BIOMARIN PHARMACEUTICAL INC
Form 424B5
February 21, 2003
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Filed Pursuant to Rule 424(b)(5)

File Number 333-102866

PROSPECTUS SUPPLEMENT

(To Prospectus dated February 21, 2003)

7,500,000 Shares

Common Stock

We are selling all of the 7,500,000 shares of common stock offered by this prospectus supplement.

Our common stock is quoted on the Nasdaq National Market and the Swiss SWX New Market under the symbol BMRN. On February 20, 2003, the last reported sale price of our common stock on the Nasdaq National Market was $10.25 per share.

Investing in our common stock involves a high degree of risk. Before buying any shares you should carefully read the discussion of material risks of investing in our common stock in Risk factors beginning on page 3 of the accompanying prospectus.

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.

	Per share	Total
Public offering price	$10.00	$ 75,000,000
Underwriting discounts and commissions	$ 0.60	$ 4,500,000

Proceeds, before expenses, to us	$ 9.40	$ 70,500,000

The underwriters may also purchase from us up to an additional 1,125,000 shares of our common stock at the public offering price less the underwriting discount, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

The underwriters are offering the shares of our common stock as described in Underwriting. Delivery of the shares will be made on or about February 26, 2003.

UBS Warburg

CIBC World Markets

SG Cowen

The date of this prospectus supplement is February 21, 2003

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You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide information different from that contained or incorporated by reference into this prospectus supplement or the accompanying prospectus. Neither the delivery of this prospectus supplement, nor any sale of common stock, shall, under any circumstances, create any implication that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is correct after the date of this prospectus supplement. These documents are not an offer to sell or a solicitation of an offer to buy these shares of common stock in any circumstance under which the offer or solicitation is unlawful.

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BioMarin, Neutralase, Aryplase, Vibrilase and NeuroTrans are trademarks of BioMarin Pharmaceutical Inc. Aldurazyme® is a registered trademark of BioMarin/Genzyme LLC. All other trademarks or trade names referred to in this prospectus supplement are the property of their respective owners.

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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 section, and other information incorporated by reference before making an investment decision.

BUSINESS OVERVIEW

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, 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 currently being evaluated for market approval in the United States, the European Union, Canada and Australia for the treatment of Mucopolysaccharidosis I (MPS I) disease. MPS I is a debilitating and life-threatening genetic disease caused by the deficiency of (alpha)-L-iduronidase, an enzyme responsible for breaking down certain carbohydrates. MPS I is a progressive disease that afflicts patients from birth and frequently leads to severe disability and early death. There are currently no drugs on the market for the treatment of MPS I. Aldurazyme has received both fast track designation from the U.S. Food and Drug Administration (FDA) and orphan drug designation for the treatment of MPS I in the United States, the European Union and Australia. We are developing Aldurazyme through a joint venture with Genzyme Corporation. In collaboration with Genzyme, we submitted a rolling Biologics License Application (BLA) to the FDA, which was completed on July 29, 2002, and submitted a Marketing Authorization Application (MAA) to the European Medicines Evaluation Agency (EMEA) on March 1, 2002. On January 15, 2003, an FDA-appointed advisory committee voted unanimously that the data on Aldurazyme demonstrated clinically meaningful improvements in endurance and pulmonary function in MPS I patients. The advisory committee stated that any remaining safety issues could be addressed with appropriate labeling and post-approval monitoring. On January 28, 2003, the FDA issued a complete response letter for Aldurazyme. We expect a response on the MAA in the first quarter of 2003.

