BIOMARIN PHARMACEUTICAL INC
Form 424B5
July 15, 2005
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File Number 333-102066

PROSPECTUS SUPPLEMENT
(To Prospectus dated February 21, 2003)

8,500,000 Shares

Common Stock

We are selling 8,500,000 shares of our common stock.

Our common stock is quoted on The Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN. On July 13, 2005, the last sale price of our shares as quoted on The Nasdaq National Market was $7.56 per share.

Investing in our common stock involves risks, including those described in the Risk Factors section beginning on page S-4 of this prospectus supplement and page 3 of the accompanying prospectus.

	Per share	Total
Public offering price	$ 7.05	$ 59,925,000
Underwriting discount	$ 0.3525	$ 2,996,250
Proceeds, before expenses, to us	$ 6.6975	$ 56,928,750

Neither the Securities and Exchange Commission nor any state securities regulators have 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 July 19, 2005.

Merrill Lynch & Co.

The date of this prospectus supplement is July 14, 2005

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Prospectus Supplement

Prospectus

You should rely on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriter has 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. We are not, and the underwriter is 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 their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

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.

For investors outside the United States: Neither we nor the underwriter have done anything that would permit this offering or possession or distribution of this prospectus supplement or the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus supplement and the accompanying prospectus.

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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, or 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 both this prospectus supplement and the accompanying prospectus together with the additional information described under the heading Where you can find more information.

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 (FSMA) by virtue of one or more of the criteria set out in section 86 of FSMA.

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PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the Risk Factors sections, and other information incorporated by reference before deciding to invest in our common stock.

Business Overview

We develop and commercialize innovative biopharmaceuticals for serious diseases and medical conditions. We select product candidates for diseases and conditions that represent a significant medical need, have well-understood biology and provide an opportunity to be first-to-market.

Our product portfolio is comprised of three approved products and multiple investigational product candidates. Approved products include Aldurazyme ® (laronidase), Orapred® (prednisolone sodium phosphate oral solution), and Naglazyme (galsulfase). 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 Medicines Evaluation Agency (EMEA) and in other countries for the treatment of mucopolysaccharidosis I (MPS I). MPS I is a progressive and debilitating life-threatening genetic disease that frequently results in death during childhood or early adulthood. It is caused by the deficiency of alpha-L-iduronidase, an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs). As the first drug approved for MPS I, Aldurazyme has been granted orphan drug status in the U.S. and the E.U., which gives Aldurazyme seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS I. We have developed Aldurazyme through a joint venture with Genzyme Corporation (Genzyme).

In May 2004, we completed the transaction to acquire the business of Ascent Pediatrics from Medicis Pharmaceutical Corporation (Medicis). The Ascent Pediatrics business includes Orapred, a drug primarily used to treat asthma exacerbations in children and other inflammatory conditions, two additional proprietary formulations of Orapred in development, and a U.S.-based sales force.

Aldurazyme net revenue recorded by our joint venture for 2004 and the first quarter of 2005 totaled $42.6 million and $15.9 million, respectively, compared to $11.5 million and $7.4 million for 2003 and the first quarter of 2004, respectively. Orapred net product sales from the acquisition in May 2004 through March 31, 2005 totaled $23.6 million. Our cash, cash equivalents, short-term investments, restricted cash and cash balances related to long-term debt totaled $62.3 million as of March 31, 2005.

On June 1, 2005, we announced that 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. In June 2004, we announced the positive results of our Phase 3 trial of Naglazyme. The clinical trial demonstrated that Naglazyme provides clinically important benefits for MPS VI patients, specifically, improved endurance as demonstrated by a 12-minute walk test and 3-minute stair climb. Additionally, data from the trial demonstrated that Naglazyme reduced the excess GAGs that are excreted in the urine of patients with MPS VI, an indication of enzymatic bioactivity. Naglazyme has been granted orphan drug status in the U.S. and the E.U., which confers seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS VI. We have also filed for marketing authorization of Naglazyme in the E.U.

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We are developing several product candidates for the treatment of genetic diseases including: Phenoptin (6R-BH4), a proprietary oral form of tetrahydrobiopterin, for the treatment of moderate to mild forms of phenylketonuria (PKU); and Phenylase (recombinant phenylalanine ammonia lyase), a preclinical candidate for the treatment of the more severe form of PKU.

In December 2004, we announced that we initiated our Phase 2 clinical trial of Phenoptin for PKU. Patients identified in the Phase 2 clinical trial that meet certain criteria will be eligible to enroll in the Phase 3 trial which began in May 2005. The Phase 3 clinical trial of Phenoptin is expected to be a six-week, multi-center, international, double-blind, placebo-controlled study. We anticipate the trial will enroll patients on an ongoing basis until it is fully enrolled. As a primary efficacy endpoint, the trial will measure the changes in blood Phenylalanine (Phe) level in patients receiving Phenoptin compared to patients receiving placebo. In July 2004, we announced positive results from an investigator sponsored pilot clinical study of 6R-BH4, the active agent in Phenoptin, in 20 patients with PKU. We have received orphan drug designation for Phenoptin for the treatment of PKU in both the U.S. and E.U.

PKU is an inherited metabolic disease that affects at least 50,000 diagnosed patients under the age of 40 in the developed world, an estimated half of whom have a moderate to mild form of the disease. PKU is caused by a deficiency of an enzyme, phenylalanine hydroxylase (PAH), which is required for the metabolism of Phe. Phe is an amino acid found in most protein-containing foods. Without sufficient quantity or activity of PAH, Phe accumulates to abnormally high levels in the blood resulting in a variety of serious neurological complications. Phenoptin, our lead product candidate for the treatment of PKU, is a proprietary oral form of 6R-BH4, a small-molecule therapeutic that is a co-factor for PAH. If approved, Phenoptin could become the first drug for the treatment of PKU.

Phenylase is currently in preclinical development. It is being developed as a subcutaneous injection and is intended for those who suffer from classic PKU, the more severe form of the disease and those who suffer from the mild to moderate form of the disease but do not respond to Phenoptin. Phenoptin and Phenylase are being developed with Serono S.A. (Serono) pursuant to a Development License and Commercialization Agreement that we entered into with a subsidiary of Serono. Pursuant to this agreement, Serono has acquired exclusive rights to market these products outside of the U.S. and Japan.

We are evaluating other enzyme-based therapies for serious medical conditions including Vibrilase, a topical investigational 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 technologies to overcome limitations associated with the delivery of existing pharmaceuticals.

In May 2005, we announced the appointment of Jean-Jacques Bienaimé as our new Chief Executive Officer and as a director. As a result of this appointment, Louis Drapeau and Jeffrey H. Cooper (who since August 2004 served as our Acting Chief Executive Officer and Acting Chief Financial Officer, respectively) resumed their positions as Senior Vice President Finance, Chief Financial Officer and Secretary and Vice President, Controller, respectively. In June 2005, we announced that Stephen Aselage was appointed as our Senior Vice President of Global Commercial Operations.

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

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THE OFFERING

Common stock offered by us	8,500,000 shares
Shares outstanding after the offering	73,244,955 shares
Use of proceeds	We intend to apply the net proceeds of this offering towards the commercialization of our products; additional clinical trials of Phenoptin 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; and working capital. 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 64,744,955 shares of common stock outstanding as of July 6, 2005, and excludes the following items calculated on such date:

- 11,348,954 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $9.47 per share; and
- 8,922,198 shares of our common stock issuable upon the conversion of our $125,000,000 3.50% Convertible Subordinated Notes due 2008.

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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, before deciding to invest in our common stock. 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.

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 $70.0 million in net sales revenue to our joint venture from the product s launch (May 2003) through March 31, 2005. We acquired exclusive rights to Orapred in May 2004 and reported $23.6 million in Orapred net product sales following the acquisition through March 31, 2005. On June 1, 2005 we announced that the FDA granted marketing approval for Naglazyme for the treatment of MPS VI. We have no revenues from sales of our product candidates. As of March 31, 2005, we had an accumulated deficit of $511.3 million. We expect to continue to operate at a net loss for the foreseeable future. Our future profitability depends on our marketing and selling of Orapred and Naglazyme, the successful commercialization of Aldurazyme by our joint venture partner, Genzyme, our receiving regulatory approval of our product candidates and our ability to successfully manufacture and market any approved drugs, either by ourselves or jointly with others. The extent of our future losses and the timing of profitability are highly uncertain. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

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

We will require additional financing to fund our future operations, including the commercialization of our 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.

