BIOMARIN PHARMACEUTICAL INC
Form 424B5
March 24, 2006
Table of Contents

Filed Pursuant to Rule 424(b)(5).

A filing fee of $14,396.85, calculated in accordance with

Rule 457(r), has been transmitted to the SEC in connection

with the securities offered from the registration statement

(File No. 333-132566) by means of this prospectus supplement.

PROSPECTUS SUPPLEMENT

(To Prospectus dated March 20, 2006)

9,000,000 Shares

Common Stock

We are offering 9,000,000 shares of our common stock.

The shares are quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN . On March 23, 2006, the last sale price of the shares as reported on the Nasdaq National Market was $13.13 per share.

We are concurrently offering $150,000,000 principal amount, or $172,500,000 principal amount if the underwriter exercises its overallotment option in full, of senior subordinated convertible notes due 2013 pursuant to a separate prospectus supplement.

Investing in our common stock involves risks, including those described in the Risk Factors section beginning on page S-8 of this prospectus supplement.

	Per Share	Total
Public offering price	$13.00	$117,000,000
Underwriting discount	$.65	$5,850,000
Proceeds, before expenses, to us	$12.35	$111,150,000

The underwriters may also purchase up to an additional 1,350,000 shares of common stock from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover overallotments, if any.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about March 29, 2006.

Merrill Lynch & Co.

Cowen & Company
Leerink Swann & Company
Pacific Growth Equities, LLC

Rodman & Renshaw

The date of this prospectus supplement is March 23, 2006.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

Prospectus

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference therein. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date on those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, when making your investment decision. You should also read and consider the information in the documents we have referred you to in the sections of the prospectus entitled Where You Can Find More Information and Information Incorporated by Reference.

General information about us can be found on our website at http://www.BMRN.com . The information on our website is for information only and should not be relied on for investment purposes. The information on our website is not incorporated by reference into either this prospectus supplement or the accompanying prospectus and should not be considered part of this or any other report filed with the Securities and Exchange Commission.

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission (SEC), utilizing a shelf registration process. This prospectus supplement provides you with the specific details regarding this offering, including the price, the amount of common stock being offered and the risks of investing in our common stock. The accompanying prospectus provides you with more general information, some of which does not apply to the offering of our common stock. To the extent information in this prospectus supplement is inconsistent with the accompanying prospectus or any of the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, you should rely on this prospectus supplement. You should read and consider the information in both this prospectus supplement and the accompanying prospectus together with the additional information described under the headings Where You Can Find More Information and Information Incorporated by Reference .

This prospectus supplement and the accompanying prospectus have not been approved by the Financial Services Authority. The shares may not be offered or sold to any person in the United Kingdom except where the offer is exempt from the general prohibition against the offer of securities to the public under section 85 of the Financial Services and Markets Act 2000 (FMSA) by virtue of one or more of the criteria set out in section 86 of FMSA.

This prospectus supplement and the accompanying prospectus is directed only at (i) persons outside the United Kingdom, (ii) persons who have professional experience in matters relating to investments and who are investment professionals within the meaning of Article 19(5) of FMSA (Financial Promotion) Order 2005 of the United Kingdom (the Financial Promotion Order), (iii) persons who fall within Article 49(2)(a) through (d) (high net worth companies, unincorporated associations, etc.) of the Financial Promotion Order, or (iv) any other persons to whom this prospectus supplement and the accompanying prospectus for the purposes of Section 21 of FSMA can otherwise lawfully be made (all such persons together being referred to as Relevant Persons), and must not be acted on or relied upon by persons other than Relevant Persons.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus, the prospectus supplement or any document incorporated by reference in this prospectus or any prospectus supplement regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects and plans and objectives of management are forward-looking statements.

Forward-looking statements include, but are not limited to, statements about:

- our expectations with respect to regulatory submissions and approvals and our clinical trials;
- our expectations with respect to our collaborations with Serono S.A. (Serono) and Genzyme Corporation (Genzyme); and
- our estimates regarding our capital requirements and our need for additional financing.

The words anticipates , believes , estimates , expects , intends , may , plans , projects , will , would and similar expressions are inte forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. We have identified some of the important factors that could cause future events to materially differ from our current expectations and they are described in this prospectus supplement under the caption Risk Factors as well as in our most recent Annual Report on Form 10-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statement.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement. This summary does not contain all the information that you should consider before investing in our common stock. You should read the entire prospectus supplement and the accompanying prospectus carefully, including Risk Factors , the financial statements and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making an investment decision. This prospectus supplement contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from the results anticipated in these forward-looking statements as a result of factors described under the Risk Factors section and elsewhere in this prospectus supplement. Unless the context otherwise requires, any reference to BioMarin, we, our and us in this prospectus supplement refers to BioMarin Pharmaceutical Inc., and its subsidiaries.

BioMarin Pharmaceutical Inc.

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 two approved products and multiple investigational product candidates. Approved products include Aldurazyme® (laronidase) and Naglazyme (galsulfase). Additionally, we have rights to receive payments and royalties related to Orapred® (see Recent Developments Orapred License Agreement).

Marketed Products

Aldurazyme

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). Aldurazyme has been granted orphan drug exclusivity 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. Aldurazyme net revenue recorded by our joint venture for 2005 totaled $76.4 million, compared to $42.6 million for 2004.

Naglazyme

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 exclusivity 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.

Table of Contents

Products in Development

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.

Phenoptin

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 clinical trial, which began in April 2005. The Phase 3 clinical trial of Phenoptin was a six-week, multi-center, international, double-blind, placebo-controlled study. On March 15, 2006, we announced positive results from the Phase 3 clinical trial (see Recent Developments Phase 3 Phenoptin Data). 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. If Phenoptin is approved for marketing, it 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. We believe that 30% to 50% of those with PKU 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 Phenylalanine (Phe). Phe is an amino acid found in 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.

In May 2005, the Company entered into an agreement with Serono for the further development and commercialization of Phenoptin and Phenylase for PKU, and 6R-BH_4, the active ingredient in Phenoptin, for other diseases including those associated with 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.

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 Programs

We are evaluating other therapies for serious medical conditions including Phenylase and Vibrilase (vibriolysin).

Table of Contents

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.

Vibrilase is 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.

Recent Developments

Phase 3 Phenoptin Data

On March 15, 2006, Serono and we announced positive results of a Phase 3, double-blind, placebo-controlled clinical study of Phenoptin for the treatment for PKU. Results confirmed that all pre-specified primary and secondary endpoints were met and data from the Phase 3 study demonstrate a statistically significant reduction at six weeks in blood Phe levels in patients receiving Phenoptin, compared with those receiving placebo.

Following the six-week double-blind study, patients were eligible to enroll into an on-going 22 week Phase 3 open-label extension study designed to further evaluate the long-term safety and efficacy of Phenoptin, as well as dose titration. Serono and we expect to file marketing authorization applications for Phenoptin for PKU in the U.S. and E.U. in 2007. We have licensed to Serono exclusive rights for Phenoptin outside of the U.S. and Japan.

The Phase 3 study enrolled 89 patients with elevated blood Phe levels aged eight years and above at 29 sites in the U.S., Europe and Canada. All patients demonstrated a reduction in blood Phe levels (approximately 30% or more) following treatment with Phenoptin in a Phase 2 screening study.

The patients were randomly assigned to receive placebo or 10 mg/kg of Phenoptin daily for six weeks. Patients were evaluated every two weeks for changes in blood Phe levels and adverse events. The primary endpoint of the study was the difference in mean blood Phe levels between the placebo and Phenoptin groups at Week 6, adjusted for baseline levels. A total of 87 patients completed six weeks of treatment.

Results from the Phase 3 double-blind study are summarized below:

Primary Endpoint

Patients treated with Phenoptin for six weeks had a mean decrease in blood Phe level of 236 μM (29%) compared to an increase of 3 μM (3%) in the placebo group ($p<0.0001$). Prior to treatment, patients in the Phenoptin group and placebo group had mean blood Phe levels of 843 μM and 888 μM, respectively.

