BIOMARIN PHARMACEUTICAL INC
Form S-3
June 17, 2004
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As filed with the Securities and Exchange Commission on June 17, 2004

Registration No. 333-_____

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

BioMarin Pharmaceutical Inc.

(Exact name of registrant as specified in its charter)

Delaware	**68-0397820**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

371 Bel Marin Keys Boulevard, Suite 210

Novato, California 94949

(415) 506-6700

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Louis Drapeau

Chief Financial Officer

BioMarin Pharmaceutical Inc.

371 Bel Marin Keys Boulevard, Suite 210

Novato, California 94949

(415) 506-6700

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:

Siobhan McBreen Burke

Paul, Hastings, Janofsky & Walker LLP

515 South Flower Street, 25th Floor

Los Angeles, California 90071-2371

(213) 683-6000

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If delivery of the prospectus is expected to be made pursuant to Rule 434 under the Securities Act, please check the following box. ¨

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered (1)	Proposed Maximum Offering Price Per Share (2)	Proposed Maximum Aggregate Offering Price (1) (2)	Amount of Registration Fee
Common Stock, par value $0.001	6,992,999	$6.135	$42,902,048.87	$5,435.69

(1) Estimated solely for the purpose of computing the registration fee required pursuant to Section 6(b) of the Securities Act and computed pursuant to Rule 457(c) of the Securities Act.

(2) Estimated solely for the purpose of computing the registration fee required pursuant to Section 6(b) of the Securities Act and computed pursuant to Rule 457(c) of the Securities Act, based on the average of the high and low prices of the Common Stock on June 10, 2004 as reported on the NASDAQ National Market.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE SECURITIES AND EXCHANGE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities, and is not soliciting an offer to buy these securities, in any state where the offer or sale is not permitted.

PROSPECTUS

SUBJECT TO COMPLETION, DATED JUNE 17, 2004

BIOMARIN PHARMACEUTICAL INC.

6,992,999 Shares of

Common Stock

par value $.001

This prospectus relates to an aggregate of 6,992,999 shares of common stock of BioMarin Pharmaceutical Inc. that may be offered for sale by Medicis Pharmaceutical Corporation (Medicis) or Medicis Pediatrics, Inc., formerly known as Ascent Pediatrics, Inc. (Ascent), who may acquire such shares in private transactions. We have registered the aggregate number of shares under the Securities Act of 1933 on behalf of Medicis and Ascent so that they can sell such shares in a public offering or other distribution after they have obtained such shares. We will not receive any of the proceeds from the offer and sale of the shares.

Our common stock currently trades on the Nasdaq National Market and the SWX Swiss Exchange under the symbol BMRN.

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 June _____, 2004

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As used in this prospectus, the terms we, us, our, the Company and BioMarin means BioMarin Pharmaceutical Inc. and its subsidiaries (unle the context indicates a different meaning), and the term common stock means our common stock, $.001 par value per share.

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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 innovative biopharmaceuticals and commercialize therapeutics for serious pediatric diseases. We select product candidates for diseases and conditions that represent both a significant medical need and also have well-understood biology.

Our first pediatric-focused product, Aldurazyme® (laronidase), has been approved for marketing in the United States by the U.S. Food and Drug Administration (FDA), in the European Union (E.U.) by the European Medicines Evaluation Agency (EMEA) and other countries 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 normally required for breaking down certain complex carbohydrates. MPS I is a progressive disease that afflicts patients from birth and leads to severe disabilities and early death. As the first drug approved for MPS I, Aldurazyme has been granted orphan drug status in the U.S. and the E.U., which gives Aldurazyme seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS I. We have developed Aldurazyme through a joint venture with Genzyme Corporation (Genzyme).

We are developing other pediatric-focused product candidates including: Aryplase™ (recombinant, human N-acetylgalactosamine 4-sulfatase) for the treatment of mucopolysaccharidosis VI (MPS VI); Phenoptin™, a proprietary oral form of tetrahydrobiopterin (6R-BH4), for the treatment of moderate to mild forms of phenylketonuria (PKU); and Phenylase™ (recombinant phenylalanine ammonia lyase) for those who do not respond to Phenoptin, likely those with the more severe form of PKU.

On June 3, 2004, we announced the positive results of our Phase 3 trial of Aryplase for the treatment of MPS VI, a progressive and seriously debilitating genetic disease for which no drug treatment currently exists. MPS VI is caused by the deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B), an enzyme normally required for the breakdown of certain complex carbohydrates. The clinical trial demonstrated a statistically significant improvement in endurance in patients receiving Aryplase compared to patients receiving placebo, as measured by the distance walked in 12 minutes, the primary end point of the trial. Additionally, the data demonstrated a statistically significant improvement in reduction of glycosaminoglycans (GAGs) and a positive trend in a 3 minute stair climb, the secondary end points of the trial. Based on this data, we expect to file for marketing authorization in the U.S. and E.U. in the fourth quarter of 2004. Aryplase has received orphan drug designation for the treatment of MPS VI in the U.S. and the E.U.