We are developing our second product candidate, Neutralase, for reversal of anticoagulation by heparin. Heparin is a carbohydrate drug commonly used as an anticoagulant in a range of surgical procedures such as coronary artery bypass graft (CABG) surgery and angioplasty. Neutralase is a carbohydrate-modifying enzyme that cleaves heparin, allowing coagulation of blood and potentially aiding patient recovery following surgery. We believe that Neutralase has the potential to address a broad market with multiple potential medical indications. Our first target indication for Neutralase is for the reversal of anticoagulation by heparin in CABG surgery. We expect to begin enrolling patients in a Phase III trial of Neutralase for the reversal of heparin in CABG surgery in February 2003 and we anticipate that this trial will be completed in the fourth quarter of 2003 or the first quarter of 2004. We also plan to evaluate Neutralase in interventional cardiology procedures such as angioplasty, and in other procedures such as hip and knee surgeries, where heparin or heparin-like anticoagulants such as Lovenox® (a low molecular weight heparin) or Arixtra® (a pentasacharride) are used. We have retained all worldwide commercial rights to Neutralase.

In addition to Aldurazyme and Neutralase, we are developing other enzyme-based therapeutics for the treatment of a variety of diseases and conditions. In March 2002, we began a Phase II trial of Aryplase

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for the treatment of Mucopolysaccharidosis VI (MPS VI), another seriously debilitating genetic disease for which no treatment currently exists. The six month treatment phase of the Phase II trial ended in January 2003 and patients are continuing to receive Aryplase as part of an extension phase of the trial. We have received orphan drug designation for Aryplase in the United States and the European Union. We also are developing Vibrilase, a topical enzyme product for use in removing burned skin tissue in preparation for skin grafting or other therapy. We initiated a Phase I clinical trial of this product in the United Kingdom in the second quarter of 2002 and we expect to begin a Phase II clinical trial in either the United States or the United Kingdom following the completion of this Phase I trial. In addition, we are pursuing preclinical development of several other enzyme product candidates for genetic and other diseases. We have retained all worldwide commercial rights to these product candidates.

RECENT DEVELOPMENTS

FDA issues complete response letter

On January 28, 2003, the FDA issued a complete response letter related to our marketing application for Aldurazyme. The FDA noted that the data submitted in the application supported the safety and effectiveness of Aldurazyme in patients with MPS I. The FDA has not requested any additional clinical data in order to grant final approval of Aldurazyme. To satisfy the FDA s requirements, and in collaboration with Genzyme, we plan to provide additional information to the FDA and take further action with respect to the following three issues outlined in its letter: post-marketing commitments, final product labeling, and follow-up on pre-marketing manufacturing inspection observations. We expect to fully respond to the FDA on these matters in the near future. The FDA also noted that they would work with the companies to make this drug available to patients.

Unanimous FDA advisory committee recommendations

On January 15, 2003, the FDA s Endocrinologic and Metabolic Drugs Advisory Committee voted unanimously that the clinical data on Aldurazyme demonstrated efficacy. In two separate votes, the panel voted 12 to 0 that our Phase III trial showed a meaningful treatment effect in both primary endpoints pulmonary capacity, as measured by percent predicted forced vital capacity, and endurance, as measured by the distance covered in a six-minute walk test. The panel stated that any remaining safety and efficacy issues could be addressed with appropriate labeling and post-approval monitoring.

Glyko Biomedical acquisition

On August 22, 2002, we announced the completion of the acquisition of all the outstanding shares of Glyko Biomedical Ltd. Glyko Biomedical s principal asset was 11,367,617 shares of our common stock, an approximate 21% ownership in us as of the closing date. In exchange for all outstanding shares of Glyko Biomedical, the shareholders of Glyko Biomedical received 11,367,617 shares of our common stock. As a result of the transaction, the shares of our common stock previously held by Glyko Biomedical have been retired, with the number of outstanding shares of our common stock remaining the same.

ALDURAZYME

Our lead product candidate, Aldurazyme, is being developed for the treatment of MPS I. MPS I is a genetic disease caused by the deficiency of (alpha)-L-iduronidase. Patients with MPS I have multiple debilitating symptoms resulting from the buildup of carbohydrate residues in all tissues in the body. These symptoms include delayed physical and mental growth, enlarged livers and spleens, skeletal and joint deformities, airway obstruction, heart disease, reduced endurance and pulmonary function, and impaired hearing and vision. Most patients with MPS I die from complications associated with the disease as children or teenagers. About 3,400 individuals in developed countries have MPS I, including

about 1,000 in the United States and Canada.

