BIOMARIN PHARMACEUTICAL INC
Form POS AM
August 16, 2001

As filed with the Securities and Exchange Commission on August 16, 2001

Registration No. 333-48800

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SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Post Effective Amendment No. 2 to
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) 884-6700
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Raymond W. Anderson
Chief Financial Officer
BioMarin Pharmaceutical Inc.
371 Bel Marin Keys Boulevard, Suite 210
Novato, California 94949
(415) 884-6700
(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
555 South Flower Street, 23rd 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, please check the following box. |_|

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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Explanatory Note

As last amended on January 29, 2001, this registration statement provided for the issuance and sale of 4,000,000 shares of our common stock. Pursuant to this post-effective amendment to the registration statement on Form S-3 (SEC File No. 333-48800), we hereby amend the registration statement to deregister a total of 1,500,000 shares of the 4,000,000 shares. The 1,500,000 shares of common stock deregistered hereby remain unsold as of the date of the filing of this post-effective amendment.

PROSPECTUS

2,500,000 Shares

BioMarin Pharmaceutical Inc.

Common Stock

This prospectus will allow us to issue and sell up to the remaining 2,500,000 shares of our common stock over time. On August 15, 2001, we entered into a common stock purchase agreement with Acqua Wellington North American Equities Fund, Ltd., pursuant to which, we may sell them shares of our common stock from time to time as described in the "Plan of Distribution."

- We will provide a prospectus supplement each time we issue shares of our common stock.
- The prospectus supplement will inform you about the specific terms of the offering and also may add, update or change information contained in this document.
- You should read this document and any prospectus supplement carefully before you invest.

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

See "Risk Factors" beginning on page 5 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 August 16, 2001

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WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference rooms in Washington, D.C., New York, NY and Chicago, IL. 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 supersede 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, 2000;

2. Our Definitive Proxy Statement dated April 3, 2001 filed in connection with our 2001 Annual Meeting of Stockholders;

3. Our Quarterly Reports on Form 10-Q for quarters ended March 31, 2001 and June 2001;

4. Our current reports on Form 8-K as filed on May 18, 2001 and June 25, 2001; and

5. The description of our common stock set forth in our Amendment No. 4 Registration Statement on Form S-1, filed with the SEC on July 22, 1999

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

BioMarin Pharmaceutical Inc.
Attention: Investor Relations
371 Bel Marin Keys Boulevard, Suite 210
Novato, CA 94949
(415) 884-6700

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 are a developer of carbohydrate enzyme therapies for debilitating, life-threatening, chronic genetic diseases and other diseases and conditions. In September 1998, we established a joint venture with Genzyme for the worldwide development and commercialization of our lead drug product, Aldurazyme(TM), for the treatment of mucopolysaccharidosis-I or MPS I, a serious genetic disease. Aldurazyme has received fast track designation for the treatment of the more severe forms of MPS I. The U.S. Food and Drug Administration (FDA) has granted Aldurazyme for the treatment of MPS I an orphan drug designation giving us exclusive rights to market Aldurazyme to treat MPS I for seven years from the date of FDA approval if Aldurazyme is the first product to be approved by the FDA for the treatment of MPS I. In addition, the European Commission has designated Aldurazyme for the treatment of MPS I as an orphan medical product in the European Community, giving us similar market exclusivity in Europe for 10 years.

MPS I is a life-threatening genetic disease caused by the lack of a sufficient quantity of the enzyme (alpha)-L-iduronidase, which affects about 3,400 patients in developed countries, including approximately 1,000 in the United States and Canada. Patients with MPS I have multiple debilitating symptoms resulting from the buildup of carbohydrate residues in all tissues in the body. These symptoms include delayed physical and mental growth, enlarged livers and spleens, skeletal and joint deformities, airway obstruction, heart disease, reduced endurance and pulmonary function, and impaired hearing and vision. Most children with MPS I will die from complications associated with the disease before adulthood.

Aldurazyme is a specific form of recombinant human (alpha)-L-iduronidase that replaces a genetic deficiency of (alpha)-L-iduronidase in MPS I patients. In April 1999, we completed a twelve-month patient evaluation for the initial clinical trial of Aldurazyme. This trial treated and evaluated ten patients with MPS I at six medical centers in the United States. The results of the trial were presented at the American Society for Human Genetics in October 1999. Based on data collected during the initial twelve-month evaluation period, Aldurazyme met the primary endpoints set forth in the investigational new drug application. In addition, Aldurazyme demonstrated efficacy according to various secondary endpoints in each of the patients. We continue to collect data from the ongoing treatment of these original patients. We recently released the data from the two-year follow-up evaluation, which continued to suggest the efficacy of Aldurazyme. In collaboration with Genzyme, we initiated a six-month Phase III clinical trial of Aldurazyme in December 2000 with the intention to file a

Biologics License Application (BLA) with the FDA, pending the successful outcome of the Phase III trial. By August 3, 2001, all 45 MPS I patients enrolled in this trial had received at least 23 of their planned 26 weekly infusions and 26 of the 45 patients have received all 26 weekly infusions.