In February 2004, we initiated a clinical trial related to our PKU program. Our PKU program is comprised of two investigational therapies: Phenoptin for mild to moderate PKU and Phenylase for more severe PKU. PKU is a genetic disease that affects at least 50,000 diagnosed patients under the age of 40 in the developed world, half of whom have a moderate to mild form of the disease. PKU is caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH), which is required for the metabolism of phenylalanine (Phe). Phe is an amino acid found in most protein-containing foods. Without sufficient quantity or activity of PAH, Phe accumulates to abnormally high levels in the blood resulting in a variety of serious neurological complications. Phenoptin, our lead product candidate for the treatment of PKU, is a proprietary oral form of tetrahydrobiopterin (6R-BH4), an oral enzyme cofactor that works in combination with PAH to metabolize Phe. If approved, it could become the first drug for the treatment of PKU. In November 2003, we entered into an agreement with Merck Eprova AG, a subsidiary of Merck KGaA, for the development and manufacturing of Phenoptin. Phenylase, an enzyme therapy currently in preclinical development, is being developed as a

subcutaneous injection and is intended for those who do not respond to Phenoptin, likely those with the more severe form of PKU.

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On May 18, 2004, we completed the acquisition of the business related to Orapred®, certain other oral liquid prednisolone solution products and oral dissolving tablet prednisolone products (the Pediatrics Business) conducted by Ascent, a subsidiary of Medicis. Under the terms of an asset purchase agreement, securities purchase agreement and license agreement that govern our acquisition of the Pediatrics Business, we (i) acquired from Medicis, Ascent and Medicis Manufacturing Corporation, a wholly-owned subsidiary of Medicis, certain pharmaceutical assets relating to the Pediatrics Business, including Orapred inventory, tangible assets, sales-related materials, contracts and copyrights, (ii) obtained from Medicis an option to purchase, in approximately five years (subject to acceleration), all of the issued and outstanding capital stock of Ascent, and (iii) obtained from Ascent a worldwide, exclusive license, with the right to sublicense, to certain assets used in or relating to the Pediatrics Business, including technology, trademarks and improvements. In connection with the acquisition of the Pediatrics Business, we also employed approximately 70 employees of Ascent involved in the sales and marketing activities of the Pediatrics Business.

Outside of pediatrics, we are evaluating multiple enzyme-based therapies for serious medical conditions: Vibrilase™, an investigational topical enzyme therapy for use in the debridement of serious burns, and preclinical candidates including Chondroitinase for spinal cord injuries and Extravase™ for reperfusion injury. We completed enrollment in a Phase 1 clinical trial of Vibrilase in the United Kingdom in April 2004 and we expect to announce data in the third quarter of 2004. We are pursuing preclinical development of several other enzyme product candidates for genetic and other diseases. We have retained all worldwide commercial rights to all of our product candidates. Additionally, we are evaluating two platform technologies, NeuroTrans™ and Immune Tolerance, to overcome limitations associated with existing pharmaceuticals.

Our principal executive offices are located at 371 Bel Marin Keys Boulevard, Suite 210, Novato, CA 94949 and our telephone number is (415) 506-6700. Information contained in our website, www.BMRN.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.

Since we began operations in March 1997, we have been engaged primarily in research and development and have operated at a net loss for the entire time. Our first product, Aldurazyme, was approved for commercial sale in the U.S. and the E.U. and has generated approximately $18.9 million in sales revenue to our joint venture through March 31, 2004. We acquired exclusive rights to Orapred in May 2004 and have not yet reported sales with respect to Orapred. We have no sales revenues from our product candidates. As of March 31, 2004, we had an accumulated deficit of $321.3 million. We expect to continue to operate at a net loss for the foreseeable future. Our future profitability depends on the successful commercialization of Aldurazyme by our joint venture partner, Genzyme, our marketing of Orapred through the newly-acquired Ascent sales force, our receiving regulatory approval of our product candidates and our ability to successfully manufacture and market any approved drugs, either by ourselves or jointly with others. The extent of our future losses and the timing of profitability are highly uncertain. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

If we fail to obtain the capital necessary to fund our operations, 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:

- our ability to successfully commercialize Aldurazyme and Orapred;
- the progress, timing and scope of our preclinical studies and clinical trials;
- the level of investment required to integrate the former Ascent pediatrics business;

the time and cost necessary to obtain regulatory approvals;

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

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

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

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

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

additional leases for new facilities and capital equipment;

additional licenses and collaborative agreements;

additional contracts for consulting, maintenance and administrative services;

additional contracts for product manufacturing; and

additional financing facilities.

We believe that our cash, cash equivalents and short-term investment securities balances at March 31, 2004, will be sufficient to meet our operating and capital requirements through the third quarter of 2005. 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 or maintain regulatory approval to commercially manufacture or sell our future drug products, or if approval is delayed, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.