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

- our ability to successfully market and sell Naglazyme;
- our joint venture partner s ability to successfully commercialize Aldurazyme;

the progress, timing and scope of our preclinical studies and clinical trials;

our ability to successfully market and sell Orapred, including our ability to protect our existing market share and regain market share against generic competition,

the time and cost necessary to obtain regulatory approvals;

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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, restricted cash balances and cash balances related to long-term debt at March 31, 2005 will be sufficient to meet our operating and capital requirements into the fourth quarter of 2005. These estimates are based on assumptions and estimates, including the availability of a $25 million loan from Medicis in July 2005. These assumptions and estimates may prove to be wrong. Additionally, we are required to maintain a total unrestricted cash balance of at least $45.0 million or a greater amount defined by a calculation provided for in our credit facility with Comerica Bank. We amended our credit facility to reduce the total unrestricted cash balance requirement for each of the months ended November and December 2004 and April and June 2005. If we are unable to obtain additional liquidity prior to July 31, 2005, we would need to obtain a further waiver of the total unrestricted cash balance requirement or risk being in violation under the credit facility. We may 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 manufacture or sell our drugs or fail to obtain regulatory approval to commercially manufacture drug products, 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 has received regulatory approval to be commercially marketed and sold in the E.U. and several 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.

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

After any of our products receive regulatory approval, they remain subject to ongoing FDA regulation, including, for example, changes to the product labeling, new or revised regulatory requirements for manufacturing practices and reporting adverse reactions and other information. If we do not comply with the FDA s regulations, the range of possible sanctions includes FDA issuance of adverse publicity, product recalls or seizures, fines, total or partial suspensions of production and/or distribution, suspension of FDA s review of marketing applications, enforcement actions, including injunctions and civil or criminal prosecution. The FDA can withdraw a product s approval under some circumstances, such as the failure to comply with existing or future regulatory requirements, or unexpected safety issues. Further, the FDA may condition approval of our product candidates on the completion of additional post-marketing clinical studies. These post-marketing studies may suggest that a product causes undesirable side effects or may present a risk to safety. If data we collect from post-marketing studies suggest that one of our approved products may present a risk to safety, the FDA could withdraw our product approval, suspend production or place other marketing restrictions on our products. If regulatory sanctions are applied or if regulatory approval is delayed or withdrawn, our management s credibility, the value of our company and our operating results will be adversely affected. Additionally, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased.

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

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

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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 cGMP regulations. The cGMP 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 cGMP warehouse facilities have been inspected and licensed by the State of California for clinical pharmaceutical manufacture and have been approved by the FDA, the EMEA and Health Canada and health agencies in other countries for the commercial manufacture of Aldurazyme and by the FDA 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 cGMP regulations in a cost effective manner. As anticipated by cGMP requirements, manufacturing deviations and deviations from cGMP 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 cGMP. 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 European Community 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

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eligible drugs, we plan to rely on the exclusivity period under the orphan drug designation to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have patent protection, our competitors may then sell the same drug to treat the same condition and our revenues will be reduced.

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

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

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

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

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

Many states have adopted laws similar to the federal antikickback statute, some of which apply to referral of patients for health care services reimbursed by any source, not just governmental payers. In addition,

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California recently passed a law that requires pharmaceutical companies to comply with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and the July 2002 PhRMA Code on Interactions with Healthcare Professionals.

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

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

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

Ascent Pediatrics had reimbursement agreements for Orapred with many of the major U.S. third-party payers. We have agreed with these third parties to maintain the existing agreements at this time and have renegotiated certain agreements. In the future, we expect to enter into additional agreements with other third-party payers and we expect to evaluate and renegotiate additional existing agreements. Reimbursement strategy is a complicated process that is based on a number of factors, including competition, patient profile and the condition being treated, among others.

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. In addition, we will need to develop our own reimbursement expertise for future drug candidates and as necessary to support Orapred and Naglazyme. For our future products and for Naglazyme outside the U.S., we will not know what the reimbursement rates will be until we are ready to market the product and we actually negotiate the rates. If we are unable to obtain sufficiently high reimbursement rates, our products may not be commercially viable or our future revenues and gross margins may be adversely affected.

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 would 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.

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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 a prescription drug benefit under the Medicare program, will take effect January 1, 2006. While it is difficult to predict the business impact of this legislation prior to 2006, there is additional risk associated with increased pricing pressures. While the MMA prohibits the Secretary of Health and Human Services (HHS) from directly negotiating prescription drug prices with manufacturers, we expect continued challenges to that prohibition over the next several years. Also, the MMA retains the authority of the HHS to prohibit the importation of prescription drugs, but we expect Congress to consider several measures that could remove that authority and allow for importation of products into the U.S. regardless of their safety or cost. If adopted, such legislation would likely have a negative effect on our U.S. sales.

As a result of the passage of the MMA, aged and disabled patients jointly eligible for Medicare and Medicaid will receive their prescription drug benefits through Medicare, instead of Medicaid, beginning January 1, 2006. This may relieve some state budget pressures but is unlikely to result in reduced pricing pressures. Many states have begun to implement supplemental rebates and restricted formularies in their Medicaid programs, and these programs are expected to continue in the post-MMA environment. Additionally, in the U.S., we are required to provide rebates to state governments on their purchases of certain of our products under state Medicaid programs. Other cost containment measures have been adopted or proposed by federal, state, and local government entities that provide or pay for health care. In most international markets, we operate in an environment of government-mandated cost containment programs, which may include price controls, reference pricing, discounts and rebates, restrictions on physician prescription levels, restrictions on reimbursement, compulsory licenses, health economic assessments, and generic substitution. Several states are also attempting to extend discounted Medicaid prices to non-Medicaid patients. Additionally, notwithstanding the federal law prohibiting pharmaceutical importation, several states have implemented importation schemes for their citizens, usually involving a website that links patients to selected Canadian pharmacies. At least one state has such a program for its state employees. In the absence of federal action to curtail state activities, we expect other states to launch importation efforts. As a result, we expect pressures on pharmaceutical pricing to continue.

International operations are also generally subject to extensive price and market regulations, and there are many proposals for additional cost-containment measures, including proposals that would directly or indirectly impose additional price controls or reduce the value of our intellectual property portfolio.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, we expect that pressures on pharmaceutical pricing will continue in the near term.

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, 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 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.

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

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.

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

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

The USPTO has issued three patents to a third-party that include composition-of-matter, isolated genomic nucleotide sequences, vectors including the sequences, host cells containing the vectors, and method of use claims for human, recombinant alpha-L-iduronidase. Our lead drug product, Aldurazyme, is based on human, recombinant alpha-L-iduronidase. We believe that these patents are invalid or not infringed on a number of grounds. A corresponding patent application was filed by a third party in the European Patent Office claiming composition-of-matter for human, recombinant alpha-L-iduronidase, and it was rejected over prior art and withdrawn and cannot be re-filed. However, corresponding applications are still pending in Canada and Japan, and these applications are being prosecuted by the applicants. We do not know whether any of these applications will issue as patents or the scope of the claims that would issue from these applications. In addition, under U.S. law, issued patents are entitled to a presumption of validity, and our challenges to the U.S. patents may be unsuccessful. Even if we are successful, challenging the U.S. patents may be expensive, require our management to devote significant time to this effort and may adversely impact commercialization of Aldurazyme in the U.S.

The holder of the patents described above has granted an exclusive license for products relating to these patents to one of our competitors, Transkaryotic Therapies Inc (TKT). 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.