In August 2000, our Galli Drive manufacturing facility and a smaller clinical manufacturing laboratory in our Bel Marin Keys Boulevard facility were both subjected to an extensive inspection by the State of California Food and Drug Branch and were granted licenses to produce clinical product.

We submitted an Investigational New Drug Application for recombinant human N-acetylgalactosamine-4-sulfatase also known as arylsulfatase B or rhASB and received FDA acceptance to begin a Phase I/II clinical trial in enzyme replacement therapy for MPS VI, which was initiated on October 11, 2000. By the end of July 2001, all six patients in this trial had received all of their planned twenty-four weekly infusions. In accordance with the original protocol of the trial, we expect to release the results of this trial in September 2001. MPS VI, also known as Maroteaux-Lamy syndrome, is similar in its clinical symptoms to MPS I. However, MPS VI does not appear to have the central nervous system involvement and mental retardation characteristics of the most severe form of MPS I. We are manufacturing clinical bulk rhASB in our Bel Marin Keys Boulevard clinical manufacturing facility. RhASB has received fast track designation and has received orphan drug designation for the treatment of MPS VI by the FDA. In addition, the European Commission has designated rhASB for the treatment of MPS VI as an orphan medical product in the European Community.

We have successfully conducted preclinical studies of our burn enzyme, Vibriolysin Topical, for use in burn debridement and grafting in pigs and mice. In June 2001, we filed a Clinical Trial Exemption application with the Medicines Control Agency in the United Kingdom for permission to begin a clinical trial for Vibriolysin Topical. We expect to begin a clinical trial in the second half of 2001.

Our principal executive offices are located at 371 Bel Marin Keys Boulevard, Suite 210, Novato, CA 94949 and our telephone number is (415) 884-6700.

THE OFFERING

Common stock offered in this prospectus.....	2,500,000 shares
Common stock outstanding after the offering.....	44,456,093 shares
Use of proceeds.....	For operating expenses, capital

	needs, including costs associat manufacturing, and potential co for our research and developmen pipeline products including rec (rhASB) and Vibriolysin Topical purposes. We will receive proc to Acqua Wellington as describe but we will receive no proceeds shares by Acqua Wellington. Se
Nasdaq National Market and SWX New Market symbol.....	BMRN

The number of shares of common stock outstanding after this offering is based on the number of shares outstanding as of August 8, 2001 and assumes that we have issued all of the shares of our common stock offered in this prospectus, but excludes:

- 6,804,870 shares subject to options outstanding as of August 8, 2001, at a weighted average exercise price of $10.78 per share;
- 752,427 additional shares issuable upon exercise of outstanding warrants, at a weighted average exercise price of $12.99 per share.
- 1,402,407 additional shares that we could issue under our stock option plans; and
- 504,496 additional shares that we could issue under our employee stock purchase plan.

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," "may," "plans," "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.

RISK FACTORS

An investment in our common stock involves a high degree of risk. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. Before purchasing these securities, you should carefully consider the following risk factors, as well as other information contained in this prospectus or incorporated by reference into this prospectus, to evaluate an investment in the securities offered by this prospectus. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our common stock to decline, and you may lose all or part of your investment.

If we continue to incur operating losses for a period longer than anticipated, we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

We are in an early stage of development and have operated at a net loss since we were formed. Since we began operations in March 1997, we have been engaged primarily in research and development. We have no sales revenues from any of our drug products. As of March 31, 2001, we had an accumulated deficit of approximately $90.2 million. We expect to continue to operate at a net loss at least through 2002. Our future profitability depends on our receiving regulatory approval of our drug 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.

Because of the relative small size and scale of our wholly-owned subsidiary, Glyko, Inc., profits from its products and services will be insufficient to offset the expenses associated with our pharmaceutical business. As a result, we expect that operating losses will continue and increase for the foreseeable future.

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 cannot be certain that any financing will be available when needed. If we fail to raise additional financing as we need it, 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. Activities which will require additional expenditures include:

- Research and development programs
- Preclinical studies and clinical trials
- Process development, including quality systems for product manufacture
- Regulatory processes in the United States and international jurisdictions
- Commercial scale manufacturing capabilities
- Expansion of sales and marketing activities

The amount of capital we will need depends on many factors, including:

- The progress, timing and scope of our research and development programs
- The progress, timing and scope of our preclinical studies and clinical trials
- The time and cost necessary to obtain regulatory approvals

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- The time and cost necessary to develop commercial processes, including quality systems
- The time and cost necessary to build our manufacturing facilities and obtain the necessary regulatory approvals for those facilities
- 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
- Any new collaborative, licensing and other commercial relationships that we may establish

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

- Additional leases for new facilities and capital equipment
- Additional licenses and collaborative agreements
- Additional contracts for consulting, maintenance and administrative services
- Additional contracts for product manufacturing

We believe that the cash, cash equivalents and short-term investment securities balances at June 30, 2001, together with the proceeds from our recent private placement of our common stock, will be sufficient to meet our operating and capital requirements at least through the end of 2002. This estimate is based on assumptions and estimates, which may prove to be wrong. As a result, we may need or choose to obtain additional financing during that time.