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There are currently no approved drugs for the treatment of MPS I. Bone marrow transplantation has been used to treat severely affected patients, generally under the age of two, with limited success. Bone marrow transplantation is associated with high morbidity and mortality rates as well as with problems inherent in the procedure itself, including graft vs. host disease, graft rejection, and donor availability, which severely limit its utility and application.

Aldurazyme is a specific form of recombinant human (alpha)-L-iduronidase that replaces a genetic deficiency of (alpha)-L-iduronidase in MPS I patients, thus reducing or eliminating the build-up of certain carbohydrates in the lysosomes of cells. By eliminating this carbohydrate build-up, Aldurazyme is able to significantly reduce symptoms experienced by these patients. In clinical trials to date, researchers have observed significant clinical and biochemical improvement in patients treated with Aldurazyme, including improved pulmonary function, improved endurance, decreased joint stiffness, decreased fatigue, improved vision, reduced airway obstruction, weight and height gain, improved cardiac function and the elimination of severe headaches.

In September 1998, we formed a 50/50 joint venture with Genzyme for the worldwide development and commercialization of Aldurazyme. We are responsible for product development, manufacturing and United States regulatory submissions. Genzyme is responsible for sales, marketing, distribution, obtaining reimbursement for Aldurazyme worldwide and international regulatory submissions.

In collaboration with Genzyme, we completed a 45-patient, double-blinded, placebo-controlled Phase III clinical trial of Aldurazyme in August 2001. All patients completed the trial and elected to receive Aldurazyme in an open label extension study. On November 2, 2001, we announced positive results from this trial. In July 2002, we announced that, together with Genzyme, we submitted the final portion of our rolling BLA to the FDA. The BLA was formally accepted and granted priority review status in September 2002. On January 15, 2003, the FDA s Endocrinologic and Metabolic Drugs Advisory Committee voted unanimously that the clinical data contained in the application demonstrated the efficacy of Aldurazyme. On January 28, 2003, the FDA issued a complete response letter related to the Aldurazyme application.

In accordance with the terms of our joint venture, Genzyme submitted an MAA to the EMEA in the first quarter of 2002 for marketing in the European Union. We expect a response in the first quarter of 2003. In December 2002, Genzyme submitted applications for market approval of Aldurazyme in Canada and Australia. In Canada, the application has been accepted and was given priority review status under Health Canada s Therapeutic Products Program. Genzyme also requested priority review status in Australia, where the Therapeutic Goods Administration has previously given Aldurazyme orphan drug designation.

The FDA has granted Aldurazyme orphan drug designation, which will result in exclusive rights to market Aldurazyme to treat MPS I for seven years from the date of FDA approval if Aldurazyme is the first product to be approved by the FDA for the treatment of MPS I. In addition, in the European Union, Aldurazyme has been designated as an orphan medicinal product for the treatment of MPS I, giving the potential for ten years of market exclusivity in the European Union.

NEUTRALASE

We are developing Neutralase for the reversal of anticoagulation by heparin in patients undergoing CABG surgery and angioplasty. Patients undergoing CABG surgery are treated with heparin to prevent coagulation during surgery. Once the procedure is completed, protamine is administered to reverse the effect of heparin and therefore prevent excessive bleeding. Currently, protamine is the only commercially available therapeutic for the reversal of heparin anticoagulation. Protamine has been associated with

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adverse side effects, such as abnormal changes in blood pressure, depression of heart function and acute allergic reactions.

We believe Neutralase has the potential to reverse heparin anticoagulation without many of the serious side effects associated with protamine. Neutralase is a carbohydrate-modifying enzyme that breaks down heparin in a manner that reverses heparin s anticoagulation effect and restores the normal coagulation of blood. We believe Neutralase has the potential for use as a reversal agent for heparin anticoagulation in open-heart surgery such as CABG procedures, interventional cardiology procedures such as angioplasty, and in other procedures where heparin or heparin-like anticoagulants are used, such as hip and knee surgeries.