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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 the joint venture is terminated and we retain the rights to Aldurazyme, we could experience significant difficulties and delays in obtaining third-party reimbursement or we could fail to obtain foreign regulatory approvals, any of which could hurt our business and results of operations. Since Genzyme funds 50% of the joint venture s product inventory and operating expenses, the termination of the joint venture would double our financial burden and reduce the funds available to us for other product programs.

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

Serono may terminate the agreement forming our strategic alliance with them at any time by giving 90 days prior written notice if such termination occurs prior to the commercialization of any of the products licensed under our agreement, or by giving 180 days prior written notice if such termination occurs after the commercialization of such a product. Either Serono or we may terminate our strategic alliance under certain circumstances, including if the other party is in material breach of the agreement and does not remedy the breach within a specified period of time, or has suffered certain financial difficulties, including filing for bankruptcy or making an assignment for the benefit of creditors. Although we are not currently in breach of the agreement and we believe that Serono is not currently in breach of the agreement, there is a risk that either party could breach the agreement in the future. Upon a termination of the agreement by Serono by giving notice or by us for a material breach by Serono, all rights licensed to us under the agreement become irrevocable and fully-paid except in those countries where restricted by applicable law or for all intellectual property that Serono does not own. Upon a termination of the agreement by Serono for a material breach by us or based on our financial difficulty, or upon the expiration of the royalty term of the products licensed under the agreement, all rights licensed to Serono under the agreement become irrevocable and fully-paid upon the payment of amounts due by Serono to us which accrued prior to the expiration of the royalty term, except in those countries where restricted by applicable law or for all intellectual property that we do not own and for which we do not have a royalty-free license. Upon a termination of the agreement for a material breach by us or for our financial difficulty, all rights and licenses granted by Serono to us under or pursuant to the agreement will automatically terminate. Under the terms of our agreement with Serono, Serono is responsible to pay for a portion of the development costs of

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

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

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

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

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

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

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

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

scale large enough to support their respective commercial markets or at acceptable margins.

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

- design, construction and qualification of manufacturing facilities that meet regulatory requirements;
- schedule;
- reproducibility;
- production yields;
- purity;
- costs;
- quality control and assurance systems;
- raw material suppliers;
- shortages of qualified personnel; and
- compliance with regulatory requirements.

Improvements in manufacturing processes typically are very difficult to achieve and are often very expensive and may require extended periods of time to develop. If we contract for manufacturing services with an unproven process, our contractor is subject to the same uncertainties, high standards and regulatory controls, and may therefore experience difficulty if further process development is necessary. Even a developed manufacturing process can encounter difficulties due to changing regulatory requirements, human error, mechanical breakdowns, and other events that cannot always be prevented or anticipated.

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

Although we have entered into contractual relationships with third-party manufacturers to produce Orapred, if those manufacturers are unwilling or unable to fulfill their contractual obligations, we may be unable to meet demand for that product or sell that product at all, and we may lose potential revenue.

We have built-out approximately 54,000 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

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required with acceptable yield and costs or may not result in adequate shelf-lives of the final products. If we are not able to develop efficient manufacturing processes, the investment in manufacturing capacity sufficient to satisfy market demand will be much greater and will place heavy financial demands upon us. If we do not achieve our manufacturing cost targets we may be unable to meet demand for our products and lose potential revenue, have reduced margins or be forced to terminate a program.

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

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

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

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

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

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

Our Galli Drive facility is our only manufacturing facility for Aldurazyme and Naglazyme. It is located in the San Francisco Bay Area near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We, and the third-party manufacturers with whom we contract and our single-source suppliers of raw materials, are also vulnerable to damage from other types of disasters, including fires, floods, power loss and similar events. If any disaster were to occur, our ability to manufacture Aldurazyme and Naglazyme, or to have Orapred manufactured for us, could be seriously, or potentially completely impaired, and our Aldurazyme, Naglazyme and Orapred commercialization efforts and revenue from the sale of Aldurazyme, Naglazyme and Orapred 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 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;
- labor interruptions;

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changes in our sources for manufacturing;

the timing and delivery of shipments;

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

conditions affecting the cost and availability of raw materials.

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

A significant portion of our revenue comes from sales of Orapred and decreased sales or increased operational costs related to Orapred could have an adverse affect on our revenues and operating expenses.

A significant portion of our revenue comes from sales of Orapred, and we anticipate that this will continue in the near term. As such, our operating results are and will be dependent on the sales and performance of Orapred. Decreased sales or increased operational costs related to Orapred, whether due to increased competition, pricing pressure from managed care organizations, increased costs of raw materials or otherwise, could have an adverse affect on our revenues and operating expenses.

In the third quarter of 2004 and the first six months of 2005, the FDA approved several generic products that have the same strength and active ingredient as Orapred. Although there are several other products on the market that have the same or similar ingredients, these newly-approved products have the exact same drug substance and concentration as Orapred. Furthermore, the generic products have an AA equivalence rating to Orapred and, therefore, may be substituted at pharmacies without consulting the prescribing physician. These products have caused Orapred to lose significant market share and we expect that our revenue will continue to decrease. While we are implementing strategies to mitigate the loss of market share, at this time we cannot estimate the magnitude of this impact or if the impact will be short-term or permanent. However, we expect that the impact will continue to be significant and that our revenues and operating expenses will be adversely affected.

Additionally, a significant amount of Orapred that was originally sold by Medicis before our acquisition of the product is maintained by our wholesaler customers and either has expired or is near its expiration date. We have replaced and expect to continue to replace the expired product with new product, which will not be recorded as net product sales. As a result, the replacement product will be utilized to supply the retail demand during its shelf life and may result in decreased sales by us in the future.

We depend on a limited number of customers, and if we lose any of them, our business could be harmed.

Our Orapred customers include some of the nation s leading wholesale pharmaceutical distributors, such as AmerisourceBergen, Cardinal and McKesson. For the three months ended March 31, 2005, product sales to these three customers accounted for 85% of our net product sales. The loss of any of these customers accounts or a material reduction in their purchases could harm our business, financial condition or results of

operations. In addition, we may face pricing pressure from our customers.

The distribution network for pharmaceutical products has, in recent years, been subject to increasing consolidation. As a result, a few large wholesale distributors control a significant share of the market. In addition, the number of independent drug stores and small chains has decreased as retail consolidation has occurred. Further consolidation among, or any financial difficulties of, distributors or retailers could result in the combination or elimination of warehouses which may result in product returns to our company, cause a reduction

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in the inventory levels of distributors and retailers, or otherwise result in reductions in purchases of our products, any of which could harm our business, financial condition and results of operations.

Fluctuations in demand for our products create inventory maintenance uncertainties.

We sell our products primarily to major wholesalers and retail pharmacy chains. Consistent with pharmaceutical industry patterns, approximately 75% to 90% of our revenues are derived from three major drug wholesale concerns. While we attempt to estimate inventory levels of our products at our major wholesale customers, using historical prescription information and purchase patterns, this process is inherently imprecise. We rely wholly upon our wholesale and drug chain customers to effect the distribution allocation of our products. There can be no assurance that these customers will adequately manage their local and regional inventories to avoid spot outages.

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

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

We recently 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. With respect to Naglazyme, if our competitors successfully commercialize a product that treats MPS VI in the E.U. before we do, we may effectively be precluded from developing a product to treat that disease because the patient population of the disease is so small. If we do not compete successfully, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product.

There are a number of competitive products with Orapred that have the same active ingredient. Some of these products are less expensive than Orapred. Additionally, in the third quarter of 2004 and the first six months of 2005, the FDA approved several generic products that have the same strength and active ingredient as Orapred. Although there are several other products on the market that have the same or similar ingredients, these

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products have the exact same drug substance and concentration as Orapred. Furthermore, the generic products have an AA equivalence rating to Orapred and therefore may be substituted at pharmacies without consulting the prescribing physician. Our revenue from Orapred has been adversely affected by these generic products and will be further adversely affected if we are not able to implement effective defensive strategies or if our existing defensive strategies are not effective.