If we fail to obtain regulatory approval to commercially manufacture or sell any of our future drug products, or if approval is delayed, we will be unable to generate revenue from the sale of our products.

We must obtain regulatory approval before marketing or selling our drug products in the U.S. and in foreign jurisdictions. In the United States, we must obtain FDA approval for each drug that we intend to commercialize. The FDA approval process is typically lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. None of our drug products has received regulatory approval to be commercially marketed and sold. If we fail to obtain regulatory approval, we

will be unable to market and sell our drug products. Because of the risks and uncertainties in biopharmaceutical development, our drug candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. If regulatory approval is delayed, our management's credibility, the value of our Company and our operating results will be adversely affected.

To obtain regulatory approval to market our products, preclinical studies and costly and lengthy clinical trials may 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 candidate. We expect the number of preclinical studies and clinical trials that the regulatory authorities will require will vary depending on the drug product, the disease or condition the drug is being developed to address and regulations applicable to the particular drug. We may need to perform multiple preclinical studies using various doses and formulations before we can begin clinical trials, which could result in delays in our ability to market any of our drug products. Furthermore, even if we obtain favorable results in preclinical studies on animals, the results in humans may be significantly different.

After we have conducted preclinical studies in animals, we must demonstrate that our drug products are safe and efficacious for use on the target human patients in order to receive regulatory approval for commercial sale. Adverse or inconclusive clinical results would stop us from filing for regulatory approval of our products. Additional factors that can cause delay or termination of our clinical trials include:

- Slow patient enrollment

- Longer treatment time required to demonstrate efficacy
- Lack of sufficient supplies of the drug candidate
- Adverse medical events or side effects in treated patients
- Lack of effectiveness of the drug candidate being tested
- Regulatory requests for additional clinical trials

Typically, if a drug product is intended to treat a chronic disease, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more. In addition, clinical trials on humans are typically conducted in three phases. The FDA generally requires two pivotal clinical trials that demonstrate substantial evidence of safety and efficacy and appropriate dosing in a broad patient population at multiple sites to support an application for regulatory approval. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, fewer clinical trials may be sufficient to prove safety and efficacy under the FDA's Modernization Act of 1997.

In April 1999, we completed a twelve-month patient evaluation for the initial clinical trial of our lead drug product, Aldurazyme, for the treatment of MPS I. The results were presented at the American Society for Human Genetics in October 1999. We continue to collect data from the ongoing treatment of these original patients. The initial clinical trial treated ten patients with MPS I at six medical centers in the United States. Two of the original ten patients enrolled in the first clinical trial of Aldurazyme died in 2000. Based on medical data collected from clinical investigative sites, neither case directly implicated treatment with Aldurazyme as the cause of death. The data suggest that one patient died due to a combination of systemic viral illness, residual MPS I coronary disease, and external factors. This patient had received 103 weeks of Aldurazyme administration. For the other patient, the data suggest that the patient died due to complications following posterior spinal fusion for scoliosis. This patient had received 127 weeks of Aldurazyme administration.

The fast track designation for our product candidates may not actually lead to a faster review process.

Although Aldurazyme and rhASB have obtained fast track designations, we cannot guarantee a faster review process or faster approval compared to the normal FDA procedures.

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 facility and process. In addition, manufacture of our drug products must comply with the FDA's current Good Manufacturing Practices regulations, commonly known as cGMP. The cGMP regulations govern 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. We cannot guarantee that these facilities will pass federal or international regulatory inspection. We cannot guarantee that we, or any potential third-party manufacturer of our drug products, will be able to comply with cGMP regulations.

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

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

As part of our business strategy, we intend to develop drugs that may be eligible for FDA and European Community orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, defined as a patient population of less than 200,000 in the United States. The company that obtains

the first FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. However, different drugs can be approved for the same condition. Similar regulations are available in the European Community with a ten-year period of market exclusivity.

Because the extent and scope of patent protection for our drug products is limited, orphan drug designation is particularly important for our products that are eligible for orphan drug designation. 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, which do not have patent protection, our competitors may then sell the same drug to treat the same condition.

We received orphan drug designation from the FDA for Aldurazyme for the treatment of MPS I in September 1997. In February 1999, we received orphan drug designation from the FDA for rhASB for the treatment of MPS VI. In February 2001, we received orphan drug designation from the European Community for both products. Even though we have obtained orphan drug designation for these drugs and even if we obtain orphan drug designation for other products we develop, we cannot guarantee that we will be the first to obtain marketing approval for any orphan indication or that exclusivity would effectively protect the product from competition. Orphan drug designation neither shortens the development time or regulatory review time of a drug so designated nor gives the drug any advantage in the regulatory review or approval process.

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

Our initial drug candidates target diseases with small patient populations. As a result, our per patient prices must be high enough to recover our development costs and achieve profitability. For example, two of our initial drug products in genetic diseases, Aldurazyme and rhASB, target patients with MPS I and MPS VI, respectively. We estimate that there are approximately 3,400 patients with MPS I and 1,100 patients with MPS VI in the developed world. We believe that we will need to market worldwide to achieve significant market share. In addition, we are developing other drug candidates to treat conditions, such as other genetic diseases and serious burn wounds, with small patient populations. We cannot be certain that we will be able to obtain sufficient market share for our drug products at a price high enough to justify our product development efforts.