Data from Phase I and Phase II clinical trials indicate that Neutralase can reverse heparin anticoagulation without the adverse changes in blood pressure associated with protamine usage. We expect to begin enrolling patients in a Phase III trial of Neutralase for the reversal of heparin in CABG surgery in February 2003. This Phase III trial of Neutralase is being conducted in patients undergoing CABG surgery, both in instances where heart-lung bypass machines are and are not used. The trial is expected to enroll approximately 600 to 800 patients at 30 sites (24 sites in the United States and 6 sites in Canada). The protocol compares Neutralase to protamine for its ability to reverse anticoagulation by heparin following CABG surgery. If the trial is successful, we anticipate that we will commence a second Phase III study shortly thereafter.

ARYPLASE

We are developing Aryplase as an enzyme replacement therapy for the treatment of MPS VI, a debilitating genetic disease similar to MPS I. Aryplase is a specific form of recombinant human *N*-acetylgalactosamine 4-sulfatase (also known as arylsulfatase B). Aryplase has received fast track designation from the FDA as well as orphan drug designation for the treatment of MPS VI in the United States and in the European Union. In September 2001, we reported positive results from a Phase I clinical trial of Aryplase. We initiated an open-label, multi-national Phase II clinical trial in March 2002 to evaluate the efficacy, safety and pharmacokinetics of weekly intravenous infusions of 1.0 mg/kg of Aryplase in ten MPS VI patients. The trial was completed in January 2003 and results will be presented at The American College of Medical Genetics, 9th Annual Clinical Genetics Meeting, to be held March 13-16, 2003 in San Diego, California.

OTHER PRODUCT DEVELOPMENT PROGRAMS

Vibrilase

We are developing Vibrilase for use in removing burned skin in preparation for skin grafting or other therapy. In the second quarter of 2002, we initiated a Phase I clinical trial of this product candidate in the United Kingdom and we expect to begin a Phase II clinical trial in either the United States or the United Kingdom following the completion of this Phase I trial.

Phenylase

Phenylase is being developed as an oral enzyme therapy for patients with phenylketonuria (PKU), a genetic disease in which the body cannot properly metabolize the amino acid phenylalanine. If left untreated, elevated levels of phenylalanine lead to brain damage and severe mental retardation.

Compliance with existing treatment, consisting of highly restricted and generally unpalatable diets, usually only occurs through middle childhood to ensure normal brain development. Recent data demonstrates that adolescent and adult PKU sufferers who no longer follow restricted diets suffer from a

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number of psychological and neurological symptoms. Phenylase is intended to enable disease control without the need for restrictive diets. Phenylase is currently in preclinical development.

NeuroTrans

NeuroTrans is a novel technology that is designed to allow large molecules such as proteins to be transported efficiently across the blood-brain barrier after administration by traditional intravenous delivery. The technology is based on a protein, p97 or melanotransferrin. Brain capillaries have a high concentration of receptors that actively transport p97 into the brain. We are exploring the delivery of lysosomal enzymes to the brain and will be seeking partners on the delivery of other therapeutics such as neurotrophic factors and cancer drugs.

OUR STRATEGY

Our strategy is to develop therapeutic enzyme products to treat a variety of diseases and conditions. The principal elements of this strategy are to:

Develop and successfully commercialize Aldurazyme

We are seeking to develop and globally commercialize Aldurazyme for the treatment of MPS I. In collaboration with our joint venture partner, Genzyme, we have established commercialization and launch plans for this product. We believe that we will benefit from Genzyme s marketing organization, which has extensive world-wide experience marketing drugs to well-defined patient populations with chronic genetic diseases.

Continue to build a portfolio of medically-important product candidates

We are developing a pipeline of product candidates in various stages of clinical and preclinical development in a variety of therapeutic areas. We believe this strategy increases the likelihood of successful product commercialization, while reducing our exposure to the risk inherent in the development of any one drug or focusing on a single therapeutic area. We currently have one product awaiting marketing approval, one product in Phase III, one product that has completed Phase II, one product in Phase I clinical trials and additional products in late preclinical development.