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

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

After any of our products receive regulatory approval, they remain subject to ongoing FDA regulation, including, for example, changes to the product labeling, new or revised regulatory requirements for manufacturing practices, reporting adverse reactions and other information, and

product recall. The FDA can withdraw a product s approval under some circumstances, such as the failure to comply with existing or future regulatory requirements, or unexpected safety issues. If regulatory approval is delayed, or withdrawn, our management s credibility, the value of our company and our operating results will be adversely affected. Additionally, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased.

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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 targeted human patients in order to receive regulatory approval for commercial sale.

Adverse or inconclusive clinical results would stop us from filing for regulatory approval of our 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.

The independent DSMB for the Neutralase Phase 3a clinical study recommended termination of the Phase 3a study as it determined that the advantages of Neutralase would be unlikely to outweigh its side effects. The study data included two patient deaths. One patient that died was found to have used protamine and not Neutralase. The other patient that died used Neutralase; however, it is our belief, based on the data that has been unblinded to date, that the cause of death was not likely related to Neutralase. Based upon the expected risk/benefit profile of Neutralase, we terminated the Neutralase development program for all indications.

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.

Aryplase has obtained fast track designation, which provides certain advantageous procedures and guidelines with respect to the review by the FDA of the Common Technical Document (CTD) for this product and which may result in our receipt of an initial response from the FDA earlier than would be received if this product 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 product had not received fast track designation. If the review process or approval for Aryplase is delayed, realizing revenue from the sale of Aryplase will be delayed and the capital necessary to fund this program will be increased.

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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 cGMP regulations. 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 and our Galli Drive facility has been approved by the FDA and the EMEA for the commercial manufacture of Aldurazyme. We have entered into contracts with third party manufacturers to produce Orapred.

Due to the complexity of the processes used to manufacture Aldurazyme and our product candidates, 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 Aldurazyme or our product candidates may be unable to comply with cGMP regulations in a cost effective manner. If we, or the third party manufacturers with whom we contract, are unable to comply with manufacturing regulations, we will not be able to sell our products.

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

As part of our business strategy, we intend to develop some drugs that may be eligible for FDA and European Community orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, defined as a patient population of less than 200,000 in the U.S. The company that first obtains FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. Similar regulations are available in the E.U. with a 10-year period of market exclusivity.

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

Even though we have obtained orphan drug designation for certain of our product candidates and even if we obtain orphan drug designation for 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. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

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

Aldurazyme and Aryplase both target diseases with small patient populations. As a result, our per-patient prices must be relatively high in order to recover our development costs and achieve profitability. Aldurazyme targets patients with MPS I and 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 penetration. In addition, we are developing other drug candidates to treat conditions, such as other genetic diseases, with small patient populations. Due to the expected costs of treatment for Aldurazyme and 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.

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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.

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

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

We currently have limited expertise obtaining reimbursement. We rely on the expertise of our joint venture partner Genzyme to obtain reimbursement for the costs of Aldurazyme. In addition, we will need to develop our own reimbursement expertise for future drug candidates and as necessary to support Orapred. For our future products, we will not know what the reimbursement rates will be until we are ready to market the product and we actually negotiate the rates. If we are unable to obtain sufficiently high reimbursement rates, our products may not be commercially viable or our future revenues and gross margins may be adversely affected.

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

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

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

The patent positions of biopharmaceutical products are complex and uncertain. The scope and extent of patent protection for some of our products are particularly uncertain because key information on some of the products we are developing has existed in the public domain for

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

For enzymes or compounds with no prospect of broad composition-of-matter patents, other forms of patent protection or orphan drug status may provide us with a competitive advantage. As a result of these uncertainties,

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investors should not rely on patents as a means of protecting our products or product candidates, including Aldurazyme or Orapred.

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

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

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

- Enforcing patents is expensive and may absorb significant time of our management. Management would spend less time and resources on developing products, which could increase our 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 U.S. are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how.

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

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If we do not obtain required licenses or rights, we could encounter delays in 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 three patents to a third party that relate to alpha-L-iduronidase. If we are not able to successfully challenge these patents, we may be prevented from producing Aldurazyme in the U.S. unless and until we obtain a license.

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

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

On October 8, 2003, Genzyme and Transkaryotic Therapies, Inc. announced their collaboration to develop and commercialize an unrelated drug product. In connection with the collaboration agreement, Genzyme and Transkaryotic Therapies, Inc. signed a global legal settlement involving an exchange of non-suits between the companies. As part of this exchange, Transkaryotic Therapies, Inc. has agreed not to initiate any patent litigation against Genzyme or our joint venture relating to Aldurazyme.

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

We 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 Aldurazyme. We have no experience selling, marketing or obtaining reimbursement for orphan pharmaceutical products. In addition, without Genzyme we would be required to pursue foreign regulatory approvals. We have limited experience in seeking foreign regulatory approvals.

Either we or Genzyme 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.

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

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out option without exercise by the non-terminating party as described above, all right and title to Aldurazyme is to be sold to the highest bidder, with the proceeds to be split equally between Genzyme and us.