Secondary Endpoints

At Week 6, the percentage of patients in the Phenoptin group with blood Phe levels less than or equal to 600 μM was 54% compared to 23% in the placebo group ($p=0.004$). At baseline the proportions were 17% and 19% for the Phenoptin and placebo groups, respectively.

Table of Contents

The mean blood Phe level at each visit among patients receiving Phenoptin showed a consistent reduction compared to the blood Phe levels in patients receiving placebo ($p<0.001$) throughout the six-week period.

The type and incidence of adverse events was similar in the Phenoptin and placebo groups. Phenoptin was generally well tolerated and investigators reported no serious adverse events occurred.

Orapred License Agreement

On March 15, 2006, we entered into an agreement with Alliant Pharmaceuticals (Alliant) pursuant to which we licensed to Alliant exclusive North American rights to the Orapred (prednisolone sodium phosphate oral solution) product line, including Orapred ODT (prednisolone sodium phosphate orally disintegrating tablets).

Under the terms of the agreement, Alliant paid us $2.5 million upon signing of the definitive agreement and will make milestone payments of up to $15.5 million contingent primarily on the approval and commercial launch of Orapred ODT in the U.S., both of which are anticipated to occur in the second half of 2006. Upon approval and commercial launch of Orapred ODT in the U.S., we will be required to make milestone payments of $3.2 million to a third party. Alliant will pay us royalties ranging from 25% to 30% on net sales of Orapred ODT, net of royalties owed to a third party, in exchange for the exclusive rights to commercialize Orapred products in North America. We have retained commercial rights outside of North America.

Net sales of Orapred, including the branded and authorized generic products, for the 12 months ended December 31, 2005 were $6.9 million.

Orapred ODT, a new formulation of Orapred currently under review by the FDA, utilizes a proprietary orally disintegrating tablet technology to provide a taste-masked, non-refrigerated and easy-to-administer formulation of prednisolone. In August 2005, we filed a New Drug Application for Orapred ODT with the FDA. Pursuant to the Prescription Drug User Fee Act, we expect that the FDA will take action on the application by June 1, 2006. If approved, Orapred would be the first orally disintegrating tablet corticosteroid dosage form available in the U.S.

Company Information

Our principal executive offices are located at 105 Digital Drive, Novato, California 94949 and our telephone number is (415) 506-6700. BioMarin, Naglazyme, Phenoptin, Vibrilase, and Phenylase are our trademarks. Aldurazyme is a registered trademark of BioMarin/Genzy LLC. Orapred is a registered trademark of Medicis Pediatrics, Inc., and is used under license. All other service marks and all brand names or trademarks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective holders.

Concurrent Convertible Note Offering

Concurrently with this offering of common stock, we are offering $150,000,000, or $172,500,000 if the underwriter exercises its overallotment option in full, aggregate principal amount of senior subordinated convertible notes due 2013 to the public, which we refer to herein as the convertible note offering. The convertible note offering is being conducted as a separate public offering by means of a separate prospectus

supplement. This offering is not contingent upon the convertible note offering, and the convertible note offering is not contingent upon this offering.

Table of Contents

THE OFFERING

Common stock offered by us	9,000,000 shares
Common stock to be outstanding after the offering	83,748,424 shares
Overallotment option	We have granted to the underwriters an option to purchase up to an additional 1,350,000 shares of common stock, exercisable solely to cover overallotments, if any, at the public offering price less the underwriting discount shown on the cover page of this prospectus supplement. The underwriters may exercise this option at any time until 30 days from the date of this prospectus supplement.
Use of proceeds	We intend to apply the net proceeds of this offering and of the concurrent offering of convertible notes described above, towards the commercialization of our products; additional clinical trials of Phenoptin, BH_4 for other indications, Phenylase and Vibrilase; preclinical studies and clinical trials for our other product candidates; potential licenses and acquisitions of complementary technologies, products and companies; general corporate purposes, including acquisition costs related to the purchase of our facility located at 46 Galli Drive for which we are currently under contract; and working capital. We may also use a portion of the proceeds of these offerings to purchase some or all of our 3.50% convertible subordinated notes due 2008 pursuant to the redemption provisions of the indenture governing such notes whereby we have the right to call the notes beginning June 20, 2006, or in one or more privately negotiated transactions from time to time. This offering is not contingent on the concurrent convertible note offering. See Use of Proceeds.
Risk factors	See Risk Factors and other information included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq National Market and SWX Swiss Exchange symbol	BMRN

The number of shares of our common stock to be outstanding after this offering is based on 74,748,424 shares of common stock outstanding as of March 14, 2006, and excludes the following items calculated as of that date:

- 8,049,183 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $9.33 per share;
- 8,922,198 shares of our common stock issuable upon the conversion of our $125 million 3.50% convertible subordinated notes due 2008; and

Table of Contents

Shares of common stock reserved for issuance upon conversion of the convertible notes concurrently being offered by us in connection with our convertible note offering.

Unless otherwise specifically stated, information throughout this prospectus supplement assumes:

No exercise of outstanding options to purchase shares of common stock; and

No exercise of the underwriters overallotment options in this offering or the convertible note offering.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. You should carefully consider the following risk factors, together with all of the other information contained in this prospectus supplement and the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus. 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 common stock to decline, and you may lose all or part of your investment.

Risks Related to Our Business

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 Naglazyme, the successful commercialization of Aldurazyme by our joint venture partner, Genzyme, the amount of royalties we receive from our license of Orapred, the receipt of 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;

Table of Contents

- the amount of royalties we receive from our license of Orapred;
- 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 $25.0 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

Table of Contents

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.

Table of Contents

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

Table of Contents

eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have 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.

Table of Contents

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 definitive guidance on the application of these laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. While we believe we have structured our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, 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 for our products, they 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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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

The U.S. Patent and Trademark Office (USPTO) has issued three patents to a third-party that relate to alpha-L-iduronidase. 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. 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.

Table of Contents

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, our royalty revenues from Orapred would be reduced or eliminated.

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 or sublicense 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 would 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

Table of Contents

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.

Pursuant to our agreement with Alliant, 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. 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;

Table of Contents

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.

Table of Contents

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, could be seriously, or potentially completely impaired, and our Aldurazyme and Naglazyme commercialization efforts, revenue from the sale of Aldurazyme and Naglazyme, royalties from the sales of 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;

Table of Contents

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 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.

Actions by wholesalers relating to the purchase of Orapred could affect the timing of royalty revenues.

Orapred is sold to major wholesalers and retail pharmacy chains. Consistent with pharmaceutical industry patterns, most Orapred sales are to three major drug wholesale concerns. Distribution allocation is determined by wholesale and drug chain customers. There can be no assurance that these customers will adequately manage their local and regional inventories to avoid spot outages.

It is difficult to 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. 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 Orapred 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 royalty revenue from sales of Orapred by our licensee in subsequent periods due to overstocking or low end-user demand.

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 of 2005, 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.

Table of Contents

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, 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 limited 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 limited 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

Table of Contents

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.

Table of Contents

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.

Table of Contents

Risks Related to Our Common Stock

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 and Naglazyme and royalties received from 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.

If you purchase our common stock pursuant to this prospectus supplement and the accompanying prospectus, depending on the terms of the offering, you will incur immediate dilution in the book value of your shares.

Based on our most recent balance sheet and the recent trading price of our common stock, you will incur an immediate dilution in the net tangible book value per share of our common stock purchased pursuant to this prospectus supplement and the accompanying prospectus. The magnitude of this dilution will depend on the offering price per share, the total net proceeds received by us in the offering and the net tangible book value of our common stock immediately before the offering.

Table of Contents

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.

Our management will have broad discretion in how we use the net proceeds of this offering and the concurrent convertible note offering.

We have not determined the specific allocation of the net proceeds from this offering and the concurrent convertible note offering. Our management will have broad discretion over the use and investment of the net proceeds, and, accordingly, investors in this offering will need to rely upon the judgment of our management with respect to the use of proceeds, with only limited information concerning management s specific intentions. Our management may spend a portion or all of the net proceeds in ways that our securityholders may not desire or that may not yield a favorable return. The failure of our management to apply the net proceeds from this offering and the concurrent convertible note offering effectively could harm our business, financial condition and results of operations.