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

Our competitors compete with us to attract organizations for acquisitions, joint ventures, licensing arrangements or other collaborations. To date, several of our product programs have been acquired through acquisitions, such as NeuroTrans, and several of our product programs have been developed through licensing or collaborative arrangements, such as Aldurazyme, Naglazyme, Orapred, Phenoptin and Vibrilase. These collaborations include licensing proprietary technology from, and other relationships with, academic research institutions. If our competitors successfully enter into partnering arrangements or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Since each of these opportunities is unique, we may not be able to find a substitute. Several pharmaceutical and biotechnology companies have already established themselves in the field of enzyme therapeutics, including Genzyme, our joint venture partner. These companies have already begun many drug development programs, some of which may target diseases that we are also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

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

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

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

We 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 effect our ability to execute our business plan and harm our operating results.

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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 approval of Aldurazyme in the U.S. and E.U., and other countries, we expect that our joint venture with Genzyme will be required to devote additional resources in the immediate future to support the commercialization of Aldurazyme. Similarly, in light of the FDA approval of Naglazyme for the treatment of MPS VI, we expect to devote additional resources in the immediate future to support the commercialization of Naglazyme.

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

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

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

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

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

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

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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 in the U.S. of $15.0 million plus additional clinical liability coverage with lower loss limits in other countries where clinical studies are conducted. Pharmaceutical companies must balance the cost of insurance with the level of coverage based on estimates of potential liability. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with the commercial use of Orapred, our clinical trials and commercial use of Aldurazyme and Naglazyme, our clinical trials for Phenoptin and Vibrilase, or our clinical trials for our terminated program for Neutralase, for which our insurance coverage may not be adequate.

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

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

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

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

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

- product sales and profitability of Aldurazyme, Naglazyme and Orapred;
- manufacture, supply or distribution of Aldurazyme, Naglazyme or Orapred;

progress of our product candidates through the regulatory process;

results of clinical trials, announcements of technological innovations or new products by us or our competitors;

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- 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 SWX Swiss Exchange. 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.

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

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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.

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FORWARD LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement or 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 supplement and the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus 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 or 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 included important factors in the cautionary statements included in this prospectus supplement and the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, particularly in the section entitled Risk Factors , that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. 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 statements.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 8,500,000 shares of our common stock in this offering will be approximately $56.6 million. Net proceeds are what we expect to receive after deducting underwriting discounts and commissions and estimated expenses payable by us.

We intend to apply the net proceeds of this offering towards the commercialization of our products; additional clinical trials of Phenoptin 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; and working capital.

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;
- 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 interest-bearing securities.

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CAPITALIZATION

The following table shows:

- our capitalization and cash, cash equivalents and short-term investments as of March 31, 2005; and
- our capitalization and cash, cash equivalents and short-term investments as of March 31, 2005, on an as adjusted basis giving effect to the completion of this offering and after deducting underwriting discounts and commissions and estimated expenses payable by us.

	As of March 31, 2005	
	Actual	As adjusted
(in thousands, except for share and per share data)	(unaudited)	
Cash, cash equivalents and short-term investments	$ 29,759	$ 86,408
Long-term debt	$ 220,473	$ 220,473
Stockholders deficit		
Common stock, par value $0.001 per share: 150,000,000 shares authorized; 64,511,159 shares issued and outstanding, actual and 73,011,159 shares issued and outstanding, as adjusted	$ 65	$ 73
Additional paid in capital	421,214	477,855
Accumulated other comprehensive loss	(235)	(235)
Accumulated deficit	(511,279)	(511,279)
Total stockholders deficit	$ (90,235)	$ (33,586)
Total liabilities and stockholders deficit	$ 180,933	$ 237,582

The number of shares of our common stock in the actual and as adjusted columns in the table above excludes:

- 11,348,954 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $9.47 per share as of July 6, 2005; and
- 8,922,198 shares of our common stock issuable upon the conversion of our $125,000,000 3.50% Convertible Subordinated Notes Due 2008.

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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.

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DILUTION

Our net tangible book value on March 31, 2005 was $(127.7) million or approximately $(1.98) 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 8,500,000 shares of our common stock in this offering and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of March 31, 2005 would have been $(0.97) per share. This amount represents an immediate increase in net tangible book value of $1.01 per share to existing stockholders and an immediate dilution in net tangible book value of $8.02 per share to purchasers of common stock in this offering, as illustrated in the following table:

Public offering price per share		$ 7.05
Net tangible book value per share as of March 31, 2005	$(1.98)	
Increase in net tangible book value per share attributable to this offering	1.01	
Pro forma net tangible book value per share as of March 31, 2005 after giving effect to this offering		(0.97)
Dilution per share to new investors in this offering		$ 8.02

This table:

- assumes no exercise of options to purchase 11,987,700 shares of common stock at a weighted average exercise price of $9.65 per share outstanding as of March 31, 2005; and
- excludes the 8,922,198 shares of our common stock issuable upon the conversion of our $125,000,000 3.50% Convertible Subordinated Notes Due 2008.

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UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated is acting as the underwriter in connection with this offering. Subject to the terms and conditions described in a purchase agreement between the underwriter and us, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, all 8,500,000 of the shares of common stock sold under the purchase agreement.

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

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

Commissions and Discounts

The underwriter has advised us that it proposes initially to offer the shares to the public at the public offering price on the cover page of this prospectus supplement. After the public offering, the public offering price, concession and discount may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us.

	Per Share	Total
Public offering price	$ 7.05	$ 59,925,000
Underwriting discount	$ 0.3525	$ 2,996,250
Proceeds, before expenses, to us	$ 6.6975	$ 56,928,750

The expenses of the offering payable by us, not including the underwriting discount, are estimated at $280,000.

No Sales of Similar Securities

We 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 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.

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This lockup provision applies to our common stock and to securities convertible into or exchangeable or exercisable for our common stock.

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, Securities and Exchange Commission rules may limit the underwriter from bidding for and purchasing our common stock. However, the underwriter may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

If the underwriter creates a short position in the common stock in connection with the offering, i.e., if it sells more shares than are listed on the cover of this prospectus supplement, the underwriter may reduce that short position by purchasing shares in the open market. 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.

Neither the underwriter 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 underwriter nor we make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this offering, the underwriter and selling group members 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 marker 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

From time to time, the underwriter and certain of its 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

Internet Distribution

Merrill Lynch may be facilitating Internet distributions for this offering to certain of its Internet subscription customers. Merrill Lynch may allocate a limited number of shares for sale to its online brokerage customers. An electronic prospectus may be available on the Internet web site maintained by Merrill Lynch. Other than the prospectus supplement and accompanying prospectus in electronic format, the information on the Merrill Lynch web site is not part of this prospectus supplement and accompanying prospectus.

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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 underwriter in connection with this offering.

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PROSPECTUS

$150,000,000

Common Stock, par value $0.001

We may offer from time to time the shares of our common stock described in this prospectus in amounts, at prices, and on terms to be determined at the time of the offering. This prospectus describes the general manner in which our common stock may be offered using this prospectus. We will provide the specific terms of the offering in supplements to this prospectus. This prospectus may not be used to offer and sell our common stock unless accompanied by a prospectus supplement.

Our common stock currently trades on the Nasdaq National Market and the Swiss SWX New Market under the symbol BMRN. The last reported sale price for our common stock on the Nasdaq National Market on February 20, 2003, was $10.25 per share.

We will provide the specific terms of the offering in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. See Risk factors beginning on page 3 to read about risks that you should consider before buying shares of our common stock.

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

The date of this prospectus is February 21, 2003

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About this prospectus

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission under a shelf registration process. Under this shelf process, we may sell the shares of our common stock described in this prospectus in one or more offerings, up to a total dollar amount of $150,000,000. Each time we offer common stock, we will provide a prospectus supplement that will describe the specific terms of the offering. The prospectus supplement and any pricing supplement may also add to, update or change the information contained in this prospectus. Please carefully read this prospectus, the prospectus supplement and any pricing supplement, in addition to the information contained in the documents we refer to under the heading Where you can find more information.

SUMMARY

This prospectus contains forward looking statements which involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward looking statements as a result of certain factors appearing under Risk factors and elsewhere in this prospectus.