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

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

Termination of the joint venture in which we retain the rights to Aldurazyme could cause us significant 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 product inventory and operating expenses, the termination of the joint venture would double our financial burden and reduce the funds available to us for other product programs.

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

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

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

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

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

become due on the accelerated closing date for the purchase of shares under the option.

If the option were accelerated, we may not have sufficient funds at that time to exercise the option and/or to make the license payments, and may not be able to obtain the financing to do so, in which case we would not be able to consummate the transaction to acquire such shares and would be in breach of the license agreement and the securities purchase agreement. If we are in breach of the license agreement, Ascent may terminate the license and

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we would no longer have the ability to manufacture, market, sell, or distribute Orapred and our revenue could decrease significantly.

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

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

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

- design, construction and qualification of manufacturing facilities that meet regulatory requirements;
- schedule;
- reproducibility;
- production yields;
- purity;
- costs;
- quality control and assurance systems;
- 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 capacity 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 result in equivalent margins.

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

We have built-out approximately 54,000 square feet at our 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 developing manufacturing processes for all of our product candidates, including Aryplase, will require significant time and resources before we can begin to manufacture them (or have them manufactured by third parties) in commercial quantity at an acceptable cost.

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

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

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

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

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

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

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

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

Our sole manufacturing facility for Aldurazyme and Aryplase is located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facility and equipment, which could materially impair our ability to manufacture Aldurazyme and Aryplase.

Our Novato, California facility is our only manufacturing facility for Aldurazyme and Aryplase. It is located in the San Francisco Bay Area near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We, and the third party manufacturers with whom we contract, are also vulnerable to damage from other types of disasters, including fires, floods, power loss and similar events. If any disaster were to occur, our ability to manufacture Aldurazyme and Aryplase, or to have Orapred manufactured for us, could be seriously, or potentially completely, impaired, we could incur delays in our development of Aryplase, Aldurazyme and Orapred commercialization efforts and revenue from the sale of Aldurazyme and Orapred could be seriously impaired. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions.

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If we are unable to effectively integrate the Ascent operations, our revenues and operating expenses will be adversely affected.

In connection with the integration of the Ascent operations, we will need to incorporate functions and operations that are new to our business, including sales and marketing functions. If we are not able to effectively integrate operations, we could experience higher than expected employee turnover, reduced revenue from Orapred, and higher than expected operating costs associated with the sales and marketing operations.

Additionally, we expect to use the Ascent sales force we obtained to support the anticipated launch and commercialization of our product candidates. If we do not effectively integrate the operations, the sales force may not be able to provide the anticipated level of support, and we may be required to utilize a third party to commercialize the products, which would adversely affect our operating expenses.

A majority of our revenue is expected to come from sales of Orapred and decreased sales or increased operational costs related to Orapred could have an adverse affect on our revenues and operating expenses.

We expect that a majority of our revenue in the near term will be from sales of Orapred. As such, our operating results will be dependent on the sales and performance of Orapred. Decreased sales or increased operational costs related to Orapred, whether due to increased competition, pricing pressure from managed care organizations, increased costs of raw materials or otherwise, could have an adverse affect on our revenues and operating expenses.

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 Aryplase, if our competitors successfully commercialize a product that treats MPS VI before we do, we may effectively be precluded from developing a product to treat that disease because the patient population of the disease is so small. If one of our competitors gets orphan drug exclusivity, we could be precluded from marketing our version for seven years in the U.S. and 10 years in the E.U. 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 NeuroTrans, and several of our product programs have been developed through licensing or collaborative arrangements, such as Aldurazyme, Aryplase, Orapred, Phenoptin and Vibrilase. These collaborations include licensing proprietary technology from, and other relationships with, academic research institutions. If our competitors successfully enter into partnering arrangements or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Since each of these opportunities is unique, we may not be able to find a substitute. Several pharmaceutical and biotechnology companies have already established themselves in the field of enzyme therapeutics, including Genzyme, our joint venture partner. These companies have already begun many drug development programs, some of which may target diseases that we are

also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

Universities and public and private research institutions also compete with us. While these organizations primarily have educational or basic research objectives, they may develop proprietary technology and acquire patents that we may need for the development of our drug products. We will attempt to license this proprietary technology, if

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available. These licenses may not be available to us on acceptable terms, if at all. If we are unable to compete successfully with respect to acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to develop new products and to continue to expand our product pipeline.

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

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

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. Based on the approval of Aldurazyme in the U.S. and E.U., and other countries, we expect that our joint venture with Genzyme will be required to devote additional resources in the immediate future to support the commercialization of Aldurazyme. Additionally, we acquired approximately 70 new employees through the acquisition of the Ascent field sales force. This has required that we expand our managerial organization to cover several new functional areas, such as sales and marketing.

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 and Chief Scientific Officer, 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. For example if in the future gene therapy becomes widely used as a treatment of genetic diseases, the use of enzyme replacement therapy, like Aldurazyme, in MPS diseases could be greatly reduced. Changes in treatment method can be caused by the introduction of other companies products or the development of

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new technologies or surgical procedures which may not directly compete with ours, but which have the effect of changing how doctors decide to treat a disease.