Table of Contents

USE OF PROCEEDS

We expect to receive approximately $110.9 million from the sale of our common stock in this offering, or $127.6 million if the underwriters exercise their overallotment option in full, after deducting the estimated underwriting discount and offering expenses that we are to pay. We estimate that the net proceeds from the convertible note offering will be approximately $145.2 million, or $167.1 million if the underwriter exercises its overallotment option in full, after deducting the underwriting discount and our estimated offering expenses.

We intend to apply the net proceeds of the offerings towards the commercialization of our products; additional clinical trials of Phenoptin, BH_4 for other indications, Phenylase and Vibrilase; preclinical studies and clinical trials for our other product candidates; potential licenses and acquisitions of complementary technologies, products and companies; general corporate purposes, including acquisition costs related to the purchase of our facility located at 46 Galli Drive for which we are currently under contract; and working capital. We may also use a portion of the proceeds of these offerings to purchase some or all of our 3.50% convertible subordinated notes due 2008 pursuant to the redemption provisions of the indenture governing such notes whereby we have the right to call the notes beginning June 20, 2006, or in one or more privately negotiated transactions from time to time.

The time and amount of our actual expenditures are subject to change and will be based on many factors, including:

- the amount of cash actually generated in this offering and the concurrent offering of convertible notes;
- the progress, timing and scope 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 capability;
- the time and cost necessary to respond to technological and market developments; and
- 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.

We have discussions from time to time regarding potential acquisitions and licensing opportunities. Although we may use a portion of the net proceeds for this purpose, we currently have no material agreements or commitments in this regard. We reserve the right, at the sole discretion of our Board of Directors, to reallocate our use of proceeds in response to these and other factors. Until we use the net proceeds of this offering, we intend to invest the funds in investment grade, interest-bearing securities.

Table of Contents

PRICE RANGE OF COMMON STOCK

Our common stock is quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN. The following table shows the high and low closing sale prices for our common stock as reported by the Nasdaq National Market during the periods indicated:

	High	Low
Year Ended December 31, 2003		
First Quarter	$ 12.30	$ 5.79
Second Quarter	13.67	9.16
Third Quarter	10.89	7.00
Fourth Quarter	8.47	6.60
Year Ended December 31, 2004		
First Quarter	8.87	7.09
Second Quarter	8.12	5.53
Third Quarter	6.66	4.50
Fourth Quarter	6.49	3.87
Year Ended December 31, 2005		
First Quarter	6.41	4.40
Second Quarter	7.77	4.75
Third Quarter	9.47	7.02
Fourth Quarter	11.70	6.94
Year Ended December 31, 2006		
First Quarter (through March 23, 2006)	15.29	10.55

The last reported sale price of our common stock on the Nasdaq National Market on March 23, 2006 was $13.13 per share. As of March 14, 2006, there were 89 holders of record of our common stock. Additionally, on such date, options to acquire 8,049,183 shares of our common stock were outstanding under our stock option plans.

Table of Contents

CAPITALIZATION

The following table shows:

- our actual capitalization as of December 31, 2005; and
- our capitalization as adjusted to give effect to both our issuance and sale of 9,000,000 shares of common stock in this offering and our concurrent issuance of $150,000,000 aggregate principal amount of convertible notes in the convertible note offering, after deducting the underwriting discount and estimated offering expenses payable by us.

	As of December 31, 2005	
(in thousands, except for share and per share data)	**Actual**	**As Adjusted**
Cash, cash equivalents and short-term investments and cash balances related to long-term debt[1]	$ 64,841	$ 320,969
Long-term debt, including current portion		
2.50% senior subordinated convertible notes due 2013	$	$ 150,000
3.50% convertible subordinated notes due 2008	125,000	125,000
Acquisition obligation, net of discount	78,350	78,350
Equipment and facility loan	20,909	20,909
Total long-term debt	$ 224,259	$ 374,259
Stockholders equity		
Common stock, par value $0.001 per share: 150,000,000 shares authorized; 74,301,610 shares issued and outstanding, actual and 83,301,610 shares issued and outstanding, as adjusted	$ 75	$ 84
Additional paid-in capital	485,570	596,460
Accumulated other comprehensive loss	(16)	(16)
Accumulated deficit	(563,091)	(563,091)
Total stockholders equity/(deficit)	$ (77,462)	$ 33,437
Total capitalization	$ 146,797	$ 407,696

(1) Cash, cash equivalents, short-term investments and cash balances relating to long-term debt includes $17.0 million of cash balances relating to long-term debt that is a portion of the $25.0 million that we are required to keep on deposit with the lender pursuant to the terms of the equipment and facility loan that we entered into in May 2004.

Table of Contents

The table above assumes no exercise of the underwriters overallotment option in this offering or the concurrent convertible note offering. In addition, the number of shares of our common stock in the actual and as adjusted columns in the table above excludes:

- 6,968,569 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $8.60 per share as of December 31, 2005;
- 8,922,198 shares of our common stock issuable upon the conversion of our $125.0 million 3.50% convertible subordinated notes due 2008; and
- shares of common stock reserved for issuance upon conversion of the senior subordinated convertible notes being offered by us in the concurrent convertible note offering.

The table set forth above assumes that none of the proceeds from this offering or the concurrent convertible note offering will be applied to the purchase of our 3.50% convertible subordinated notes due 2008.

Table of Contents

DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance operations and the expansion of our business and do not intend to declare or pay cash dividends on our capital stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors and will depend upon our results of operations, financial condition, current and anticipated cash needs, contractual restrictions, restrictions imposed by applicable law and other factors that our Board of Directors deems relevant.

Table of Contents

DILUTION

Our net tangible book value on December 31, 2005 was ($114.0) million or approximately $(1.53) per share. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding.

Net tangible book value dilution per share to new investors in this offering represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after completion of this offering. After giving effect to the sale of 9,000,000 shares of our common stock in this offering and after deducting the underwriting discount and estimated offering expenses payable by us, our net tangible book value as of December 31, 2005 would have been $(0.04) per share. This amount represents an immediate increase in net tangible book value of $1.49 per share to existing stockholders and an immediate dilution in net tangible book value of $13.04 per share to purchasers of common stock in this offering, as illustrated in the following table:

Public offering price per share		$ 13.00
Net tangible book value per share as of December 31, 2005	$ (1.53)	
Increase in net tangible book value per share attributable to this offering	1.49	
Pro forma net tangible book value per share as of December 31, 2005 after giving effect to this offering		(0.04)
Dilution per share to new investors in this offering		$ 13.04

This table:

- assumes no exercise of options to purchase 6,968,569 shares of common stock at a weighted average exercise price of $8.60 per share outstanding as of December 31, 2005;
- excludes the 8,922,198 shares of our common stock issuable upon the conversion of our $125.0 million 3.50% convertible subordinated notes due 2008;
- excludes the shares of common stock reserved for issuance upon conversion of the senior subordinated convertible notes being offered by us in the concurrent convertible note offering; and
- assumes that none of the proceeds from this offering or the concurrent convertible note offering will be applied to the purchase of our 3.50% convertible subordinated notes due 2008.

This table also assumes no exercise of the underwriters overallotment option in this offering. If the underwriters exercised the overallotment option in full, then the dilution per share to new investors in this offering would be $12.84.

Table of Contents

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of certain material U.S. federal income tax considerations relating to the purchase, ownership and disposition of our common stock applicable to non-U.S. holders as we define that term below. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended (Code), Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service (IRS) with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. Except as provided in the discussion of estate tax, the term non-U.S. holder means a beneficial owner of our common stock that, for U.S. federal income tax purposes, is not a partnership or any other entity taxable as a partnership, or any of the following:

- an individual citizen or resident of the U.S.;
- a corporation or other entity taxable as a corporation for U.S. federal income tax purposes created or organized in the U.S. or under the laws of the U.S., any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more U.S. persons or (2) has a valid election in effect under applicable Treasury Regulations to be treated as a U.S. person.