The following summary does not contain all the information that may be important to you. You should read the entire prospectus, including the financial statements and other information incorporated by reference in this prospectus, before making an investment decision.

We develop enzyme therapies to treat serious, life-threatening diseases and conditions. We leverage our expertise in enzyme biology to develop product candidates for the treatment of genetic diseases, including Mucopolysaccharidosis I (MPS I), Mucopolysaccharidosis VI (MPS VI) and Phenylketonuria (PKU), as well as other critical care situations such as cardiovascular surgery and serious burns. Our product candidates address markets for which no products are currently available or where current products have been associated with major deficiencies.

Our lead product candidate, Aldurazyme is being developed with our joint venture partner, Genzyme Corporation (Genzyme), for the treatment of MPS I, a life threatening genetic disease for which no specific drug treatments currently exist. On July 31, 2002, we announced that the U.S. Patent and Trademark Office had issued U.S. Patent No. 6,426,208 covering Aldurazyme for the treatment of MPS I. The patent claims unique characteristics of the pharmaceutical composition of Aldurazyme, including, but not limited to, the purity of (alpha)-L-iduronidase in the final formulation. This patent, which protects a highly purified form of (alpha)-L-iduronidase, supports the intellectual property position for using Aldurazyme to treat MPS I.

In July 2002, we announced that together with Genzyme, we submitted the final portion of our rolling Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA). The BLA is the application to market Aldurazyme in the U.S. The BLA was formally accepted and granted priority review status in September 2002. On October 28, 2002, Genzyme and we announced that the FDA informed us that the Aldurazyme BLA had been scheduled for review by the Endocrinologic and Metabolic Drugs Advisory Committee on January 15, 2003. We received a response from the FDA regarding the BLA on January 28, 2003. A Marketing Authorization Application or MAA, was submitted to the European Agency for the Evaluation of Medicinal Products (EMEA) in the first quarter of 2002. The MAA is the application to market Aldurazyme in the European Community. We expect a response on the MAA in the first half of 2003.

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On November 24, 2002, Genzyme and we released 36-week data from the ongoing open label Phase-3 extension study of Aldurazyme. This data was submitted to the FDA for review as part of the BLA and was also submitted to the EMEA for review as part of the MAA.

We are developing another product candidate, Neutralase, for reversal of anticoagulation by heparin in patients undergoing coronary artery bypass graft (CABG) surgery. Heparin is a carbohydrate drug commonly used to prevent coagulation, or blood clotting, during certain types of major surgery. Neutralase is a carbohydrate-modifying enzyme that cleaves heparin, allowing coagulation of blood following CABG surgery. We completed critical steps to begin patient enrollment for our Phase 3 trial of Neutralase for reversal of heparin in CABG surgery. Neutralase may also be useful as a heparin reversal agent in coronary angioplasty. Preclinical experiments indicate that Neutralase may also reverse the newer classes of anticoagulants, such as the low molecular weight heparins and the pentasaccharide, fondiparinux.

In 2001, we announced the results of a Phase 1 trial of Aryplase for the treatment of MPS VI, another seriously debilitating genetic disease. Based on data from the Phase 1 trial we initiated a Phase 2 trial of Aryplase in the first quarter of 2002 and expect results in the first half of 2003. We are also developing Vibrilase, a topical enzyme product for use in removing burned skin tissue in the treatment of serious burns. We initiated a Phase 1 clinical trial of Vibrilase in the United Kingdom in the fourth quarter of 2001, and expect to analyze the results from this trial in the first half of 2003.

In addition, we are in preclinical development with several other enzyme product candidates for genetic and other diseases and conditions, as well as with NeuroTrans, our technology that is being investigated as a method for delivering enzymes and other drug candidates to the brain through traditional intravenous delivery. Additionally, we are actively seeking partners for licensing the NeuroTrans technology for use with non-enzyme based treatments, including for the treatment of brain cancers.

Our principal executive offices are located at 371 Bel Marin Keys Boulevard, Suite 210, Novato, CA 94949 and our telephone number is (415) 884-6700. BioMarin, Aryplase, Neutralase and Vibrilase are our trademarks. Aldurazyme is a trademark of BioMarin/Genzyme LLC. All ot trademarks or trade names referred to in this prospectus are the property of their respective owners. Information contained in our website, www.biomarinpharm.com, is not part of this prospectus.

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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. Before purchasing these securities, you should carefully consider the following risk factors, as well as other information contained in this prospectus or incorporated by reference into this prospectus, to evaluate an investment in the securities offered by this 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.

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.

We are in an early stage of development and have operated at a net loss since we were formed. Since we began operations in March 1997, we have been engaged primarily in research and development. We have no sales revenues from any of our product candidates. As of December 31, 2002, we had an accumulated deficit of approximately $225.6 million. We expect to continue to operate at a net loss for at least the next few years, and we expect that our net loss for the first quarter of 2003 will be greater than that for the comparable period of 2002. Our future profitability depends on our receiving regulatory approval of our product candidates and our ability to successfully manufacture and market any approved drugs, either by ourselves or jointly with others. The extent of our future losses and the timing of profitability are highly uncertain. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations.

If we fail to obtain the capital necessary to fund our operations, we will be unable to complete our product development programs.

In the future, we may need to raise substantial additional capital to fund operations. 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.

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:

- Ø the progress, timing and scope of our preclinical studies and clinical trials;
- Ø the time and cost necessary to obtain regulatory approvals;
- Ø the time and cost necessary to develop commercial manufacturing processes, including quality systems and to build or acquire manufacturing capabilities;

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

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

- additional leases for new facilities and capital equipment;

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

We believe that our cash, cash equivalents and short term investment securities balances at December 31, 2002 will be sufficient to meet our operating and capital requirements through 2003. These estimates are based on assumptions and estimates, which may prove to be wrong. As a result, we may need or choose to obtain additional financing during that time.

If we fail to obtain regulatory approval to commercially manufacture or sell any of our future drug products, or if approval is delayed, we will be unable to generate revenue from the sale of our 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. None of our drug products has received regulatory approval to be commercially marketed and sold. If we fail to obtain regulatory approval, we will be unable to market and sell our drug products. Because of the risks and uncertainties in biopharmaceutical development, our drug products could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. If regulatory approval is delayed, our management s credibility, and 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 our 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 clinical trials will be 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 drug product. We expect the number of preclinical studies and clinical trials that the regulatory authorities will require will vary depending on the drug product, 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 drug products. 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 on the target 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 drug products. Additional factors that can cause delay or termination of our clinical trials include:

- slow or insufficient patient enrollment;

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

- adverse medical events or side effects in treated patients;
- lack of effectiveness of the product candidate being tested; and
- regulatory requests for additional clinical trials.

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

We completed a 235 week patient evaluation for the initial clinical trial of our lead drug product, Aldurazyme, for the treatment of MPS I. Two of the original ten patients enrolled in this trial died in 2000. One of these patients received 103 weeks of Aldurazyme treatment and the other received 137 weeks of treatment. A third patient from this initial trial died in 2002, after 234 weeks of treatment. One of the original forty-five patients who completed the Phase 3 clinical trial died after 16 weeks of the Phase 3 extension study. One patient treated under a single-patient use protocol died after 28 weeks of Aldurazyme treatment. Based on medical data collected from clinical investigative sites, none of these cases directly implicated treatment with Aldurazyme as the cause of death. If cases of patient complications or death are ultimately attributed to Aldurazyme, our chances of commercializing this drug would be seriously compromised.

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

Aldurazyme and Aryplase have obtained fast track designations, which provides certain advantageous procedures and guidelines with respect to the review by the FDA of the BLA for these products and which may result in our receipt of an initial response from the FDA earlier than would be received if these products had not received a fast track designation. However, these procedures and guidelines do not guarantee 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 products had not received fast track designation. If the review process or approval for either product is delayed, realizing revenue from the sale of the products will be delayed and the capital necessary to fund these programs will be increased.

We will not be able to sell our products if we fail to comply with manufacturing regulations.