If we fail to obtain an adequate level of reimbursement for our drug products by third-party payers, there would 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 rhASB 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 rhASB without reimbursement from third-party payers.

Third-party payers, such as government or private health care insurers, carefully review and increasingly challenge the price 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 cannot be certain that third-party payers will pay for the costs of our drugs and the courses of treatment. Even if we are able to obtain reimbursement from third-party payers, we cannot be certain that reimbursement rates will be enough to allow us to profit from sales of our drugs or to justify our product development expenses.

We currently have no expertise obtaining reimbursement. We expect to rely on the expertise of our joint venture partner Genzyme to obtain reimbursement for the costs of Aldurazyme. We cannot predict what the reimbursement rates will be. In addition, we will need to develop our own reimbursement expertise for future drug candidates unless we enter into collaborations with other companies with the necessary expertise.

We expect that in the future, reimbursement will be increasingly restricted both in the United States and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. Governmental and private third-party payers have proposed health care reforms and cost reductions. A number of federal and state proposals to control the cost of health care, including the cost of drug treatments have been made in the United States. In some foreign markets, the government controls the pricing

which would affect the profitability of drugs. Current government regulations and possible future legislation regarding health care may affect our future revenues from sales of our drugs and may adversely affect our business and prospects.

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. Meaningful patent protection may not be available for some of the enzymes we are developing, including Aldurazyme and rhASB. If we must spend significant time and money protecting our patents, designing around patents held by others or licensing, for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed.

The patent positions of biotechnology products are complex and uncertain. The scope and extent of patent protection for some of our products are particularly uncertain because key information on some of the enzymes we are developing has existed in the public domain for many years. Other parties have published the structure of the enzymes, the methods for purifying or producing the enzymes or the methods of treatment. The composition and genetic sequences of animal and/or human versions of many of our enzymes, including those for Aldurazyme and rhASB, have been published and are believed to be in the public domain. The composition and genetic sequences of other MPS enzymes which we intend to develop as products have also been published. Publication of this information may prevent us from obtaining composition-of-matter patents, which are generally believed to offer the strongest patent protection. For enzymes with no prospect of composition-of-matter patents, we will depend on orphan drug status to provide us a competitive advantage.

In addition, our owned and licensed patents and patent applications do not ensure the protection of our intellectual property for a number of other

reasons:

- We do not know whether our patent applications will result in actual 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. 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. In litigation, a competitor could claim that our issued patents are not valid for a number of reasons. If the court agrees, we would lose that patent.

- Even if we receive a patent, it 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. There are many patents in our field of technology, and we cannot guarantee 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:

- 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 will provide useful protection. While we use reasonable efforts to protect our trade secrets, our

employees or consultants may unintentionally or willfully disclose our information to competitors. Enforcing a claim that someone else illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how.

We may also support and collaborate in research conducted by government organizations or by universities. We cannot guarantee that we will be able to acquire any exclusive rights to technology or products derived from these collaborations. 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 recently issued two patents that related to (alpha)-L-iduronidase. If Aldurazyme infringes on these patents and we are not able to successfully challenge them, we may be prevented from producing Aldurazyme unless and until we obtain a license.

The United States Patent and Trademark Office recently issued two patents that include claims related to (alpha)-L-iduronidase. Our lead drug product, Aldurazyme, may infringe on these patents. We believe that these patents are invalid on a number of grounds. Two patents making the same claims were filed in Europe and have been rejected and cannot be refiled. Our challenges to the U.S. patents may be unsuccessful, but the rejection of the European applications supports our strategy to challenge the validity of the U.S. patents. Even if we are successful, challenging the U.S. patents may be expensive, require our management to devote significant time to this effort and may delay commercialization of our product in the United States.

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

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

We are relying on Genzyme to apply the expertise it has developed through the launch and sale of Ceredase(R) and Cerezyme(R) enzymes for Gaucher disease, a rare genetic disease, to the marketing of our initial drug product, Aldurazyme. Because it is our initial product, our operations are substantially dependent upon the development of Aldurazyme. We have no experience selling, marketing or obtaining reimbursement for pharmaceutical products. In addition, without Genzyme we would be required to pursue foreign regulatory approvals. We have no experience in seeking foreign regulatory approvals.

We cannot guarantee that Genzyme will devote the resources necessary to successfully market Aldurazyme. In addition, either party 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. Either party may also terminate the agreement upon one-year prior written notice for any reason. Furthermore, we may terminate the joint venture if Genzyme fails to fulfill its contractual obligation to pay us $12.1 million in cash upon the approval of the

BLA for Aldurazyme.

Upon termination of the joint venture one party must buy out the other party's interest in the joint venture. The party who buys out the other will then also obtain, exclusively, all rights to Aldurazyme and any related intellectual property and regulatory approvals.