Target underserved markets

We intend to continue to target market opportunities where there is little or no competition, such as the markets for MPS I and MPS VI. We also target markets where we believe that our technology will enable us to become a market leader in a relatively short time period, such as the market for Neutralase. Our strategy is to avoid markets where product differentiation is a function of marketing strength rather than superior technology.

Seek to license or acquire complementary products and technologies

We intend to supplement our internal drug discovery efforts through the acquisition of products and technologies that complement our general product development strategy. We intend to continue to identify, evaluate and pursue the licensing or acquisition of other strategically valuable products and organizations.

Leverage our core competencies

We believe that we have significant expertise in enzyme biology and production, which we have used to establish a strong platform for the development of enzyme-related pharmaceutical products. We intend to leverage these competencies to develop high-value products for markets with unmet medical needs. When strategically advantageous, we may seek partnerships with industry leaders for the further advancement of our product candidates.

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The offering

Common stock offered	7,500,000 shares
Common stock to be outstanding after the offering	61,321,913 shares
Use of proceeds	We intend to use the net proceeds of this offering to fund development and commercialization of our lead product candidate, Aldurazyme; additional clinical trials and manufacturing of Neutralase; 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.
Nasdaq National Market and Swiss SWX New Market symbol	BMRN

The number of shares of our common stock to be outstanding after this offering in the table above is based on the number of shares outstanding on February 1, 2003, and does not include, as of that date:

- 779,846 shares of common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of $13.35 per share; and
- 7,785,121 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $10.77 per share.

The number of shares of our common stock to be outstanding after this offering in the table above does not give effect to the possible sale and issuance promptly after this offering of up to $1.0 million of our common stock to Acqua Wellington North American Equities Fund, Ltd. on the same terms as the shares offered in this offering pursuant to their rights under the Securities Purchase Agreement with us dated August 15, 2001, as amended.

Unless otherwise stated, all information contained in this prospectus supplement assumes that the underwriters do not exercise their over-allotment option.

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Summary condensed consolidated financial data

This section presents our summary consolidated financial data. You should carefully read the financial statements included in the reports incorporated by reference in this prospectus supplement and the accompanying prospectus, including the notes to the financial statements included in those reports. The selected data in this section is not intended to replace the financial statements.

We derived the condensed consolidated statements of operations data for years ended December 31, 1999, 2000, 2001 and 2002 from audited financial statements. Historical results are not necessarily indicative of results that we may expect in the future. See notes to our consolidated financial statements incorporated by reference in this prospectus supplement and the accompanying prospectus for a description of the number of shares used in the computation of the net loss per common share.

	Year ended December 31,			
Condensed consolidated statements of operations data:	**1999**	**2000**	**2001**	**2002**
(in thousands, except for per share data)				
Revenue from BioMarin/Genzyme LLC	$ 5,300	$ 9,714	$ 11,330	$ 13,919
Operating expenses:				
Research and development	26,341	38,882	44,914	54,455
General and administrative	4,757	6,507	6,718	17,541
In-process research and development			11,647	11,223
Loss of BioMarin/Genzyme LLC	1,673	2,912	7,333	9,547
Total operating expenses	32,771	48,301	70,612	92,766
Loss from operations	(27,471)	(38,587)	(59,282)	(78,847)
Interest income	1,832	2,979	1,871	2,017
Interest expense	(732)	(7)	(17)	(542)
Net loss from continuing operations	(26,371)	(35,615)	(57,428)	(77,372)
Loss from discontinued operations	(1,701)	(1,749)	(10,178)	(89)
Net loss	$ (28,072)	$ (37,364)	$ (67,606)	$ (77,461)
Net loss per share, basic and diluted:				
Loss from continuing operations	$ (0.88)	$ (0.99)	$ (1.40)	$ (1.45)
Loss from discontinued operations	(0.06)	(0.05)	(0.25)	
Net loss	$ (0.94)	$ (1.04)	$ (1.65)	$ (1.45)
Weighted average common shares outstanding	29,944	35,859	41,083	53,279

	December 31, 2002

Condensed consolidated balance sheet data:	Actual	As adjusted[1]
(in thousands)		(unaudited)
Cash, cash equivalents and short-term investments	$ 73,978	$ 144,108
Total current assets	81,072	151,202
Total assets	110,616	180,746
Long-term debt	5,893	5,893
Total stockholders equity	98,543	168,673

(1) As adjusted to give effect to the completion of this offering and receipt of the estimated net proceeds.