Before we can begin commercial manufacture of our products, we must obtain regulatory approval of our manufacturing facilities and processes. In addition, manufacture of our drug products must comply with the FDA s current Good Manufacturing Practices regulations, commonly known as cGMP. The cGMP regulations govern facility compliance, quality control and documentation policies and procedures. 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 Galli Drive and our Bel Marin Keys Boulevard manufacturing facilities have been inspected and licensed by the State of California for clinical pharmaceutical manufacture. Due to the complexity of the processes used to manufacture our products, we may be unable to pass federal or international regulatory inspections in a cost effective manner. For the same reason, any potential third party manufacturer of our drug products may be unable to comply with cGMP regulations in a cost effective manner.

We must pass federal, state and European regulatory inspections, and we must manufacture process qualification batches to final specifications under cGMP controls for each of our drug products before the marketing applications can be approved. Although we have completed process qualification batches for Aldurazyme, these batches may be rejected by the regulatory authorities, and we may be unable to manufacture the process qualification batches for our other products or pass the inspections in a timely manner, if at all.

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If we fail to obtain 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 European Community 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 United States. 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. However, different drugs can be approved for the same condition. Similar regulations are available in the European Community with a ten-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 particularly important for our products that are eligible for orphan drug designation. For eligible drugs, we plan to rely on the exclusivity period under the orphan drug designation to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have patent protection, our competitors may then sell the same drug to treat the same condition.

Even though we have obtained orphan drug designation for certain of our product candidates and even if we obtain orphan drug designation for other products we develop, due to the uncertainties associated with developing pharmaceutical products, we may not be the first to obtain marketing approval for any orphan indication or, if we are the first, that exclusivity would effectively protect the product from competition. 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.

Two of our lead drug candidates, Aldurazyme and Aryplase, 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 Aryplase targets patients with MPS VI. We estimate that there are approximately 3,400 patients with MPS I and 1,100 patients with MPS VI in the developed world. We believe that we will need to market worldwide to achieve significant market share. In addition, we are developing other drug candidates to treat conditions, such as other genetic diseases and serious burn wounds, with small patient populations. Due to the expected costs of treatment for Aldurazyme and Aryplase, we may be unable to obtain sufficient market share for our drug products at a price high enough to justify our product development efforts.

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 with MPS I using Aldurazyme and for patients with MPS VI using Aryplase is expected to be 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 Aryplase 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

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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 no expertise obtaining reimbursement. We expect to rely on the expertise of our joint venture partner Genzyme to obtain reimbursement for the costs of Aldurazyme. In addition, we will need to develop our own reimbursement expertise for future drug candidates unless we enter into collaborations with other companies with the necessary expertise. We will not know what the reimbursement rates will be until we are ready to market the product and we actually negotiate the rates. If we are unable to obtain sufficiently high reimbursement rates, our products may not be commercially viable or our future revenues and gross margins may be adversely affected.

We expect that, in the future, reimbursement will be increasingly restricted both in the United States 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 United States. In some foreign markets, the government controls the pricing, which would 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.

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 enzymes we are developing. If we must spend significant time and money protecting our patents, designing around patents held by others or licensing, for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed.

The patent positions of biotechnology products are complex and uncertain. The scope and extent of patent protection for some of our products are particularly uncertain because key information on some of the enzymes we are developing has existed in the public domain for many years. Other parties have published the structure of the enzymes, the methods for purifying or producing the enzymes or the methods of treatment. The composition and genetic sequences of animal and/or human versions of many of our enzymes have been published and are believed to be in the public domain. The composition and genetic sequences of other MPS enzymes that we intend to develop as products have also been published. Publication of this information may prevent us from obtaining composition-of-matter patents, which are generally believed to offer the strongest patent protection. For enzymes 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 product candidates, including Aldurazyme.

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

Ø 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.

Ø 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 research and development 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 United States 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 or by universities. These government organizations and universities may be unwilling to grant us any exclusive rights to technology or products derived from these collaborations prior to entering into the relationship. If we do not obtain required licenses or rights, we could encounter delays in product development while we attempt to design around other patents or even be prohibited from developing, manufacturing or selling products requiring these licenses. There is also a risk that disputes may arise as to the rights to technology or products developed in collaboration with other parties.

The United States Patent and Trademark Office has issued two 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 unless and

until we obtain a license.

The United States Patent and Trademark Office has issued two patents to a third party that include composition-of-matter and method of use claims for human recombinant (alpha)-L-iduronidase. Our

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lead drug product, Aldurazyme, is based on human recombinant (alpha)-L-iduronidase. We believe that these patents are invalid on a number of grounds. A corresponding patent application was filed 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 pending in Canada and Japan, and these applications are being prosecuted by the applicants. It is not known 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 delay commercialization of Aldurazyme in the United States.

The patent holder has granted an exclusive license for products relating to these patents to one of our competitors. If we are unable to successfully challenge the patents, we may be unable to produce Aldurazyme in the United States (or in Canada or Japan, should patents issue in these countries) unless we can obtain a sublicense from the current licensee. The current licensee is not required to grant us a license and even if a license is available, we may have to pay substantial license fees, which could adversely affect our business and operating results.

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

We are relying on Genzyme to apply the expertise it has developed through the launch and sale of other enzyme-based products to the marketing of our initial drug product, Aldurazyme. We have no experience selling, marketing or obtaining reimbursement for pharmaceutical products. In addition, without Genzyme we would be required to pursue foreign regulatory approvals. We have no 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 or 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. Furthermore, we may terminate the joint venture if Genzyme fails to fulfill its contractual obligation to pay us $12.1 million in cash upon the approval of the BLA for Aldurazyme.

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

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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 the product.

Termination of the joint venture in which we retain the rights to Aldurazyme could cause us significant delays in product launch in the United States, difficulties in obtaining third-party reimbursement and delays or failure to obtain foreign regulatory approval, any of which could hurt our business and results of operations. Since Genzyme funds 50% of the joint venture s operating expenses, the termination of the joint venture would double our financial burden and reduce the funds available to us for other product programs.

If we are unable to manufacture our drug products in sufficient quantities and at acceptable cost, we may be unable to meet demand for our products and lose potential revenues or have reduced margins.

Although we have successfully manufactured Aldurazyme 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:

- Ø design, construction and qualification of manufacturing facilities that meet regulatory requirements;
- Ø schedule;
- Ø reproducibility;
- Ø production yields;
- Ø purity;
- Ø costs;

- quality control and assurance systems;

- 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.

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

The manufacture of Neutralase involves the fermentation of a bacterial species. We have never used a bacterial production process for the production of any commercial product. IBEX Technologies Inc., from which we acquired Neutralase, had contracted with a third party for the manufacture of the Neutralase used in prior clinical trials. We have also contracted with a third party for the manufacture of additional quantities of Neutralase.

We have built-out approximately 51,800 square feet at our Novato facilities for manufacturing capability for Aldurazyme and Aryplase 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 the manufacturing process of all of our new drug products, including Aryplase and Neutralase, will require significant time and resources before we can begin to manufacture them (or have them manufactured by third parties) in commercial quantity at acceptable cost.

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

- Ø improving the product yield from our current cell lines, which are colonies of cells that have a common genetic makeup;
- Ø improving the manufacturing processes licensed from others; or
- Ø 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 have otherwise produced. The development of a stable, high production cell line for any given enzyme 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 will have lower margins and reduced profitability in commercial production and larger losses in manufacturing start-up phases.

If we are unable to create marketing and distribution capabilities or to enter into agreements with third parties to do so, our ability to generate revenues will be diminished.

If we cannot expand capabilities either by developing our own sales and marketing organization or by entering into agreements with others, we may be unable to successfully sell our products. We believe that developing an internal sales and distribution capability will be expensive and time consuming. Alternatively, we may enter into agreements with third parties to market our products. For example, under our joint venture with Genzyme, Genzyme is responsible for marketing and distributing Aldurazyme. However, these third parties may not be capable of successfully selling any of our drug products.