If the joint venture is terminated by Genzyme for a breach on our part, Genzyme 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 our interest in the joint venture. We would then effectively be unable to develop and commercialize Aldurazyme. If we terminated the joint venture for

a breach by Genzyme, we would be obligated to buy out Genzyme's interest in the joint venture and, we would then be granted all of these rights to Aldurazyme exclusively. While we could then continue to develop Aldurazyme, that development would be slowed because we would have to divert substantial capital to buy out Genzyme's interest in the joint venture. We would then either have to search for a new partner to commercialize the product and to obtain foreign regulatory approvals or have to develop these capabilities ourselves.

If the joint venture is terminated by us without cause, Genzyme would have the option, exercisable for one year, to immediately buy out our interest in the joint venture and obtain all rights to Aldurazyme exclusively. If the agreement is terminated by Genzyme without cause, we would have the option, exercisable for one year, to immediately buy out Genzyme's interest in the joint venture and obtain these exclusive rights. In event of termination of the buy out option without exercise by the non-terminating party as described above, all right and title to Aldurazyme is to be sold to the highest bidder, with the proceeds to be split equally between Genzyme and us.

If the joint venture is terminated by us because Genzyme fails to make the $12.1 million payment to us upon FDA approval of the BLA for Aldurazyme, we would be obligated to buy Genzyme's interest in the joint venture and would obtain all rights to Aldurazyme exclusively. 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 delays in product launch in the United States, difficulties in obtaining third-party reimbursement and delays or failure to obtain foreign regulatory approval, any of which could hurt our business and results of operations. Since Genzyme funds 50% of the joint venture's operating expenses, the termination of the joint venture would double our financial burden and reduce the funds available to us for other product programs.

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

With the exception of Aldurazyme, we have no experience manufacturing drug products in volumes that will be necessary to support commercial sales. Our manufacturing processes may not meet initial expectations as to schedule, reproducibility, yields, purity, costs, quality, and other measurements of performance. Improvements in manufacturing processes typically are very difficult to achieve and are often very expensive. We cannot know with certainty how long it might take to make improvements if it became necessary to do so. If we contract for manufacturing services with an unproven process, our contractor is subject to the same uncertainties, high standards and regulatory controls.

If we are unable to establish and maintain commercial scale manufacturing within our planned time and cost parameters, sales of our products and our financial performance will be adversely affected.

Although we have successfully manufactured Aldurazyme at commercial scale within our cost parameters, we cannot guarantee that we will be able to manufacture rhASB, Vibriolysin or any future product candidates successfully in a scale large enough to support their respective commercial markets.

We may encounter problems with any of the following if we attempt to increase the scale or size of manufacturing:

- Design, construction and qualification of manufacturing facilities that meet regulatory requirements

- Production yields
- Purity
- Quality control and assurance systems
- Shortages of qualified personnel
- Compliance with regulatory requirements

We have constructed and built-out a total of 41,200 square feet at our Novato facilities for manufacturing capability for Aldurazyme and rhASB. We expect to expand the Galli Drive facility in stages over time, which creates

additional operational complexity and challenges. We expect that the manufacturing process of all of our new products, including rhASB, will require lengthy significant time and resources before we can begin to manufacture them (or have them manufactured by third parties) in commercial quantity. Even if we can establish the necessary capacity, we cannot be certain that manufacturing costs will be commercially reasonable, especially if third-party reimbursement is substantially lower than expected.

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, colonies of cells which have a common genetic make-up,
- Improving the 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 which is used to produce a protein that it would not have otherwise produced. The development of a stable, high production cell line for any given enzyme is risky, expensive and unpredictable and may not result in adequate yields. In addition, the development of protein purification processes is difficult and may not produce the high purity required with acceptable yield and costs or may not result in adequate shelf-lives of the final products. If we are not able to develop efficient manufacturing processes, the investment in manufacturing capacity sufficient to satisfy market demand will be much greater and will place heavy financial demands upon us. If we do not achieve our manufacturing cost targets, we will have lower margins and reduced profitability in commercial production and larger losses in manufacturing start-up phases.

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

If we cannot increase our marketing capabilities either by developing our sales and marketing organization or by entering into agreements with others, we may be unable to successfully sell our products. If we are unable to effectively sell our drug products, our ability to generate revenues will be diminished.

To increase our distribution and marketing for both our drug candidates and our Glyko, Inc. products, we will have to increase our current sales force and/or enter into third-party marketing and distribution agreements. We cannot guarantee that we will be able to hire in a timely manner, the qualified sales and marketing personnel we need, if at all. Nor can we guarantee that we will be able to enter into any marketing or distribution agreements on acceptable terms, if at all. If we cannot increase our marketing capabilities as we intend, either by increasing our sales force or entering into agreements with third parties, sales of our products may be adversely affected.

Under our joint venture with Genzyme, Genzyme is responsible for marketing and distributing Aldurazyme. We cannot guarantee that we will be able to establish sales and distribution capabilities or that the joint venture, any future collaborators or we will successfully sell any of our drug candidates.

If we fail to compete successfully, our revenues and operating results will be adversely affected.