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

We are exposed to the potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceuticals. The BioMarin/Genzyme LLC maintains product liability insurance for Aldurazyme with aggregate loss limits, including aggregate losses on other Genzyme products, of $25.0 million as a named insured under Genzyme s insurance coverage. We have obtained insurance against product liability lawsuits for commercial sale of our products and for the clinical trials of our product candidates with aggregate loss limits of $15.0 million. Pharmaceutical companies must balance the cost of insurance with the level of coverage based on estimates of potential liability. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with the commercial use of Orapred, our current clinical trials and commercial use for Aldurazyme and our current clinical trials for Aryplase, our PKU program and Vibrilase, or in connection with the clinical trials for our now terminated program for Neutralase, for which our insurance coverage is not adequate.

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

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

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

- product sales and profitability of Aldurazyme and Orapred;
- progress of Aryplase and our other drug products through the regulatory process;
- results of clinical trials, announcements of technological innovations or new products by us or our competitors;
- government regulatory action affecting our drug products or our competitors drug products in both the U.S. and foreign countries;
- developments or disputes concerning patent or proprietary rights;

general market conditions and fluctuations for the emerging growth and biopharmaceutical market sectors;

economic conditions in the U.S. or abroad;

broad market fluctuations in the U.S. or in the E.U.;

actual or anticipated fluctuations in our operating results; and

changes in company assessments or financial estimates by securities analysts.

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In addition, the value of our common stock may fluctuate because it is listed on both the Nasdaq National Market and the Swiss SWX Exchange. Listing on both exchanges may increase stock price volatility due to:

- trading in different time zones;
- different ability to buy or sell our stock;
- different market conditions in different capital markets; and
- different trading volume.

In the past, following periods of large price declines in the public market price of a company s securities, securities class action litigation has often been initiated against that company. Litigation of this type could result in substantial costs and diversion of management s attention and resources, which would hurt our business. Any adverse determination in litigation could also subject us to significant liabilities.

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.

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

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

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FORWARD LOOKING STATEMENTS

This prospectus 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 will not receive any of the proceeds from the sale of the shares offered and sold for the accounts of the selling stockholders.

The selling stockholders will not pay any of the expenses that are incurred in connection with the registration of the shares, but each selling stockholder will pay all commissions, discounts and any other compensation to any securities broker dealers through whom it sells any of the shares.

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SELLING STOCKHOLDERS

On May 18, 2004, we delivered certificates representing 3,733,015 shares of our common stock to U.S. Bank, National Association, as escrow agent, as partial security for payments totaling approximately $50 million in cash that we agreed to make to Ascent under our license agreement with Ascent. In the event that we fail to make the first two installments of the required license payments totaling $25 million under the license agreement, such shares will be transferred and released to Ascent out of the escrow.

Pursuant to a securities purchase agreement with Medicis, we obtained an option to purchase all of the issued and outstanding capital stock of Ascent from Medicis upon the exercise of the option provided therein, on or about August 17, 2009 (subject to acceleration upon certain events), for $62 million in cash plus $20 million in our common stock (as measured by the average closing sales price per share of our common stock over the twenty trading days immediately preceding the option closing date).

We are registering all of the shares of common stock offered for sale pursuant to this prospectus as required by the license agreement and securities purchase agreement discussed above.

Assuming that shares of our common stock are transferred and released to Ascent from escrow due to our failure to make the first two installments of the required license payments under our license agreement with Ascent and assuming that shares are issued to Medicis pursuant to the exercise of the option under our securities purchase agreement with Medicis, as if such events occurred as of June 10, 2004, the following table sets forth the names of each selling stockholder, the aggregate number of shares of common stock beneficially owned by each selling stockholder, and the aggregate number of shares of common stock that each selling stockholder may offer and sell pursuant to this prospectus. Because each selling stockholder may offer all or a portion of the shares of common stock offered by this prospectus at any time and from time to time after the later of the date hereof or the date that certificates representing issued shares are delivered to it, no estimate can be made of the number of shares that it may retain upon completion of this offering.

	Shares Beneficially Owned Before Offering [1]			Shares Beneficially Owned After Offering [1]	
Name and Address	Number	Percentage	Shares to be Offered	Number	Percentage
Medicis Pediatrics, Inc.	3,733,015	5.5%	3,733,015	-0-	0%
Medicis Pharmaceutical Corporation	3,259,984	4.8%	3,259,984	-0-	0%

(1) We have calculated shares of common stock beneficially owned by the selling stockholders based upon 64,364,988 shares of common stock outstanding on June 10, 2004, together with options, warrants or other convertible securities that are exercisable, or other rights to acquire common stock, within 60 days of June 10, 2004. Under the rules of the Securities and Exchange Commission, beneficial ownership includes shares over which the named stockholder exercises voting and/or investment power. We believe that the selling stockholders will have sole voting and investment power with respect to all shares beneficially owned. The information with respect to beneficial ownership of common stock held by the selling stockholders is based upon record ownership data provided by our transfer agent, information as supplied or confirmed by the selling stockholders, based upon statements filed with the Securities and Exchange Commission or based upon our actual knowledge.