This summary is limited to holders who hold our common stock as a capital asset. This summary also does not address the tax considerations arising under the laws of any foreign, state or local jurisdiction. In addition, this discussion does not address tax considerations applicable to an investor s particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, or other financial institutions;
- tax-exempt organizations;
- dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- foreign persons or entities, except to the extent specifically set forth below;
- persons that are partnerships or other pass-through entities;
- persons that own, or are deemed to own, more than 5% of our company, except to the extent specifically set forth below;

certain former citizens or long-term residents of the U.S.;

persons who hold the notes as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction; or

persons deemed to sell the common stock under the constructive sale provisions of the Code.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the federal estate or gift tax rules or under the laws of any state, local, foreign or other taxing jurisdiction or under any applicable tax treaty.

Table of Contents

Distributions on Common Stock

If we make cash or other property distributions on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our earnings and profits will constitute a return of capital that will first be applied against and reduce the non-U.S. holder s adjusted tax basis in our common stock, but not below zero. Any remaining excess will be treated as gain realized on the sale or other disposition of the common stock and will be treated as described under Gain on Disposition of Common Stock below.

Dividends paid to a non-U.S. holder that are not effectively connected with the non-U.S. holder s conduct of a trade or business in the U.S. will generally be subject to withholding of U.S. federal income tax at the rate of 30%, or if a tax treaty applies, a lower rate specified by the treaty. Non-U.S. holders should consult their tax advisers regarding their entitlement to benefits under a relevant income tax treaty.

Dividends that are effectively connected with a non-U.S. holder s conduct of a trade or business in the U.S. and, if an income tax treaty applies, are attributable to a permanent establishment in the U.S., are taxed on a net income basis at the regular graduated U.S. federal income tax rates in much the same manner as if the non-U.S. holder were a U.S. person, as defined under the Code. In such cases, we will not have to withhold U.S. federal income tax if the non-U.S. holder complies with applicable certification requirements. In addition, if the non-U.S. holder is a corporation, a branch profits tax equal to 30% (or lower applicable treaty rate) may be imposed on a portion of its effectively connected earnings and profits for the taxable year. Non-U.S. holders should consult any applicable tax treaties that may provide for different rules.

To claim the benefit of a tax treaty or an exemption from withholding because the dividends are effectively connected with the conduct of a trade or business in the U.S., a non-U.S. holder must either (a) provide a properly executed IRS Form W-8BEN or Form W-8ECI (as applicable) before the payment of dividends or (b) if our common stock is held through certain foreign intermediaries, satisfy the relevant certification requirements of applicable U.S. Treasury regulations. These forms must be periodically updated. Non-U.S. holders may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund.

Gain on Disposition of Common Stock

A non-U.S. holder generally will not be subject to U.S. federal income tax or any withholding thereof with respect to gain recognized on a sale or other disposition of our common stock unless one of the following applies:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business in the U.S. and, if an income tax treaty applies, is attributable to a permanent establishment maintained by the non-U.S. holder in the U.S.; in these cases, the non-U.S. holder will generally be taxed on its net gain derived from the disposition at the regular graduated U.S. federal income tax rates in much the same manner as if the non-U.S. holder were a U.S. person and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above may also apply;

- the non-U.S. holder is an individual who is present in the U.S. for 183 days or more in the taxable year of the disposition and meets certain other requirements; in this case, the non-U.S. holder will be subject to U.S. federal income tax at a rate of 30% (or a reduced rate under an applicable treaty) on the amount by which capital gains (including gain recognized on a sale or other disposition of our common stock) allocable to U.S. sources exceed capital losses allocable to U.S. sources; or

our common stock constitutes a United States real property interest by reason of our status as a United States real property holding corporation, (USRPHC), for U.S. federal income tax purposes

Table of Contents

at any time during the shorter of the 5-year period ending on the date you dispose of our common stock or the period you held our common stock, or the applicable period. The determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other business assets. We believe that we are currently not and do not anticipate becoming a USRPHC.

Federal Estate Tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder at the time of death will be included in such individual s gross estate for U.S. federal estate tax purposes, unless an applicable estate tax or other treaty provides otherwise.

Backup Withholding and Information Reporting

In general, you will not be subject to backup withholding and information reporting with respect to payments that we make to you, provided that we do not have actual knowledge or reason to know that you are a U.S. person and you have given us an appropriate statement certifying, under penalties of perjury, that you are not a U.S. person. In addition, you will not be subject to backup withholding or information reporting with respect to the proceeds of the sale of a share of common stock within the U.S. or conducted through certain U.S.-related financial intermediaries, if the payor receives the statement described above and does not have actual knowledge or reason to know that you are a U.S. person or you otherwise establish an exemption. However, we may be required to report annually to the IRS and to you the amount of, and the tax withheld with respect to, any dividends paid to you, regardless of whether any tax was actually withheld. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which you reside. You generally will be entitled to credit any amounts withheld under the backup withholding rules against your U.S. federal income tax liability provided that the required information is furnished to the IRS in a timely manner.

Table of Contents

CONCURRENT CONVERTIBLE NOTE OFFERING

We are concurrently offering $150,000,000 aggregate principal amount, or $172,500,000 aggregate principal amount if the underwriter exercises its option in full, of senior subordinated convertible notes due 2013. The notes will mature on March 29, 2013, unless earlier purchased or converted. The notes will bear interest at 2.50% per year on the principal amount of the notes, payable semi-annually in arrears in cash on September 29 and March 29 of each year, beginning September 29, 2006.

Holders may convert their notes into our common stock at any time prior to maturity based on an initial conversion rate, subject to adjustment, of 60.3318 shares per $1,000 principal amount of notes, which represents an initial conversion price of approximately $16.58 per share, subject to adjustment in certain circumstances.

Upon a fundamental change, which includes a termination of trading or certain changes in control, holders will have the option to require us to purchase all or any portion of the notes at a price equal to 100% of the principal amount of the notes, plus accrued and unpaid interest, if any, to, but excluding, the fundamental change repurchase date.

If certain fundamental changes occur, we will pay, to the extent described in the supplemental indenture, a make whole premium on notes converted in connection with a fundamental change by increasing the conversion rate applicable to the notes.

The notes will be unsecured obligations and will be:

- subordinated in right of payment, as provided in the indenture, to the prior payment in full of all of our existing and future senior debt,
- equal in right of payment with all of our existing and future senior subordinated debt, and
- senior in right of payment to all of our existing and future subordinated debt, including, without limitation, our $125.0 million 3.50% convertible subordinated notes due 2008.

As of March 14, 2006, we had $113.0 million in senior debt outstanding, to which the notes would effectively rank junior.

The terms of the supplemental indenture under which the notes will be issued do not limit our ability to incur additional debt, including senior debt and subordinated debt.

Table of Contents

UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated is acting as representative of the underwriters named below in connection with this offering. Subject to the terms and conditions described in a purchase agreement among us and the underwriters, we have agreed to sell to the underwriters, and the underwriters severally have agreed to purchase from us, the number of shares listed opposite their names below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	4,050,000
Cowen & Co., LLC	1,800,000
Leerink Swann & Company	1,350,000
Pacific Growth Equities, LLC	900,000
Rodman & Renshaw, LLC	900,000
Total	9,000,000

The underwriters have agreed to purchase all of the shares sold under the purchase agreement if any of these shares are purchased. If an underwriter defaults, the purchase agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the purchase agreement may be terminated. The underwriters are not required to take or pay for the shares covered by the underwriters overallotment option described below.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribute to payments the underwriters may be required to make in respect of these liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares and other conditions contained in the purchase agreement, such as the receipt by the underwriters of officers certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representative of the underwriters has advised us that the underwriters propose initially to offer the shares to the public at the public offering price on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of $.39 per share. The underwriters may allow, and the dealers may reallow, a discount not in excess of $0.10 per share to the other dealers. After the public offering, the public offering price, concession and discount may be changed.

The following table shows the public offering price, the underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their overallotment option.

	Per Share	Without Option	With Option
Public offering price	$13.00	$117,000,000	$134,550,000
Underwriting discount	$.65	$5,850,000	$6,727,500
Proceeds, before expenses, to us	$12.35	$111,150,000	$127,822,500

The estimated expenses of this offering, not including the underwriting discount, payable by us will be approximately $250,000.