Our competitors may develop, manufacture and market products that are more effective or less expensive than ours. They may also obtain regulatory

approvals for their products faster than we can obtain them, including those products with orphan drug designation, or commercialize their products before we do. If our competitors successfully commercialize a product, which treats a

given rare genetic disease before we do, we will effectively be precluded from developing a product to treat that disease because the patient populations of the rare genetic diseases are so small. If our competitor gets orphan drug exclusivity, we could be precluded from marketing our version for seven years. However, different drugs can be approved for the same condition. These companies also compete with us to attract qualified personnel and organizations for acquisitions, joint ventures or other collaborations. They also compete with us to attract academic research institutions as partners and to license these institutions' proprietary technology. If our competitors successfully enter into partnering arrangements or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Since each of these opportunities is unique, we may not be able to find a substitute. Several pharmaceutical and biotechnology companies have already established themselves in the field of enzyme therapeutics, including Genzyme, our joint venture partner. These companies have already begun many drug development programs, some of which may target diseases that we are also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

Universities and public and private research institutions are also competitors. While these organizations primarily have educational or basic research objectives, they may develop proprietary technology and acquire patents that we may need for the development of our drug products. We will attempt to license this proprietary technology, if available. These licenses may not be available to us on acceptable terms, if at all. We also directly compete with a number of these organizations to recruit personnel, especially scientists and technicians.

We believe that established technologies provided by other companies, such as laboratory and testing services firms, compete with Glyko, Inc.'s products and services. For example, Glyko's FACE(R) Imaging System competes with alternative carbohydrate analytical technologies, including capillary electrophoresis, high-pressure liquid chromatography, mass spectrometry and nuclear magnetic resonance spectrometry. These competitive technologies have established customer bases and are more widely used and accepted by scientific and technical personnel because they can be used for non-carbohydrate applications. Companies competing with Glyko may have greater financial, manufacturing and marketing resources and experience.

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

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

To manage expansion effectively, we need to continue to develop and improve our research and development capabilities, manufacturing and quality capacities, sales and marketing capabilities and financial and administrative systems. We cannot guarantee that our staff, financial resources, systems, procedures or controls will be adequate to support our operations or that our management will be able 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 Christopher M. Starr, Ph.D., our Vice President for Research and Development, could be detrimental to us if we cannot recruit suitable replacements in a timely manner. While Mr. Price and Dr. Starr are parties to employment agreements with us, we cannot 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. We cannot be certain that we will continue to attract and retain qualified personnel necessary for the development of our business.

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

We are exposed to the potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceuticals. The BioMarin/Genzyme LLC maintains product liability insurance for our clinical trials of Aldurazyme. We have obtained insurance against product liability

lawsuits for the clinical trials for rhASB. We may be subject to claims in connection with our current clinical trials for Aldurazyme and rhASB for which the joint venture's or our insurance coverages are not adequate. We cannot be certain that if Aldurazyme receives FDA approval, the product liability insurance the joint venture will need to obtain in connection with the commercial sales of Aldurazyme will be available in meaningful amounts or at a reasonable cost. In addition, we cannot be certain that we can successfully defend any product liability lawsuit brought against us. If we are the subject of a successful product liability claim which exceeds the limits of any insurance coverage we may obtain, we may incur substantial liabilities which would adversely affect our earnings and financial condition.

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

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

- Progress of Aldurazyme and our other lead drug products through the regulatory process, especially Aldurazyme regulatory actions in the United States

- Results of clinical trials, announcements of technological innovations or new products by us or our competitors

- Government regulatory action affecting our drug candidates or our competitors' drug candidates in both the United States and foreign countries

- Developments or disputes concerning patent or proprietary rights

- General market conditions for emerging growth and biopharmaceutical companies

- Economic conditions in the United States or abroad

- Actual or anticipated fluctuations in our operating results

- Broad market fluctuations in the United States or in Europe may cause the market price of our common stock to fluctuate

- Changes in company assessments or financial estimates by securities analysts

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

- Trading in different time zones

- Different ability to buy or sell our stock

- Different market conditions in different capital markets

- 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.

Substantial resales of our common stock which may be issued pursuant to this prospectus could adversely affect the price of our common stock.

The maximum shares which may be issued pursuant to this prospectus represents a significant portion of our outstanding common stock. If the persons acquiring these shares sell all or a substantial portion of these shares of common stock on the public market in a short period of time, the common stock available for sale may exceed the demand and the stock price may be adversely affected. In addition, the mere perception that such sales could occur may depress the price of our common stock.

If our officers, directors and largest stockholder elect to act together, they may be able to control our management and operations, acting in their best interests and not necessarily those of other stockholders.

Our directors and officers control approximately 44.8% of the outstanding shares of our common stock. Glyko Biomedical Ltd. owns 27.0% of the outstanding shares of our capital stock. The president and chief executive officer of Glyko Biomedical and a significant shareholder of Glyko Biomedical serve as two of our directors. As a result, due to their concentration of stock ownership, directors and officers, if they act together, may be able to control our management and operations, and may be able to prevail on all matters requiring a stockholder vote including:

- The election of all directors;
- The amendment of charter documents or the approval of a merger, sale of assets or other major corporate transactions; and
- The defeat of any non-negotiated takeover attempt that might otherwise benefit the public stockholders.