None of the selling stockholders representative have held any position or office with us within the past three years and, except for (a) the asset purchase agreement, pursuant to which we obtained certain pharmaceutical assets of Medicis and Ascent, including assets related to Orapred and assets concerning the Ascent field sales force; (b) the license agreement, pursuant to which we obtained the exclusive worldwide rights to

Orapred; and (c) the securities purchase agreement, pursuant to which we obtained an option to purchase all of the issued and outstanding capital stock of Ascent upon the exercise of the option provided therein, none of the selling stockholders have entered into a material relationship with us within the past three years.

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PLAN OF DISTRIBUTION

We are registering the shares of common stock offered for sale by this prospectus on behalf of the selling stockholders. As used in this section, selling stockholders includes donees, pledgees, distributees, transferees or other successors-in-interest, including, without limitation, their respective affiliates, members and limited or general partners, all of which are referred to as a group below as transferees, or certain counterparties to derivative transactions with the selling stockholders or transferees. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. We will pay all costs, expenses and fees in connection with the registration of the shares. The selling stockholders will pay all brokerage commissions, underwriting discounts, commissions, transfer taxes and other similar selling expenses, if any, associated with the sale of the shares of common stock by them.

An aggregate of 6,992,999 shares of common stock may be issued to and purchased by the selling stockholders, as partial security for certain payments under a license agreement and partial consideration for certain securities that may be acquired from one of the selling stockholders by one of our subsidiaries. All of these shares of common stock are expected to be issued and sold pursuant to an exemption from the registration requirements of the Securities Act as provided Section 4(2) of the Securities Act. This section of this prospectus contemplates that shares of our common stock are transferred and released to Ascent from escrow due to our failure to make the first two installments of the required license payments under our license agreement with Ascent and assumes that shares are issued to Medicis pursuant to the exercise of the option under our securities purchase agreement with Medicis, as if such events occurred as of June 10, 2004.

Shares of common stock may be sold by the selling stockholders from time to time in one or more types of transactions (which may include block transactions) on the Nasdaq National Market or on any other market on which our common stock may from time to time be trading, in the over-the-counter market, in privately negotiated transactions, through put or call options transactions relating to the shares, through short sales of such shares, or a combination of such methods of sale, at market prices prevailing at the time of sale, fixed prices, varying prices determined at the time of sale or at negotiated prices. The selling stockholders will have the sole discretion not to accept any purchase offer or make any sale of shares if it deems the purchase price to be unsatisfactory at any particular time. Such transactions may or may not involve brokers or dealers. To the best of our knowledge, the selling stockholders have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of the securities, nor is there an underwriter or coordinating broker acting in connection with the proposed sale of shares of common stock offered by this prospectus; however, the selling stockholders may enter into agreements, understandings or arrangements with an underwriter or broker-dealer regarding the sale of the shares in the future.

The selling stockholders may effect such transactions by selling shares of common stock directly to purchasers or to or through broker-dealers, which may act as agents or principals, or other agents. Such broker-dealers or other agents may receive compensation in the form of discounts, concessions, or commissions from the selling stockholders and/or the purchasers of shares of common stock for whom such broker-dealers or other agents may act as agents or to whom they sell as principal, or both (which compensation as to a particular broker-dealer or other agent might be in excess of customary commissions). Market makers and block purchasers purchasing the shares will do so for their own account and at their own risk. It is possible that the selling stockholders will attempt to sell shares of common stock in block transactions to market makers or other purchasers at a price per share which may be below the then market price. There can be no assurance that all or any part of the shares offered hereby will be sold by the selling stockholders.

The selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions with respect to the shares. In connection with these transactions, broker-dealers or other financial institutions may engage in short sales of the shares in the course of hedging the positions they assume with the selling stockholders. The selling stockholders may also sell the shares short and redeliver the shares to close out the short positions. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions that require the delivery to the broker-dealer or other financial institutions of the shares. The selling stockholders may also loan or pledge the shares to a financial institution or a broker-dealer and the financial institution or the broker-dealer may sell the shares loaned or upon a default the financial institution or the broker-dealer may effect sales of the pledged shares.

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The selling stockholders and any brokers, dealers or agents that participate in connection with the sale of shares of common stock might be deemed to be underwriters within the meaning of the Securities Act of 1933 (the Securities Act), and any commissions received by such brokers, dealers or agents and any profit on the resale of the shares sold by them while acting as principals might be deemed to be underwriting discounts or commissions under the Securities Act. We have agreed to indemnify the selling stockholders against certain liabilities, including liabilities arising under the Securities Act. The selling stockholders may agree to indemnify any agent, dealer, broker-dealer or underwriter that participates in transactions involving sales of the shares of common stock offered pursuant to this prospectus against certain liabilities, including liabilities arising under the Securities Act.