With our acquisition of Neutralase we have an enzyme product that has a significantly larger potential patient population than Aldurazyme and Aryplase and will be marketed and sold to different target audiences with different therapeutic and financial requirements and needs. As a result,

we will be competing with other pharmaceutical companies with experienced and well-funded sales and marketing operations targeting these specific physician and institutional audiences. We may not be able to develop our own sales and marketing force at all, or of a size that would allow us to compete with these other companies. If we elect to enter into third-party marketing and distribution agreements in order to sell

into these markets, we may not be able to enter into these agreements on acceptable terms, if at all. If we cannot compete effectively in these specific physician and institutional markets, it would adversely affect sales of Neutralase.

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.

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. With respect to Aldurazyme and Aryplase, if our competitors successfully commercialize a product that treats MPS I or MPS VI, respectively, before we do, we may effectively be precluded from developing a product to treat that disease because the patient populations of the diseases are so small. If one of our competitors gets orphan drug exclusivity, we could be precluded from marketing our version for seven years in the U.S. and ten years in the European Union. However, different drugs can be approved for the same condition. 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.

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 Neutralase and NeuroTrans, and several of our product programs have been developed through licensing or collaborative arrangements, such as Aldurazyme 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 are also competitors 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 drug products. 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

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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.

If we fail to manage our growth or fail to recruit and retain personnel, our product development programs may be delayed.

Our rapid growth has strained our managerial, operational, financial and other resources. We expect this growth to continue. We have entered into a joint venture with Genzyme. If we receive FDA and/or foreign government approval to market Aldurazyme, the joint venture will be required to devote additional resources to support the commercialization of Aldurazyme.

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.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. The loss of key scientific, technical and managerial personnel may delay or otherwise harm our product development programs. Any harm to our research and development programs would harm our business and prospects.

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 Fredric D. Price, our Chairman and Chief Executive Officer, or Emil D. Kakkis, M.D., Ph.D., our Senior Vice President of Business Operations or Christopher M. Starr, Ph.D., our Senior Vice President of Scientific Operations, could be detrimental to us if we cannot recruit suitable replacements in a timely manner. While Mr. Price, Dr. Kakkis and Dr. Starr are parties to employment agreements with us, these agreements do not guarantee that they will remain employed with us in the future. In addition, these agreements do not restrict their ability to compete with us after their employment is terminated. The competition for qualified personnel in the biopharmaceutical 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.

Changes in methods of treatment of disease could reduce demand for our products.

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.

Examples include the potential use in the future of effective gene therapy for the treatment of genetic diseases. The use of gene therapy could theoretically reduce or eliminate the use of enzyme replacement therapy in MPS diseases. Sometimes, this change 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. For example, Neutralase is being developed for heparin reversal in CABG surgery. It is possible that alternative non-surgical methods of treating heart disease could be developed. If so, then the demand for Neutralase would likely decrease.

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Risk factors

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. The BioMarin/Genzyme LLC maintains product liability insurance for our clinical trials of Aldurazyme with aggregate loss limits of $5.0 million. We have obtained insurance against product liability lawsuits for the clinical trials for Aryplase, Vibrilase and Neutralase with aggregate loss limits of $6.0 million. 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 our current clinical trials for Aldurazyme, Aryplase, Vibrilase and Neutralase for which our insurance coverage is not adequate.

If Aldurazyme, Aryplase, Vibrilase or Neutralase receives FDA or foreign regulatory approval, the product liability insurance we will need to obtain in connection with the commercial sales of Aldurazyme, Aryplase, Vibrilase or Neutralase 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.

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:

- progress of Aldurazyme, Neutralase, Aryplase and our other lead drug products through the regulatory process, especially regulatory actions in the United States related to Aldurazyme;
- results of clinical trials, announcements of technological innovations or new products by us or our competitors;
- government regulatory action affecting our drug products or our competitors drug products in both the United States and foreign countries;
- developments or disputes concerning patent or proprietary rights;
- general market conditions and fluctuations for the emerging growth and biopharmaceutical market sectors; economic conditions in the United States or abroad;
- actual or anticipated fluctuations in our operating results;
- broad market fluctuations in the United States or in Europe, which may cause the market price of our common stock to fluctuate; and

Ø 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 Exchange s SWX New Market. 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, 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. 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.

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 the certificate of incorporation providing that stockholders meetings may only be called by the board of directors and a provision in the bylaws providing that the stockholders may not take action by written consent. 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 the 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.

On September 11, 2002, our board of directors authorized a stockholders rights plan and related dividend of one preferred share purchase right for each share of our common stock outstanding at the close of business on September 23, 2002. 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 one-hundredth of a share of our Series B Junior Participating Preferred Stock at a price of $35.00 per one-hundredth of a Preferred Share, subject to adjustment.

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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.

The ability of our stockholders to recover against Arthur Andersen LLP may be limited because we have not been able to obtain, after reasonable efforts, the reissued reports of Arthur Andersen with respect to the financial statements included in this prospectus.

Our audited consolidated financial statements, the audited financial statements of IBEX Technologies Inc./Technologies IBEX Inc. Therapeutic Enzymes Division and Glyko Biomedical Ltd. incorporated by reference into this prospectus have been audited by Arthur Andersen LLP. We have not been able to obtain, after reasonable efforts, the reissued reports of Arthur Andersen with respect to the financial statements included in this registration statement of which this prospectus is a part. Therefore, in reliance on Rule 437a promulgated under the Securities Act, we have dispensed with the requirement to file with this registration statement the reissued report and consent of Arthur Andersen with respect to these financial statements. As a result, our stockholders will not be able to recover against Arthur Andersen under Section 11 of the Securities Act for any untrue statement of a material fact contained in these financial statements or any omissions to state a material fact required to be stated therein. In addition, the ability of Arthur Andersen to satisfy any claims properly brought against it may be limited as a practical matter due to recent developments involving Arthur Andersen.

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Forward looking statements

This prospectus contains forward looking statements. These statements relate to future events or our future financial performance. We have identified forward looking statements in this prospectus using words such as anticipates , believes, could, estimates, expects, intends, ma potential, predicts, should, or will or the negative of such terms or other comparable terminology. These statements are based on our beliefs as well as assumptions we made using information currently available to us. Because these statements reflect our current views concerning future events, these statements involve risks, uncertainties, and assumptions. These risks, uncertainties, assumptions and other factors, including the risks outlined under Risk factors, that may cause our or our industry s actual results, levels of activity, performance or achievements to be materially different from future results, levels of actual activity, performance or achievements expressed or implied by such forward looking statements.

Although we believe that the expectations reflected in the forward looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of such statements. We are under no duty to update any of the forward looking statements after the date of this prospectus to conform such statements to actual results, unless required by law.

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Use of proceeds

We cannot guarantee that we will receive any proceeds in connection with this offering. Unless we inform you otherwise in a prospectus supplement or any pricing supplement, we expect to use the net proceeds from any and all offerings of the common stock registered hereunder for general corporate purposes and working capital, which may include some or all of the following purposes:

- to fund our share of costs associated with our joint venture with Genzyme for the development and commercialization of Aldurazyme;
- to fund research and development including clinical trials, regulatory processes, process development and scale-up and start-up of manufacturing activities for our other pharmaceutical product programs, including Neutralase, Aryplase and Vibrilase, and other products in earlier stages of development; and
- to fund research, development, clinical and commercial manufacturing facilities, including related equipment.

A portion of the proceeds may also be used to acquire or invest in businesses or products or to obtain rights to use other technologies. There are currently no commitments or agreements with respect to any such acquisitions.

We have not identified precisely the amounts we plan to spend on each of these areas or the timing of such expenditures. Accordingly, our management will have significant flexibility in applying such proceeds. The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from this offering, progress with the regulatory approval, manufacturing and commercialization of Aldurazyme, Neutralase, Aryplase and Vibrilase and progress with our other development programs. In addition, expenditures will also depend upon the establishment of additional collaborative arrangements with other companies, the availability of other financing and other factors. Pending use for these or other purposes, we intend to invest the net proceeds of this offering in short-term, investment-grade, interest-bearing securities.