Anti-takeover provisions in our charter documents 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 1,000,000 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.

USE OF PROCEEDS

We cannot guarantee that we will receive any proceeds in connection with this offering. We will receive the proceeds from any sale of the shares to Acqua Wellington as described in the Plan of Distribution but we will receive no proceeds from any subsequent sale of the shares by Acqua Wellington.

We intend to use any proceeds of this offering, together with other available funds, for the following purposes:

- To fund our share of costs associated with our joint venture with Genzyme for the development and commercialization of Aldurazyme;
- To fund research and development including clinical trials, regulatory processes, process development and scale-up and start-up of manufacturing activities for our other pharmaceutical product programs, including rhASB and Vibriolysin Topical;
- To fund research, development, clinical and commercial manufacturing facilities, including related equipment; and
- To fund general corporate purposes, including working capital.

A portion of the proceeds may also be used to acquire or invest in complementary businesses or products or to obtain rights to use complementary technologies.

We may require additional funds in the 12-month period following this offering to accelerate product programs or to undertake new initiatives or enter

into collaborative arrangements.

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

We anticipate that we will be required to raise substantial additional capital to continue to accelerate product programs or to undertake new initiatives or enter into collaborative arrangements. Additional capital may be raised through additional public or private financing, as well as collaborative relationships, borrowings and other available sources. See "Risk Factors - if we fail to obtain the capital necessary to fund our operations, we will be unable to complete our product development programs."

PLAN OF DISTRIBUTION

On August 15, 2001, we entered into what is sometimes termed an equity line arrangement with Acqua Wellington North American Equities Fund, Ltd. Specifically, we entered into a common stock purchase agreement with Acqua Wellington, which provides that, subject to the satisfaction of certain conditions, we may issue and sell and Acqua Wellington will be obligated to purchase, from time to time until October 15, 2002, up to an aggregate of $27,700,000 of our common stock. The total amount of securities available under the purchase agreement, as amended, may not exceed 10% of the aggregate market value of our outstanding common stock that was held by our non-affiliates as of August 15, 2001. In connection with entering into the new agreement, we have terminated the common stock purchase agreement that we had entered with Acqua Wellington North American Equities Fund, Ltd. on January 26, 2001.

On February 1, 2001, we issued and sold 101,153 shares of our common stock to Acqua Wellington at a negotiated price of $9.85 per share. These 101,053 shares were issued pursuant to this prospectus and are included in the total 2,500,000 related to this agreement

At our discretion, we may present Acqua Wellington with draw down notices from time to time, provided that there must be at least five trading days between the end of each pricing period and the next draw down, requiring that Acqua Wellington purchase shares of our common stock. For each draw down, we will determine the minimum sale price per share and the total dollar amount of each draw down, subject to a limit of between $500,000 and $4,000,000 determined by the minimum sale price of the draw down. Over a 20 trading day period, for each trading day the volume weighted average price for our common stock exceeds the minimum purchase price, Acqua Wellington will be obligated to purchase a pro rata portion of the total draw down amount at a price per share equal to the volume weighted average price of our common stock less a discount of between 3.33% to 5%.

Additionally, at our discretion, in connection with any draw down, we may issue Acqua Wellington call options of up to the amount of the draw down. The call options give Acqua Wellington the right, but not the obligation, to purchase an additional amount of our common stock concurrent with the draw down. Acqua Wellington may exercise all or any unexercised portion of these options at any time during the pricing period of the draw down and for a purchase price equal to the volume weighted average price of our common stock on the day of exercise less a discount of 3.33% to 5%.

All of the shares purchased under a draw down and upon the exercise of any related call options will be settled on the second trading day after the end of the related pricing period. Prior to each settlement, we will file a prospectus supplement that describes the number of shares being purchased and the price per share. The maximum aggregate amount of common stock that Acqua Wellington will be required to purchase from us will not exceed an aggregate of $27,700,000. Additionally, Acqua Wellington will have no obligation to purchase our common stock if the volume weighted average trading price of our common stock is below $7.00 per share.

We have entered into a placement agreement with Reedland Capital Partners, an Institutional Division of Financial West Group, which is not affiliated with either Acqua Wellington or us, pursuant to which the shares to be issued and sold to Acqua Wellington will be placed through Reedland Capital Partners. Reedland Capital Partners is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act. Pursuant to the terms of this placement agent agreement, in connection with each draw down and call option settlement, Reedland Capital Partners will receive a placement agent fee from us of between 1% and 0.67% of the dollar amount of the shares purchased. The net proceeds we receive on each settlement will be 4% to 6% less than the volume weighted average price of our common stock as a result of the total effect of the placement agent fee and the discount to Acqua Wellington.

In addition to our offer and sale of shares of common stock to Acqua Wellington through Reedland Capital Partners pursuant to the purchase and placement agreements, this prospectus also covers the offer and sale of shares so purchased from time to time by Acqua Wellington to the public. Acqua Wellington is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act.