Because the selling stockholders may be deemed to be underwriters within the meaning of the Securities Act, the selling stockholders will be subject to the prospectus delivery requirements of the Securities Act and the rules promulgated thereunder and they may be subject to certain statutory liabilities under the Securities Act, including, but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Securities Exchange Act of 1934 (the Securities Exchange Act). In addition, the selling stockholders and any other person participating in the offering will be subject to applicable provisions of the Securities Exchange Act and the rules and regulations thereunder, including Regulation M under the Securities Exchange Act, which may limit the timing of purchases and sales. These restrictions may affect the marketability of the common stock and the ability of any person to engage in market-making activities with respect to the common stock.

Some of the shares of common stock covered by this prospectus may qualify for resale pursuant to Rule 144 under the Securities Act and such shares may be sold under Rule 144 rather than under the terms of this prospectus. In addition, subject to applicable state and foreign laws, the selling stockholders may sell the common stock outside the U.S. pursuant to Rules 903 and 904 of Regulation S under the Securities Act.

To comply with the securities laws of certain jurisdictions, the shares of common stock offered by this prospectus may need to be offered or sold only through registered or licensed brokers or dealers. In addition, in certain jurisdictions, the shares of common stock may not be offered or sold unless they have been registered or qualified for sale or an exemption is available and complied with.

If a selling stockholder notifies us that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker, dealer or underwriter, we will file a supplement to this prospectus, if required, pursuant to Rule 424(b) under the Securities Act. In addition, to the extent required, we will amend or supplement this prospectus to disclose other material arrangements regarding the plan of distribution.

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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 and for the years ended December 31, 2003 and 2002, have been incorporated by reference in this prospectus and in the registration statement (of which this prospectus is a part) from our Annual Report on Form 10-K as of and for the years ended December 31, 2003 and 2002 in reliance upon the reports of KPMG LLP, independent registered public accounting firm, and Pricewaterhouse Coopers LLP, independent accountants, incorporated by reference herein, and upon the authority of said firms as experts in accounting and auditing.

Our consolidated financial statements as of and for the year ended December 31, 2001, incorporated by reference in this prospectus and in the registration statement (of which this prospectus is a part) from our Annual Report on From 10-K of and for the year ended December 31, 2003 have been audited by Arthur Andersen LLP, independent accountants, as stated in their report with respect thereto and incorporated by reference herein. After reasonable efforts, we have been unable to obtain Arthur Andersen s consent to the incorporation by reference of their audit report on the financial statements and schedule from our Annual Report on Form 10-K as of and for the year ended December 31, 2001. Accordingly, Arthur Andersen LLP has not consented to the inclusion of their report in this prospectus, and we have dispensed with the requirement to file their consent in reliance on Rule 437a under the Securities Act. Because Arthur Andersen LLP has not consented to the inclusion of their report in this prospectus, you will not be able to recover against Arthur Andersen LLP under Section 11 of the Securities Act for any untrue statements of a material fact contained in the financial statements audited by Arthur Andersen LLP incorporated by reference in this prospectus or any omissions to state a material fact required to be stated therein. Additionally, due to Arthur Andersen s current financial and legal circumstances, the ability of Arthur Andersen LLP to satisfy claims will be limited as a practical matter.

The consolidated financial statements of BioMarin/Genzyme LLC incorporated by reference in this prospectus and in the registration statement (of which this prospectus is a part) from Exhibit 99.1 to our Annual Report on Form 10-K as of and for the year ended December 31, 2003 have been so incorporated in reliance upon the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

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 in Washington, D.C. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference 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, 2003 (including Exhibit 99.1 thereto);

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2. Our Definitive Proxy Statement dated March 29, 2004, filed in connection with our 2004 Annual Meeting of Stockholders;

3. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2004;

4. Our Current Reports on Form 8-K, as filed on February 3, 2004, February 4, 2004, February 24, 2004, two reports on April 22, 2004, May 5, 2004, May 19, 2004, June 2, 2004 and June 4, 2004; and

5. The description of our common stock set forth in our Form 8-A, filed with the SEC on July 15, 1999 and the description of our preferred share purchase rights set forth in our Form 8-A/A, filed with the SEC on August 8, 2003.

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) 506-6777

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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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth the costs and expenses to be paid by the registrant in connection with the sale of the common stock being registered:

Securities and Exchange Commission registration fee	$ 5,435.69
Legal fees and expenses	$ 20,000.00
Accountants fees and expenses	$ 5,000.00
Miscellaneous	$ 10,000.00
Total	$ 40,435.69

The foregoing items, except for the Securities and Exchange Commission registration fee, are estimated.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Reference is made to the Amended and Restated Certificate of Incorporation with the Registrant; the Bylaws of the Registrant; Section 145 of the Delaware General Corporation Law; which, among other things, and subject to certain conditions, authorize the Registrant to indemnify, or indemnify by their terms, as the case may be, the directors and officers of the Registrant against certain liabilities and expenses incurred by such persons in connection with claims made by reason of their being such a director or officer. Pursuant to this authority, the Registrant has entered into an indemnification agreement with each director and executive officer, whereby the Registrant has agreed to cover the indemnification obligations.

