customers' need to maintain a supply of Aldurazyme and Genzyme's similar products, the Joint Venture has not written-off any receivables and no allowance for doubtful accounts has been necessary. In the future, if the financial condition of any of the Joint Venture's customers were to deteriorate and result in an impairment of the customer's ability to make payments, an allowance for doubtful accounts may be required.

D. Funding Receivable

At December 31, 2003, both Venturers had not provided their funding commitments for December 2003 and, as a result, the Joint Venture recorded funding receivable from each Venturer of $1.9 million. Both Venturers paid their December 2003 funding commitments in January 2004 (unaudited). There were no funding amounts receivable from the Venturers at December 31, 2004 (unaudited) or December 31, 2005.

E. Inventories (amounts in thousands)

	December 31,	
	2005	2004
		(Unaudited)
Raw materials	$ 1,082	$ 2,155
Work in process – bulk material	10,424	15,451
Finished products	18,780	21,020
Total	$30,286	$ 38,626

E. Inventories (Continued)

The Joint Venture capitalizes inventory produced for commercial sale, which may result in the capitalization of inventory that has not yet been approved for sale. If a product is not approved for sale, it would likely result in the write off of the inventory and a charge to earnings. At December 31, 2005 and 2004 (unaudited), all of the Joint Venture's inventories are related to Aldurazyme, a product approved for sale.

F. Technology License Fees

In 2005, the Joint Venture paid approximately $358,000 for technology license fees, which will be amortized over their estimated useful lives, which range from approximately four to five years. Total amortization expense for the Joint Venture's technology license fees was approximately $73,000 for the year ended December 31, 2005.

The estimated future amortization expense for the Joint Venture's technology license fees for the four succeeding fiscal years is as follows:

Year Ended December 31,	Estimated Amortization Expense
2006	$ 73,575
2007	$ 73,575
2008	$ 73,575
2009	$ 63,906

G. Accrued Expenses:

Accrued expenses consist of the following (amounts in thousands):

	December 31,	
	2005	2004
		(Unaudited)
Royalties	$3,032	$ 2,095
Rebates	1,597	544
Other	198	282
Total accrued expenses	$4,827	$ 2,921

H. Venturers' Capital

In 2005, the Joint Venture distributed a total of $3.0 million of cash to each Venturer in accordance with the terms of the Collaboration Agreement.

As of December 31, 2005, Venturers' capital is comprised of capital contributions made by the Venturers to fund budgeted costs and expenses of the Joint Venture in accordance with the Collaboration Agreement and income (losses) allocated to the Venturers, net of cash distributions to the Venturers. All funding is shared equally by the two Venturers. As of December 31, 2005, the BioMarin Companies and Genzyme have each provided a total of $104.2 million of funding to the Joint Venture, net of $3.0 million of cash distributed by the Joint Venture to each Venturer. The Venturers did not make any capital contributions to the Joint Venture in 2005 because the Joint Venture had sufficient cash to meet its financial obligations.

I. Commitments and Contingencies

The Joint Venture may become subject to legal proceedings and claims arising in connection with its business. There were no asserted claims against the Joint Venture as of December 31, 2005.

J. Segment Information

The Joint Venture operates in one business segment—human therapeutics. Disclosures about revenues by geographic area and revenues from major customers are presented below.

The following table contains revenue information by geographic area (amounts in thousands):

	For the Years Ended December 31,		
	2005	2004	2003
		(Unaudited)	
Revenues:			
US	$20,408	$ 12,568	$ 4,499
Europe	49,189	27,468	6,881
Other	6,820	2,547	160
Total	$76,417	$ 42,583	$11,540

The Joint Venture's results of operations are solely dependent on sales of Aldurazyme. BioMarin manufactures Aldurazyme at a single manufacturing facility in Novato, California. The fill-finish process is completed at either Genzyme's manufacturing facility in Allston, Massachusetts or at a third party. The percentage of sales of Aldurazyme to distributors, as compared to total revenues in 2005, 2004 (unaudited) and 2003, were as follows:

	% of Total Revenues		
	2005	2004	2003
		(Unaudited)	
Sales to U.S. distributors	11%	12%	19%
Sales to European distributors	6%	6%	9%
Sales to Other distributors	3%	0%	0%
Total sales to distributors	20%	18%	28%

Sales of Aldurazyme to a single U.S. distributor were 6% in 2005, 7% in 2004 (unaudited) and 12% in 2003 of total revenues.