Table of Contents

In compliance with the guidelines of the National Association of Securities Dealers (NASD), the maximum consideration or discount to be received by any NASD member may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus supplement.

Overallotment Option

We have granted to the underwriters an option to purchase up to 1,350,000 additional shares at the public offering price less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus supplement solely to cover any overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the purchase agreement, to purchase a number of additional shares proportionate to that underwriter s initial amount reflected in the above table.

No Sales of Similar Securities

We and our executive officers and directors have agreed, with exceptions, not to sell or transfer any of our common stock for 90 days after the date of this prospectus supplement without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated. Specifically, we and these individuals have agreed not to directly or indirectly:

- offer, pledge, sell or contract to sell any of our common stock;
- sell any option or contract to purchase any of our common stock;
- purchase any option or contract to sell any of our common stock;
- grant any option, right or warrant for the sale of any of our common stock;
- otherwise dispose of or transfer any of our common stock;
- file a registration statement related to our common stock; or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any of our common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

The restrictions described in the preceding paragraph do not apply to:

- bona fide gifts; or

trusts for the direct or indirect benefit of the individuals subject to the 90 day restriction or the immediate family of any such individual (for purposes of the lock-up agreement, Immediate family shall mean any relationship by blood, marriage or adoption, not more remote than first cousin), provided that

(1) Merrill Lynch receives a signed lock-up agreement for the balance of the 90 day restriction period from each donee, trustee, distributee, or transferee, as the case may be,

(2) any such transfer shall not involve a disposition for value,

(3) such transfers are not required to be reported in any public report or filing with the SEC, or otherwise, and

(4) the individual subject to the lockup does not otherwise voluntarily effect any public filing or report regarding such transfers.

Additionally, the 90 day restriction does not apply to the exercise of stock options held by directors and officers (provided that the shares of common stock received upon exercise shall continue to be restricted by the lockup agreement).

Table of Contents

Furthermore, we and our officers and directors subject to the restriction may sell shares of our common stock purchased on the open market following this offering if and only if (i) such sales are not required to be reported in any public report or filing with the SEC, or otherwise, and (ii) a public filing or report regarding such sales is not otherwise voluntarily made.

Notwithstanding the foregoing, if:

- during the last 17 days of the 90-day period, we issue an earnings release or material news or a material event relating to us occurs; or
- prior to the expiration of the 90-day period, we announce that we will release earnings results or we become aware that material news or a material event will occur during the 16-day period beginning on the last day of the 90-day period.

the lockup restrictions will continue to apply until the expiration of the 18-day period beginning on our issuance of the earnings release or the occurrence of the material news or material event, as applicable, unless Merrill Lynch waives, in writing, such extension.

This lockup provision applies to our common stock and to securities convertible into or exchangeable or exercisable for our common stock. It also applies to common stock owned or acquired during the lockup period by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Nasdaq National Market and SWX Swiss Exchange Quotation

Our common stock is quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN.

Price Stabilization and Short Positions

Until the distribution of the shares is completed, SEC rules may limit the underwriters from bidding for and purchasing our common stock. However, the underwriters may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of more shares than are listed on the cover of this prospectus supplement. Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares from us in this offering. The underwriters may reduce the short position by purchasing shares in the open market, or by exercising all or part of the overallotment option described above. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the overallotment option. Naked short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of this offering.

Similar to the other purchase transactions, the underwriters purchases of the common stock to stabilize its price or to reduce a short position may cause the price of the common stock to be higher than it might be in the absence of such purchases.

Table of Contents

Neither the underwriters nor we make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither the underwriters nor we make any representation that the underwriters will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with the offering, the underwriters may engage in passive market making transactions in our common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker s bid, that bid must then be lowered when specified purchase limits are exceeded.

Other Relationships

Some of the underwriters and their affiliates have in the past and may in the future provide us with investment banking and advisory services. In particular, Merrill Lynch, Pierce, Fenner & Smith Incorporated provided advisory services to us in connection with our Orapred licensing agreement in March 2006, and was the sole underwriter in the July 2005 public offering of our common stock. Merrill Lynch, Pierce, Fenner & Smith Incorporated is currently acting as underwriter in a public offering of our convertible notes that is occurring concurrently with this offering. It has received, and will receive, customary fees for these transactions.

From time to time, the underwriters and certain of their affiliates may in the future engage in transactions with, and perform investment banking and/or commercial banking services, for us and our affiliates in the ordinary course of business.

Transfer Agent

The transfer agent for our common stock is Mellon Investor Services LLC.

Electronic Distribution

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters of this offering. Other than the electronic prospectus, the information on the websites of the underwriters is not part of this prospectus. The underwriters may agree to allocate a number of shares to the underwriters for sale to their online brokerage account holders. Internet distributions will be allocated to the underwriters that may make Internet distributions on the same basis as other allocations.

LEGAL MATTERS

Paul, Hastings, Janofsky & Walker LLP, Los Angeles, California, is giving us an opinion on the validity of the shares offered by this prospectus supplement. Latham & Watkins LLP, Costa Mesa, California, is counsel to the representative of the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements and financial statement schedule II as of December 31, 2005 and 2004, and for each of the years in the three-year period ended December 31, 2005, and management s assessment of the effectiveness of internal control over financial reporting as of December 31, 2005, have been incorporated by reference herein, in reliance upon the report of KPMG LLP, independent registered accounting firm, incorporated by reference herein and upon the authority of said firms as experts in accounting and auditing.

Table of Contents

The consolidated financial statements of BioMarin/Genzyme LLC as of December 31, 2005 and for the years ended December 31, 2005 and 2003 included in our Annual Report on Form 10-K, which are incorporated by reference in this prospectus supplement, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting. In addition, such financial statements, to the extent they have been incorporated in the financial statements of BioMarin Pharmaceutical Inc., have been so incorporated in reliance on the report of such independent registered public accounting firm given on the authority of said firm as experts in auditing and accounting.

Table of Contents

PROSPECTUS

BioMarin Pharmaceutical Inc.

Common Stock

Debt Securities

We may offer and sell, from time to time in one or more offerings:

- shares of our common stock;
- our unsecured debt securities, in one or more series, which may be either senior, senior subordinated or subordinated debt securities; or
- any combination of the foregoing.

We will provide the specific terms of these securities in supplements to this prospectus. A prospectus supplement may also add, update or change information in this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest. This prospectus may not be used to offer or sell securities unless it includes a prospectus supplement.

Our principal executive offices are located at 105 Digital Drive, Novato, California 94949, and our telephone number is (415) 506-6700.

Our common stock is quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN . On March 17, 2006, the closing sale price for our common stock as quoted on the Nasdaq National Market was $14.43 per share.

Investing in our securities involves various risks. See the sections entitled RISK FACTORS on page 1 and NOTE REGARDING FORWARD-LOOKING STATEMENTS on page 2. Additional risks associated with an investment in us as well as with the particular types of securities will be described in the related prospectus supplements.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 20, 2006.

Table of Contents

TABLE OF CONTENTS

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (SEC), as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, under a shelf registration process. Under this shelf registration process, we may sell from time to time in one or more offerings the following securities:

- shares of our common stock;
- our unsecured debt securities, in one or more series, which may be either senior, senior subordinated or subordinated debt securities; or
- any combination of the foregoing.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide you with a prospectus supplement that describes the specific amounts, prices and terms of the securities we offer. Any prospectus supplement and any pricing supplement may add to, update or change the information contained in this prospectus. Please carefully read this prospectus, any prospectus supplement and any pricing supplement, in addition to the information described below under Information Incorporated By Reference.

This prospectus does not contain all of the information provided in the registration statement we filed with the SEC. For further information about us or the securities offered hereby, you should refer to that registration statement, which you can obtain from the SEC as described below under Where You Can Find More Information and Information Incorporated by Reference.

You should rely only on the information contained or incorporated by reference in this prospectus or a prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus or any prospectus supplement, as well as information we have previously filed with the SEC and incorporated by reference, is accurate as of the date on those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. We may sell the securities to or through underwriters, dealers or agents or directly to purchasers. We and our agents reserve the sole right to accept or reject in whole or in part any proposed purchase of securities. The prospectus supplement, which we will provide to you each time we offer securities, will set forth the names of any underwriters, dealers or agents involved in the sale of the securities, if any, and any applicable fee, commission or discount arrangements with them. See Plan of Distribution.