This table does not give effect to the possible sale and issuance promptly after this offering of up to $1.0 million of our common stock to Acqua Wellington on the same terms as the shares offered in this offering pursuant to their rights under the Securities Purchase Agreement with us.

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Use of proceeds

We estimate that the net proceeds from the sale of shares of common stock we are offering will be approximately $70.1 million. If the underwriters fully exercise their over-allotment option, the net proceeds from the sale of the shares we are offering will be approximately $80.7 million. Net proceeds are what we expect to receive after deducting the underwriting discount and paying our other estimated expenses of this offering.

We intend to use the net proceeds of this offering for the development and commercialization of our lead product candidate, Aldurazyme; additional clinical trials and the manufacturing of Neutralase; 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 timing and amount of our actual expenditures are subject to change and will be based on many factors, including:

- 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:

Ø our actual capitalization and cash, cash equivalents and short-term investments as of December 31, 2002; and

Ø our capitalization and cash, cash equivalents and short-term investments on December 31, 2002, on an as adjusted basis giving effect to the completion of this offering and receipt of the estimated net proceeds.

	As of December 31, 2002	
	Actual	As adjusted
(in thousands)		(unaudited)
Cash, cash equivalents and short-term investments	$ 73,978	$ 144,108
Long-term debt	$ 5,893	$ 5,893
Stockholders equity:		
Common stock, par value $0.001 per share; 75,000,000 shares, authorized; 53,782,426 shares issued and outstanding, actual and 61,282,426 shares issued and outstanding, as adjusted	$ 54	$ 61
Additional paid-in capital	319,038	389,161
Warrants	5,219	5,219
Deferred compensation	(47)	(47)
Notes from stockholders	(468)	(468)
Accumulated other comprehensive income	327	327
Deficit accumulated during development stage	(225,580)	(225,580)
Total stockholders equity	$ 98,543	$ 168,673
Total liabilities and stockholders equity	$ 110,616	$ 180,746

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

Ø 7,077,509 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $11.21 per share at December 31, 2002; and

Ø

779,846 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of $13.35 per share as of December 31, 2002.

This table does not give effect to the possible sale and issuance promptly after this offering of up to $1.0 million of our common stock to Acqua Wellington on the same terms as the shares offered in this offering pursuant to their rights under the Securities Purchase Agreement with us.

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Dilution

Our net tangible book value on December 31, 2002 was $98.5 million or approximately $1.83 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 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 7,500,000 shares of our common stock in this offering and after deducting the underwriting discount and our estimated offering expenses, our net tangible book value as of December 31, 2002 would have been $2.75 per share. This amount represents an immediate increase in net tangible book value of $0.92 per share to existing stockholders and an immediate dilution in net tangible book value of $7.25 per share to purchasers of common stock in this offering, as illustrated in the following table:

Public offering price per share		$ 10.00
Net tangible book value per share as of December 31, 2002	$ 1.83	
Increase in net tangible book value per share attributable to this offering	0.92	
Pro forma net tangible book value per share as of December 31, 2002 after giving effect to this offering		2.75
Dilution per share to new investors in this offering		$ 7.25

This table:

- assumes no exercise of options to purchase 7,077,509 shares of common stock at a weighted average exercise price of $11.21 per share outstanding as of December 31, 2002;
- assumes no exercise of warrants to purchase 779,846 shares of common stock at a weighted average exercise price of $13.35 per share outstanding as of December 31, 2002; and
- assumes no exercise by Acqua Wellington of its right to purchase up to $1.0 million of our common stock promptly after this offering on the same terms as the shares offered in this offering.