The Registrant maintains directors and officers insurance providing indemnification against certain liabilities for certain of the Registrant s directors, officers, affiliates, partners or employees.

The indemnification provisions in the Registrant s Bylaws, and the indemnification agreements entered into between the Registrant and its directors and executive officers, may be sufficiently broad to permit indemnification of the Registrant s officers and directors for liabilities arising under the Act.

Reference is made to the following documents incorporated by reference into this Registration Statement regarding relevant indemnification provisions described above and elsewhere herein: (1) the Amended and Restated Certificate of Incorporation, filed as Exhibit 3.1 to Registrant s Current Report on Form 8-K filed with the Securities and Exchange Commission on June 23, 2003; (2) the Registrant s Amended and Restated Bylaws filed as Exhibit 3.2 to Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2002; and (3) the form of Indemnification Agreement entered into by the Registrant with each of its directors and executive officers filed as Exhibit 10.1 to Registrant s Registration Statement on Form S-1 filed with the Securities and Exchange Commission on May 4, 1999, each incorporated by reference into this Registration Statement.

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ITEM 16. EXHIBITS

Exhibit Number	Description of Document
2.1	Asset Purchase Agreement dated as of April 20, 2004, by and among BioMarin Pharmaceutical Inc., Medicis Pharmaceutical Corporation, Ascent Pediatrics, Inc. and BioMarin Pediatrics Inc., previously filed with the Commission on June 2, 2004 as Exhibit 2.1 to the Current Report on Form 8-K, which is incorporated herein by reference.
2.2	Securities Purchase Agreement dated as of May 18, 2004, by and BioMarin Pharmaceutical Inc., Medicis Pharmaceutical Corporation, Ascent Pediatrics, Inc. and BioMarin Pediatrics Inc., previously filed with the Commission on June 2, 2004 as Exhibit 2.2 to the Current Report on Form 8-K, which is incorporated herein by reference.
2.3	Securities Purchase Agreement dated as of May 18, 2004, by and BioMarin Pharmaceutical Inc., Medicis Pharmaceutical Corporation, Ascent Pediatrics, Inc. and BioMarin Pediatrics Inc., previously filed with the Commission on June 2, 2004 as Exhibit 2.3 to the Current Report on Form 8-K, which is incorporated herein by reference.
5.1*	Opinion of Paul, Hastings, Janofsky & Walker LLP.
23.1*	Consent of Paul, Hastings, Janofsky & Walker LLP (included with Exhibit 5.1).
23.2*	Consent of KPMG LLP, independent registered public accounting firm for BioMarin Pharmaceutical Inc.
23.3*	Consent of PricewaterhouseCoopers LLP, independent accountants for BioMarin/Genzyme LLC.
24.1*	Power of Attorney (included with signatures).

* Filed herewith

ITEM 17. UNDERTAKINGS

Insofar as indemnification for liabilities arising under the Securities Act of 1933, may be permitted to directors, officers, and controlling persons of the Registrant pursuant to the provisions described in Item 15 or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Act, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer, or controlling person of the Registrant in the successful defense of any action suit, or proceeding) is asserted by such director, officer, or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made pursuant to this registration statement: (i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933; (ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20

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percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; (iii) to include any material information with respect to the distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; and

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant s annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

The undersigned Registrant undertakes that: (1) for purpose of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b) (1) or (4) or 497(h) under the Securities Act shall be deemed to be part of the registration statement as of the time it was declared effective; and (2) for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Novato, State of California, this 17th day of June 2004.

BIOMARIN PHARMACEUTICAL INC.

By: /s/ FREDRIC D. PRICE
Fredric D. Price

Chairman, Chief Executive Officer and

Director (Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Fredric D. Price and Louis Drapeau, and each of them severally, as such persons true and lawful attorneys-in-fact and agents for such person and in such person s name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and any new Registration Statement filed under Rule 462(b) of the Securities Act of 1933 and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission and any other regulatory authority, granting unto said attorneys-in-fact and agents, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement on Form S-3 has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ FREDRIC D. PRICE **Fredric D. Price**	Chairman, Chief Executive Officer and Director (Principal Executive Officer)	June 17, 2004
/s/ LOUIS DRAPEAU **Louis Drapeau**	Chief Financial Officer, Vice President Finance and Secretary (Principal Financial and Accounting Officer)	June 17, 2004
/s/ FRANZ L. CRISTIANI **Franz L. Cristiani**	Director	June 17, 2004

/s/ ELAINE HERON	Director	June 16, 2004
Elaine Heron, Ph.D.		
/s/ PIERRE LAPALME	Director	June 15, 2004
Pierre Lapalme		
/s/ ERICH SAGER	Director	June 15, 2004
Erich Sager		
/s/ JOHN URQUHART	Director	June 16, 2004
John Urquhart, M.D.		
/s/ GWYNN R. WILLIAMS	Director	June 14, 2004
Gwynn R. Williams		

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Exhibit Index

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