RISK FACTORS

Before making an investment decision, you should carefully consider the risks described under Risk Factors in the applicable prospectus supplement and the documents incorporated by reference in this prospectus and any applicable prospectus supplement, in light of your particular investment objectives and financial circumstances. The risks so described are not the only risks we face. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may

lose all or part of your investment.

Table of Contents

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the documents incorporated by reference in this prospectus or any prospectus supplement contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus, any prospectus supplement or any document incorporated by reference in this prospectus or any prospectus supplement regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects and plans and objectives of management are forward-looking statements.

Forward-looking statements include, but are not limited to, statements about:

- our expectations with respect to regulatory submissions and approvals and our clinical trials;
- our expectations with respect to our collaborations with Serono S.A. and Genzyme Corporation; and
- our estimates regarding our capital requirements and our need for additional financing.

The words anticipates , believes , estimates , expects , intends , may , plans , projects , will , would and similar expressions are inte forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. We have identified some of the important factors that could cause future events to materially differ from our current expectations and they are described in this prospectus and any prospectus supplement under the caption Risk Factors as well as in our most recent Annual Report on Form 10-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statement.

Table of Contents

BIOMARIN PHARMACEUTICAL INC.

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 clinical and preclinical product candidates. Approved products include Naglazyme (galsulfase) for the treatment of mucopolysaccharidosis VI, a product wholly developed and commercialized by us, Aldurazyme® (laronidase) for the treatment of mucopolysaccharidosis I. Additionally, we have rights to receive payments and royalties related to Orapred® (prednisolone sodium phosphate oral solution) for the treatment of inflammatory conditions. Investigational product candidates include Phenoptin (sapropterin hydrochloride), a Phase 3 product candidate for the treatment of phenylketonuria.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the Public Reference Room. Our SEC filings are also available at the SEC s website at http://www.sec.gov. The address of our internet site is http://www.BMRN.com. We make free of charge on or through our internet site our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Other than the electronic prospectus, the information on our website is not part of this prospectus.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information we file with it. This means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is considered a part of this prospectus and any accompanying prospectus supplement, and later information we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of Securities Exchange Act of 1934, as amended (the Securities Exchange Act):

- Our Annual Report on Form 10-K for the year ended December 31, 2005, as filed with the SEC on March 7, 2006, as amended by Form 10-K/A, as filed with the SEC on March 20, 2006;
- Our Current Reports on Form 8-K, as filed with the SEC on January 30, 2006, February 28, 2006 and March 15, 2006; and
- The description of our common stock contained in our registration statement on Form 8-A, as filed with the SEC on July 15, 1999, including any amendment or report filed for the purpose of updating such description.

We will provide to you at no cost a copy of any and all of the information incorporated by reference into the registration statement of which this prospectus is a part. You may make a request for copies of this information in writing or by telephone. Requests should be directed to:

BioMarin Pharmaceutical Inc.

Attention: Susan Ferris

105 Digital Drive

Novato, CA 94949

(415) 506-6700

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus shall be deemed modified, superceded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus, or in any subsequently filed document that also is deemed to be incorporated by reference in this prospectus, modifies, supercedes or replaces such statement. Any statement so modified, superceded or replaced shall not be deemed, except as so modified, superceded or replaced, to constitute a part of this prospectus.

Table of Contents

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our securities offered hereby. Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of securities offered by this prospectus to repay or refinance debt, and for working capital, capital expenditures and other general corporate purposes. We may also use the proceeds to fund acquisitions of businesses, technologies or product lines that complement our current business. However, we currently have no commitments or agreements for any specific acquisitions. We have not identified the precise amounts we plan to spend on each of these areas or the timing of these expenditures. Accordingly, our management will have significant flexibility in applying these proceeds.

Table of Contents

GENERAL DESCRIPTION OF SECURITIES

We, directly or through agents, dealers or underwriters designated from time to time, may offer, issue and sell, together or separately, in one or more offerings:

- shares of our common stock, par value $0.001 per share;
- our unsecured debt securities, in one or more series, which may be either senior, senior subordinated or subordinated debt securities; or
- any combination of the foregoing.

We may issue the debt securities as exchangeable for and/or convertible into shares of our common stock. The common stock and the debt securities are collectively referred to herein as the securities. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide you with a prospectus supplement that describes the specific amounts, prices and terms of the securities we offer. The securities involve various risks that we will describe in a section entitled Risk Factors that will be included in each prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

Our authorized common stock consists of 150,000,000 shares, $0.001 par value per share. At March 14, 2006, there were 74,748,424 shares of our common stock issued and outstanding. The approximate number of stockholders of record of our common stock as of March 14, 2006 was 89.

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Subject to preferences that may be applicable to any outstanding preferred stock, holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of funds legally available. In the event of liquidation, dissolution or winding up of us, holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock. Holders of common stock have no preemptive rights and no right to cumulate votes in the election of directors. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable.

Our board of directors has adopted our stockholder rights plan, which provides for a dividend distribution of one right on each outstanding share of the common stock. Each right entitles stockholders to buy 1/200th of a share of our Series B Junior Participating Preferred Stock (Series B Preferred Stock) at an exercise price of $35, subject to adjustment. The rights will generally become exercisable following the tenth day after a person or group acquires 15% or more of the common stock, or announces commencement of a tender offer the consummation of which would result in ownership by the person or group of 15% or more of the common stock. We will generally be entitled to redeem the rights at $0.001 per right at any time on or before the tenth day following acquisition by a person or group that acquires 15% or more of the common stock. The plan will expire on September 23, 2012.

The Series B Preferred Stock is entitled to a liquidation preference equal to the lesser of $10,000 per share or 200 times the liquidation payment on the common stock and a quarterly dividend equal to the lesser of $0.01 per share or 200 times the dividend, if any, declared on the common stock. The Series B Preferred Stock is entitled to 200 votes per share and will vote together with the common stock.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

This prospectus describes certain general terms and provisions of our debt securities. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a prospectus supplement or a pricing supplement. We will also indicate in the supplement whether the general terms and provisions described in this prospectus apply to a particular series of debt securities. Our debt securities will be our direct obligations and they may be secured or unsecured, senior or subordinated indebtedness. We may issue our debt securities under one or more indentures and each indenture will be dated on or before the issuance of the debt securities to which it relates. Additionally, each indenture must be in the form filed as an exhibit to the Registration Statement containing this prospectus or in a form incorporated by reference to this prospectus in a post-effective amendment to the Registration Statement or a Form 8-K. The form of indenture is subject to any amendments or supplements that may be adopted from time to time. We will enter into each indenture with a trustee and the trustee for each indenture may be the same. The indenture will be subject to, and governed by, the Trust Indenture Act of 1939, as amended. Because this description of debt securities is a summary, it does not contain all the information that may be important to you. You should read all provisions of our indenture and our debt securities to assure that you have all the important information you need to make any required decisions. All capitalized terms used, but not defined, in this section shall have the meanings set forth in the form of indenture.

TERMS

The particular terms of any series of our debt securities will be described in a prospectus supplement. Additionally, any applicable modifications of or additions to the general terms of our debt securities described in this prospectus and in the applicable indenture will also be described in a prospectus supplement. Accordingly, for a description of the terms of any series of our debt securities, you must refer to both the prospectus supplement relating to those debt securities and the description of the debt securities set forth in this prospectus. If any particular terms of our debt securities described in a prospectus supplement differ from any of the terms described in this prospectus, then those terms as set forth in the relevant prospectus supplement will control.

The terms of each series of debt securities will be established by or pursuant to a resolution of our Board of Directors and detailed or determined in the manner provided in a Board of Directors resolution, an officers certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to the series, including any pricing supplement.