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Underwriting

We and the underwriters for this offering named below have entered into an underwriting agreement concerning the shares being offered hereby. Subject to conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. UBS Warburg LLC, CIBC World Markets Corp. and SG Cowen Securities Corporation are the representatives of the underwriters. UBS Warburg LLC is the sole book-running manager of this offering.

Underwriters	Number of shares
UBS Warburg LLC	3,630,000
CIBC World Markets Corp.	1,996,500
SG Cowen Securities Corporation	1,633,500
Gerard Klauer Mattison & Co., Inc.	60,000
Leerink Swann & Company	60,000
Morgan Keegan & Company, Inc.	60,000
Bank J. Vontobel & Co AG	60,000
Total	7,500,000

We may sell to Acqua Wellington up to 100,000 shares of common stock at the per share offering price set forth on the cover page of this prospectus supplement. The sale to Acqua Wellington is not being made pursuant to this prospectus supplement or through the underwriters named in this prospectus supplement. Our sale of the 7,500,000 shares pursuant to this prospectus supplement is not conditioned on the closing of a possible sale to Acqua Wellington.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have a 30-day option to buy up to 1,125,000 shares from us at the public offering price less the underwriting discounts and commissions to cover these sales. If any shares are purchased under this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table provides information regarding the amount of the discount to be paid to the underwriters by us. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 1,125,000 shares. In compliance with NASD guidelines, the maximum consideration or discount to be received by any NASD member or independent broker dealer may not exceed 8% of the aggregate amount of securities offered pursuant to this prospectus and any applicable prospectus supplement.

	No exercise	Full exercise
Per share	$ 0.60	$ 0.60

Total	$ 4,500,000	$ 5,175,000

We estimate that the total expenses of this offering payable by us, excluding underwriting discounts and commissions, will be about $370,000.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $0.36 per share from the public offering price. Any of these securities dealers may resell any shares purchased from the underwriters to other brokers or dealers at a discount of up to $0.10 per share from the public offering price. If all the shares are not sold at the public offering price, the representatives may change the offering price and the other selling terms.

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Underwriting

We and each of our directors and executive officers have agreed with the underwriters not to offer, sell, contract to sell, hedge or otherwise dispose of, directly or indirectly, any of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, subject to certain permitted exceptions, without the prior written consent of UBS Warburg LLC.

In connection with this offering, the underwriters may purchase and sell shares of our common stock in the open market. These transactions may include stabilizing transactions, short sales and purchases to cover positions created by short sales. Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of our common stock while this offering is in progress. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. Short sales may be either covered short sales or naked short sales. Covered short sales are sales made in an amount not greater than the underwriters over-allotment option to purchase additional shares in this offering. The underwriters may close out any covered short position by either exercising their over-allotment option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned there may be downward pressure on the price of shares in the open market after pricing that could adversely affect investors who purchase in this offering.

The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of that underwriter in stabilizing or short covering transactions.

These activities by the underwriters may stabilize, maintain or otherwise affect the market price of our common stock. As a result, the price of our common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued by the underwriters at any time. These transactions may be effected on the Nasdaq National Market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in the common stock on the Nasdaq National Market prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq National Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker s average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of the common stock to be higher than the price that otherwise would exist in the open market in the absence of such transactions. If passive market making is commenced, it may be discontinued at any time.

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses electronically.

We have agreed to indemnify the several underwriters against some liabilities, including liabilities under the Securities Act of 1933, as amended, and to contribute to payments that the underwriters may be required to make in respect thereof.

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Underwriting

UBS Warburg LLC has in the past provided and may in the future provide financial advisory services to us. For these services, we have paid them, or will pay them, customary compensation. We may also engage any of the other underwriters for financial advisory services in the future.

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. Dewey Ballantine LLP, New York, New York, is counsel to the underwriters 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;

- 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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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

- 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:

Ø trading in different time zones;

Ø different ability to buy or sell our stock;

Ø different market conditions in different capital markets; and

Ø 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

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Ø 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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