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Plan of distribution

We may offer the common stock covered by this prospectus by one or more of, or a combination of, the following methods:

- through agents to the public;
- to underwriters for resale to the public;
- directly to institutional investors;
- in payment of all or a portion of the purchase price from one or more acquisitions of companies, businesses or assets; or
- as consideration for rights for us to use third party technologies pursuant to one or more license, development or other similar agreements.

We will set forth in a prospectus supplement the terms of the offering of securities, including:

- the name or names of any agents or underwriters;
- the purchase price of the securities being offered and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;
- any initial public offering price; and
- any discounts or concessions allowed or reallowed or paid to dealers.

To the extent required by law, we may also provide this information by an amendment to the registration statement, of which this prospectus is a part.

SALE THROUGH AGENTS

We may designate agents to solicit purchases for the period of the agent s appointment or to sell the common stock on a continuing basis. Unless we inform you otherwise in the applicable prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of the agent s appointment.

SALE THROUGH UNDERWRITERS

If we use underwriters for a sale of the common stock, the underwriters will acquire the common stock for their own account. The underwriters may resell the common stock in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. We may offer the common stock through an underwriting syndicate or through a single underwriter. The obligations of the underwriters to purchase the common stock will be subject to the conditions set forth in the applicable underwriting agreements.

The underwriters will be obligated to purchase all the offered common stock, subject to certain conditions contained in an underwriting agreement that we will enter into with the underwriters at the time of sale to them. The underwriters may from time to time change any public offering price and any discounts or concessions allowed or reallowed or paid to dealers. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement that names the underwriter the nature of any such relationship.

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Plan of distribution

SALE THROUGH DEALERS

If we use dealers in the sale of common stock, we will sell the common stock to the dealers as principals. They may then resell that common stock to the public at varying prices determined by the dealers at the time of resale or at a fixed offering price agreed to with us at the time of sale.

COMPENSATION OF UNDERWRITERS, DEALERS AND AGENTS

Underwriters, dealers and agents that participate in the distribution of the common stock may be underwriters as defined in the Securities Act of 1933 and any discounts or commissions they receive from us, as well as any profit on their resale of the common stock, may be treated as underwriting discounts and commissions under the Securities Act of 1933. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers or agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act of 1933. Underwriters, dealers and agents may engage in transactions with or perform services for us or our subsidiaries in the ordinary course of their businesses. This includes commercial banking and investment banking transactions.

DIRECT SALES

We may sell the common stock directly. In that event, no underwriters or agents would be involved. We may sell the common stock directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of that common stock.

DELAYED DELIVERY CONTRACTS

If we so indicate in a prospectus supplement, we may authorize underwriters, dealers or agents to solicit offers from selected types of institutions to purchase common stock from us at the public offering price under delayed delivery requirements. These contracts would provide for payment and delivery on a specified date in the future. Institutions with which such contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement relating to such contracts will set forth the price to be paid for common stock under the contracts, the commission payable for solicitation of the contracts and the date or dates in the future for delivery of the common stock under the contracts.

STABILIZATION ACTIVITIES

During and after an offering through underwriters, the underwriters may purchase and sell the common stock in the open market. These transactions may include overallotment and stabilizing transactions and purchases to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, in which selling concessions allowed to syndicate members or other broker-dealers for the offered common stock sold for their account may be reclaimed by the syndicate if the offered common stock is repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the offered common stock, which may be higher than the price that might otherwise prevail in the open market. If commenced, these activities may be discontinued at any time.

PASSIVE MARKET MAKING

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the

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commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of highest independent bid for the security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid then must be lowered when certain purchase limits are exceeded.

ACQUISITIONS

We may offer the common stock in payment of all or a portion of the purchase price from one or more acquisitions of companies, businesses or assets. We expect that the terms of acquisitions in which the common stock would be issued by us would be determined by negotiations between us and the owners of the companies, businesses or assets we intend to acquire. It is anticipated that the common stock issued in any such acquisition would be valued for purposes of the acquisition at a price reasonably related to the market value of the common stock either at the time of the execution of the definitive acquisition agreement or at the time of the consummation of the acquisition.

LICENSE, DEVELOPMENT OR OTHER SIMILAR AGREEMENTS

We may offer the common stock as consideration for rights for us to use third party technologies pursuant to one or more license, development or other similar agreements. We expect that the terms of those agreements would be determined by negotiations between us and the other party or parties to a particular agreement. The common stock issued as part of any such agreement would be valued for purposes of the agreement at a price reasonably related to the market value of the common stock either at the time of the signing of the agreement, or such other date as the agreement stipulates.

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Legal matters

For the purpose of this offering, Paul, Hastings, Janofsky & Walker LLP, Los Angeles, California is giving an opinion of the validity of the issuance of the securities offered in this prospectus.

Experts

Our consolidated financial statements as of December 31, 2002, and for the year then ended, have been incorporated by reference herein and elsewhere in the registration statement in reliance upon the report of KPMG LLP, independent accountants, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

Our audited financial statements for the year ended December 31, 2001, included in our Annual Report on Form 10-K, the audited financial statements of IBEX Technologies Inc./Technologies IBEX Inc. Therapeutic Enzymes Division included in our Current Report on Form 8-K/A, as filed on January 14, 2002, and the audited financial statements of Glyko Biomedical Ltd. included in our Current Report on Form 8-K/A, as filed on October 18, 2002, which are incorporated by reference in this prospectus and elsewhere in the registration statement, have been audited by Arthur Andersen LLP, independent public accountants, as indicated in their report with respect thereto. After reasonable efforts, we have not been able to obtain a current consent of Arthur Andersen LLP to the inclusion of these financial statements, and the related report of Arthur Andersen LLP, in this prospectus. Therefore, in reliance on Rule 437a of the Securities Act, the consent of Arthur Andersen included herein has not been reissued and Arthur Andersen LLP has not consented to the inclusion of its report in this amendment to the registration statement. As a result, our stockholders may not be able to recover against Arthur Andersen LLP under Section 11 of the Securities Act for any untrue statement of a material fact contained in these financial statements or any omissions to state a material fact required to be stated in these financial statements. In addition, the ability of Arthur Andersen LLP to satisfy claims properly brought against it may be limited as a practical matter due to recent developments involving Arthur Andersen LLP.

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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 Rooms at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the Public Reference Rooms. Our SEC filings are also available at the SEC s Web site at http://www.sec.gov. In addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, Washington, D.C. 20006.

The SEC allows us to incorporate by reference information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supercede this information. Further, all filings we make under the Securities Exchange Act of 1934 after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus. 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 the Securities Exchange Act of 1934:

1. Our Annual Report on Form 10-K for the year ended December 31, 2001, as amended by Form 10-K/A, as filed on April 30, 2002;

2. Our Quarterly Report on Form 10-Q for the quarters ended March 31, 2002, June 30, 2002 and September 30, 2002;

3. Our Current Report of Form 8-K/A filed on January 14, 2002 and our Current Reports on Form 8-K, as filed on January 7, 2002, January 15, 2002; February 7, 2002; February 26, 2002; March 21, 2002; April 16, 2002; April 24, 2002; May 7, 2002; May 16, 2002; June 12, 2002, as amended and restated on June 18, 2002; June 24, 2002; June 25, 2002; July 9, 2002; July 15, 2002; July 29, 2002; August 1, 2002; August 2, 2002; August 26, 2002 as amended by Form 8-K/A on October 18, 2002; September 13, 2002; September 17, 2002; September 30, 2002; October 30, 2002; November 1, 2002; November 26, 2002; December 23, 2002; January 17, 2003; January 29, 2003; February 6, 2003; and February 10, 2003; and

4. The description of our common stock set forth in our Form 8A, filed with the SEC on July 15, 1999.

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: Joshua A. Grass

371 Bel Marin Keys Boulevard, Suite 210

Novato, CA 94949

(415) 884-6777

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 part of this prospectus.

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8,500,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

Merrill Lynch & Co.

July 14, 2005