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium or at a discount. We will set forth in a prospectus supplement (including any pricing supplement) relating to any series of debt securities being offered, the initial offering price, the aggregate principal amount and the following terms of the debt securities:

- the title of the debt securities;
- the price or prices (expressed as a percentage of the aggregate principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which we will pay the principal on the debt securities;

the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;

the place or places where the principal of, premium, and interest on the debt securities will be payable;

Table of Contents

the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities;

the dates on which and the price or prices at which we will repurchase the debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities;

the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;

if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, premium or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to or change in the events of default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any other terms of the debt securities, which may modify or delete any provision of the indenture as it applies to that series; and

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Table of Contents

EXCHANGE OF SECURITIES

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, as Depositary, or a nominee of the Depositary (we will refer to any debt security represented by a global debt security as a book-entry debt security), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a certificated debt security), as described in the applicable prospectus supplement. Except as described under Global Debt Securities and Book-Entry System below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities with the Registrar s office or paying agencies in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may transfer certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the old certificate representing those certificated debt securities and either we or the trustee will reissue the old certificate to the new holder or we or the trustee will issue a new certificate to the new holder.

Global Debt Securities And Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depositary, and registered in the name of the Depositary or a nominee of the Depositary.

The Depositary has indicated it intends to follow the following procedures with respect to book-entry debt securities.

Ownership of beneficial interests in book-entry debt securities will be limited to persons that have accounts with the Depositary for the related global debt security (we shall refer to these persons as participants) or persons that may hold interests through participants. Upon the issuance of a global debt security, the Depositary will credit, on its book-entry registration and transfer system, the participants accounts with the respective principal amounts of the book-entry debt securities represented by the global debt security beneficially owned by such participants. The accounts to be credited will be designated by any dealers, underwriters or agents participating in the distribution of the book-entry debt securities. Ownership of book-entry debt securities will be shown on, and the transfer of the ownership interests will be effected only through, records maintained by the Depositary for the related global debt security (with respect to interests of participants) and on the records of participants (with respect to interests of persons holding through participants). The laws of some states may require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to own, transfer or pledge beneficial interests in book-entry debt securities.

So long as the Depositary for a global debt security, or its nominee, is the registered owner of that global debt security, the Depositary or its nominee, as the case may be, will be considered the sole owner or holder of the book-entry debt securities represented by such global debt security for all purposes under the indenture. Except as described herein, beneficial owners of book-entry debt securities will not be entitled to have securities registered in their names, will not receive or be entitled to receive physical delivery of a certificate in definitive form representing securities and will not be considered the owners or holders of those securities under the indenture. Accordingly, to exercise any rights of a holder under the indenture, each person beneficially owning book-entry debt securities must rely on the procedures of the Depositary for the related global debt security and, if that person is not a participant, on the procedures of the participant through which that person owns its interest.

We understand, however, that under existing industry practice, the Depositary will authorize the persons on whose behalf it holds a global debt security to exercise certain rights of holders of debt securities, and the indenture provides that we, the trustee and our respective agents will treat as the holder of a debt security the

Table of Contents

persons specified in a written statement of the Depositary with respect to that global debt security for purposes of obtaining any consents or directions required to be given by holders of the debt securities pursuant to the indenture.

We will make payments of principal of, and premium and interest on book-entry debt securities to the Depositary or its nominee, as the case may be, as the registered holder of the related global debt security. We, the trustee and any other agent of ours or agent of the trustee will not have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in a global debt security or for maintaining, supervising or reviewing any records relating to such beneficial ownership interests.

We expect that the Depositary, upon receipt of any payment of principal of, premium or interest on a global debt security, will immediately credit participants accounts with payments in amounts proportionate to the respective amounts of book-entry debt securities held by each participant as shown on the records of the Depositary. We also expect that payments by participants to owners of beneficial interests in book-entry debt securities held through those participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers in bearer form or registered in street name, and will be the responsibility of those participants.

We will issue certificated debt securities in exchange for each global debt security if the Depositary is at any time unwilling or unable to continue as Depositary or ceases to be a clearing agency registered under the Securities Exchange Act, and a successor Depositary registered as a clearing agency under the Securities Exchange Act is not appointed by us within 90 days. In addition, we may at any time and in our sole discretion determine not to have any of the book-entry debt securities of any series represented by one or more global debt securities and, in that event, we will issue certificated debt securities in exchange for the global debt securities of that series. Global debt securities will also be exchangeable by the holders for certificated debt securities if an event of default with respect to the book-entry debt securities represented by those global debt securities has occurred and is continuing. Any certificated debt securities issued in exchange for a global debt security will be registered in such name or names as the Depositary shall instruct the trustee. We expect that such instructions will be based upon directions received by the Depositary from participants with respect to ownership of book-entry debt securities relating to such global debt security.

We have obtained the foregoing information in this section concerning the Depositary and the Depositary s book-entry system from sources we believe to be reliable, but we take no responsibility for the accuracy of this information.

NO PROTECTION IN THE EVENT OF A CHANGE OF CONTROL

Unless we provide otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

COVENANTS

Unless we provide otherwise in the applicable prospectus supplement, the debt securities will not contain any restrictive covenants, including covenants restricting us or any of our subsidiaries from incurring, issuing, assuming or guarantying any indebtedness secured by a lien on any of our or our subsidiaries property or capital stock, or restricting us or any of our subsidiaries from entering into any sale and leaseback transactions.

9

Table of Contents

CONSOLIDATION, MERGER AND SALE OF ASSETS

Unless we provide otherwise in the applicable prospectus supplement, we may not consolidate with or merge into, or convey, transfer or lease all or substantially all of our properties and assets to, any person (a successor person), and we may not permit any person to merge into, or convey, transfer or lease its properties and assets substantially as an entirety to us, unless:

- the successor person is a corporation, partnership, trust or other entity organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;
- immediately after giving effect to the transaction, no event of default, and no event which, after notice or lapse of time, or both, would become an event of default, shall have occurred and be continuing under the indenture; and
- certain other conditions are met.

EVENTS OF DEFAULT

Unless we provide otherwise in the applicable prospectus supplement, event of default means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of that default for a period of 30 days (unless the entire amount of such payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal on any debt security of that series when due and payable;
- default in the deposit of any sinking fund payment, when and as due in respect of any debt security of that series;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or we and the trustee receive written notice from the holders of at least 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain events of our bankruptcy, insolvency or reorganization;
- default under any of our debt created under the indenture (including a default with respect to any debt security of a different series) or of our subsidiaries, if (1) such default results from the failure to pay any such debt when it becomes due, (2) the principal amount of our debt created under the indenture, together with the principal amount of any other such debt in default for failure to pay principal at stated final maturity or the maturity of which has been so accelerated, aggregates $10.0 million or

more at any one time outstanding, and (3) such debt is not discharged or such acceleration is not rescinded or annulled within 30 days after written notice to us by the holder or holders of such debt in the manner provided for in the applicable debt instrument; or

any other event of default provided with respect to debt securities of that series that is described in the applicable prospectus supplement accompanying this prospectus.

An event of default may also be an event of default under our bank credit agreements or other debt securities in existence from time to time, including, without limitation, our 3.50% convertible subordinated notes due 2008, and under certain guaranties by us of any subsidiary indebtedness. In addition, certain events of

default or an acceleration under the indenture may also be an event of default under some of our other indebtedness outstanding from time to time.

Unless we provide otherwise in the applicable prospectus supplement, if an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing (other than certain events of our bankruptcy, insolvency or reorganization), then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by written notice to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and premium of all debt securities of that series. In the case of an event of default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) and premium of all outstanding debt securities will become and be immediately due and payable without any declaration or other act by the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before the trustee has obtained a judgment or decree for payment of the money due, the holders of a majority in principal amount of the outstanding debt securities of that series may, subject to our having paid or deposited with the trustee a sum sufficient to pay overdue interest and principal which has become due other than by acceleration and certain other conditions, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal and premium with respect to debt securities of that series, have been cured or waived as provided in the indenture. For information as to waiver of defaults see the discussion under Modification and Waiver below. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of the discount securities upon the occurrence of an event of default and the continuation of an event of default.

Unless we provide otherwise in the applicable prospectus supplement, the indenture will provide that the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any holder of outstanding debt securities, unless the trustee receives indemnity satisfactory to it against any loss, liability or expense. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

Unless we provide otherwise in the applicable prospectus supplement, no holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing event of default with respect to debt securities of that series; and
- the holders of at least 25% in principal amount of the outstanding debt securities of that series have made written request, and offered reasonable indemnity, to the trustee to institute such proceeding as trustee, and the trustee shall not have received from the holders of a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding the foregoing, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 90 days after the end of our fiscal year, to furnish to the trustee a certificate as to compliance with the indenture. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any default or event of default (except in payment on any debt securities of that series) with respect to debt securities of that series if it in good faith determines that

withholding notice is in the interest of the holders of those debt securities.

Table of Contents

MODIFICATION AND WAIVER

Unless we provide otherwise in the applicable prospectus supplement, we and the trustee may modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We and the trustee may not make any modification or amendment without the consent of the holder of each affected debt security then outstanding if that amendment will:

- change the amount of debt securities whose holders must consent to an amendment or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from that acceleration);
- make the principal of or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of and interest on those debt securities and the right of holders to institute suit for the enforcement of such payment; the right of holders to waive past defaults; the right of holders of a specified principal amount of debt securities which are denominated in a foreign currency to be deemed for the purposes of taking action under the indenture, that amount of U.S. dollars at the Market Exchange Rate; certain terms regarding judgments in foreign currencies; or to amend the limitations described in this bullet point; or
- waive a redemption payment with respect to any debt security or change any of the provisions with respect to the redemption of any debt securities.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may, on behalf of the holders of all debt securities of that series, waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of the holders of all the debt securities of that series, waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

DEFEASANCE OF DEBT SECURITIES AND CERTAIN COVENANTS IN CERTAIN CIRCUMSTANCES

Legal Defeasance. The indenture provides that, unless the terms of the applicable series of debt securities provide otherwise, we may be discharged from any and all obligations in respect of the debt securities of any series (except for certain obligations to register the transfer or exchange of debt securities of the series, to replace stolen, lost or mutilated debt securities of the series, and to maintain paying agencies and certain provisions relating to the treatment of funds held by paying agents). We will be so discharged 90 days after the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations (as described at the end

Table of Contents

of this section), that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of such payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an officers certificate and an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that holders of the debt securities of such series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amount and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

Defeasance of Certain Covenants. The indenture provides that, unless the terms of the applicable series of debt securities provide otherwise, upon compliance with certain conditions, we may omit to comply with the restrictive covenants of the indenture entitled SEC Reports, Compliance Certificate, Stay, Extension and Usury Laws, Corporate Existence, Taxes and When We May Merge, Etc., as well as any additional covenants contained in a supplement to the indenture, a board resolution or an officers certificate delivered pursuant to the indenture. The conditions include:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants to pay principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities;

such deposit does not result in a breach or constitute a default under the indenture or any other agreement to which we are a party;

no default or event of default with respect to the debt securities shall have occurred and be continuing on the date of deposit or during the period ending 90 days after such date; and

delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax in the same amount and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

Covenant Defeasance and Events of Default. In the event we exercise our option, as described above, not to comply with certain covenants of the indenture with respect to any series of debt securities and the debt securities of that series are declared due and payable because of the occurrence of any event of default, the amount of money and/or U.S. government obligations or foreign government obligations on deposit with the trustee will be sufficient to pay amounts due on the debt securities of that series at the time of their stated maturity but may not be sufficient to pay amounts due on the debt securities of that series at the time of the acceleration resulting from the event of default. However, we will remain liable for those payments.

Table of Contents

Foreign government obligations means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars:

- direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged, which are not callable or redeemable at the option of the issuer thereof; or

- obligations of a person controlled or supervised by or acting as an agency or instrumentality of that government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government, which are not callable or redeemable at the option of the issuer thereof.

CONVERSION AND EXCHANGE RIGHTS

The debt securities may be exchanged for and/or converted into shares of common stock, shares of preferred stock or other securities. The terms, if any, on which the debt securities may be exchanged for and/or converted will be set forth in the applicable prospectus supplement. Such terms may include provisions for conversion, either mandatory, at the option of the holder or at our option, in which case the number of shares of common stock, preferred stock or other securities to be received by the holders of the debt securities would be calculated as of a time and in the manner stated in the prospectus supplement.

GOVERNING LAW

The indenture and the debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time in one or more transactions through underwriters or dealers, through agents, or directly to one or more purchasers or through a combination of these methods. The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices, or at negotiated prices. Sales of securities offered pursuant to this registration statement may be effected from time to time in one or more transactions on the Nasdaq National Market or in negotiated transactions or a combination of these methods.

The applicable prospectus supplement will describe the terms of the offering of the securities, including:

- the name or names of any underwriters, if any, and if required, any dealers or agents;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any underwriting discounts and other items constituting underwriters compensation;
- any initial public offering price;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

We may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed;
- market prices prevailing at the time of sale;
- prices related to such prevailing market prices; or
- negotiated prices.

Only underwriters named in a prospectus supplement are underwriters of the securities offered by such prospectus supplement.

If we use underwriters in the sale, they will acquire the securities for their own account and may resell them from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to specific limited conditions, the underwriters will be obligated to purchase all the securities of the series offered by the applicable prospectus supplement. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time.

If we use a dealer in the sale of the securities being offered pursuant to this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the applicable prospectus supplement. Unless the applicable prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

Table of Contents

We may authorize agents or underwriters to solicit offers by institutional investors to purchase securities from us at the public offering price set forth in the applicable prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the applicable prospectus supplement.

In connection with the sale of the securities, underwriters, dealers or agents may receive compensation from us or from purchasers of the securities for whom they act as agents in the form of discounts, concessions or commissions. Underwriters may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of the securities, and any institutional investors or others that purchase securities directly and then resell the securities, may be deemed to be underwriters, and any discounts or commissions received by them from us and any profit on the resale of the securities by them may be deemed to be underwriting discounts and commissions under the Securities Act.

We may provide agents and underwriters with indemnification against particular civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to such liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

In addition, we may enter into derivative transactions with third parties (including the writing of options), or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with such a transaction the third parties may, pursuant to this prospectus and the applicable prospectus supplement, sell securities covered by this prospectus and the applicable prospectus supplement. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and the applicable prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and the applicable prospectus supplement. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement or in a post-effective amendment.

All securities we offer other than common stock will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Until the distribution of securities is completed, SEC rules may limit the underwriters from bidding for and purchasing our common stock. However, the underwriters may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of more shares than are listed on the cover of this prospectus supplement. Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares from us in this offering. The underwriters may reduce the short position by purchasing shares in the open market, or by exercising all or part of any over-allotment option which may be granted to them. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned

16

Table of Contents

that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of this offering.

Similar to the other purchase transactions, the underwriters purchases of the securities to stabilize their price or to reduce a short position may cause the price of the common stock to be higher than it might be in the absence of such purchases.

Neither the underwriters nor we make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither the underwriters nor we make any representation that the underwriters will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

LEGAL MATTERS

Paul, Hastings, Janofsky & Walker LLP, 515 South Flower Street, 25th Floor, Los Angeles, California, is giving us an opinion on the validity of the securities we are offering in this prospectus.

EXPERTS

The consolidated financial statements and financial statement schedule II as of December 31, 2005 and 2004, and for each of the years in the three-year period ended December 31, 2005, and management s assessment of the effectiveness of internal control over financial reporting as of December 31, 2005, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered accounting firm, incorporated by reference herein and upon the authority of said firms as experts in accounting and auditing.

The consolidated financial statements of BioMarin/Genzyme LLC as of December 31, 2005 and for the years ended December 31, 2005 and 2003 included in our Annual Report on Form 10-K, which are incorporated by reference in this prospectus supplement, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting. In addition, such financial statements, to the extent they have been incorporated in the financial statements of BioMarin Pharmaceutical Inc., have been so incorporated in reliance on the report of such independent registered public accounting firm given on the authority of said firm as experts in auditing and accounting.

Table of Contents

9,000,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

Merrill Lynch & Co.

Cowen & Company

Leerink Swann & Company

Pacific Growth Equities, LLC

Rodman & Renshaw

March 23, 2006