Acqua Wellington has informed us that it intends to use Carlin Equities Corp. as the broker-dealer to offer and sell shares of our common stock on the Nasdaq National Market. Such sales will be made on the Nasdaq National Market at prices and at terms then prevailing or at prices related to the then current market price. Carlin Equities Corp. is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act. Acqua Wellington has informed us that Carlin Equities Corp., which is not an affiliate of Acqua Wellington, will receive commissions from Acqua Wellington which will not exceed customary brokerage commissions. Acqua Wellington also will pay other expenses associated with the sale of the common stock it acquires pursuant to the purchase agreement. Profits on any resale of the common stock by Acqua Wellington and commissions received by either Carlin Equities Corp. or Reedland Capital Partners may be deemed to be underwriting discounts and commissions under the Securities Act.

The shares of common stock may be sold by Carlin Equities Corp. in one or more of the following manners:

- ordinary brokerage transactions and transactions in which the broker solicits purchasers; or
- a block trade in which the broker or dealer so engaged will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction.

In addition, Acqua Wellington, Reedland Capital Partners and Carlin Equities Corp. will be subject to liability under the federal securities laws and must comply with the requirements of the Securities Act and the Securities Exchange Act of 1934, as amended, including without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock by Acqua Wellington, Reedland Capital Partners or Carlin Equities Corp. Under these rules and regulations, Acqua Wellington, Reedland Capital Partners and Carlin Equities Corp.:

- may not engage in any stabilization activity in connection with our securities;
- must furnish each broker which offers shares of our common stock covered by this prospectus with the number of copies of this prospectus and any prospectus supplement which are required by each broker; and
- may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities other than as permitted under the Exchange Act.

These restrictions may affect the marketability of the shares of common stock by Acqua Wellington, Reedland Capital Partners and Carlin Equities Corp.

During the term of the purchase agreement, Acqua Wellington may sell the shares that it has the right to purchase pursuant to the purchase agreement,

but Acqua Wellington has agreed that it will not sell any other shares of our common stock.

The common stock offered hereby is being registered pursuant to our contractual obligations with Acqua Wellington, and, in addition to the placement agent fees described above, we have agreed to pay the costs of registering the shares hereunder. We have also agreed to reimburse Acqua Wellington's costs and expenses incurred in connection with the stock purchase agreement, including fees, expenses and disbursements of counsel for Acqua Wellington for the preparation of the stock purchase agreement up to a maximum of $15,000, and all reasonable fees incurred in connection with any amendment, modification or waiver, to or enforcement of the stock purchase agreement.

In the stock purchase agreement with Acqua Wellington, we have agreed to indemnify and hold harmless Acqua Wellington and Carlin Equities Corp., and each person who controls either Acqua Wellington or Carlin Equities Corp., against certain liabilities, including liabilities under the Securities Act, which may be based upon, among other things, any untrue statement or alleged untrue statement of a material fact or any omission or alleged omission of a material fact contained in any prospectus or any prospectus supplement, unless made or omitted in reliance upon written information provided to us by Acqua Wellington or Carlin Equities Corp., respectively. In the placement agent agreement with Reedland Capital Partners, we have agreed to indemnify and hold harmless Reedland Capital Partners, and each person who controls Reedland Capital Partners, against certain liabilities, including liabilities under the Securities Act, which may be based upon, among other things, any untrue statement or alleged untrue statement of a material fact or any omission or alleged omission of a material fact contained in any prospectus or any prospectus supplement, unless made or omitted in reliance upon written information provided to us by Reedland Capital Partners.

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

The financial statements included in our Annual report on form 10-K for

the year ended December 31, 2000, incorporated by reference in this prospectus and elsewhere in the registration statement have been audited by Arthur Andersen LLP, independent public accountants, as indicated in their report(s) with respect thereto, and are included herein in reliance upon the authority of said firm as experts in giving said reports.

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PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

Securities and Exchange Commission registration fee...	$14,457
Legal fees and expenses.....	$45,000
Accountants' fees and expenses.....	$7,500
Miscellaneous.....	$3,000
Total.....	$69,957

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 director's and officer's 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 3.1B to Registrant's Amendment No. 2 to Registration Statement on Form S-1 filed with the Securities and Exchange Commission on July 6, 1999; (2) the Bylaws of the Registrant filed as Exhibit

3.1 to Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2001 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.

ITEM 16. EXHIBITS

EXHIBIT NO.	DESCRIPTION OF DOCUMENT
1.1*	Engagement Letter between BioMarin Pharmaceutical Inc. and Reedland Capital Partners, an Institutional Division of Financial West Group, dated August 15, 2001
1.2*	Common Stock Purchase Agreement between BioMarin Pharmaceutical Inc. and Acqua Wellington North American Equities Fund, Ltd., dated August 15, 2001
5.1	Opinion of Paul, Hastings, Janofsky & Walker, LLP

10.1*	Letter Agreement between BioMarin Pharmaceutical Inc. and Acqua Wellington North American Equities Fund, Ltd., dated August 15, 2001 regarding Termination of the Common Stock Purchase Agreement dated January 26, 2001
23.1*	Consent of Paul, Hastings, Janofsky & Walker LLP.
23.2*	Consent of Arthur Andersen LLP
24.1	Power of Attorney

* Filed herewith. All other Exhibits filed previously.

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 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 the 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.

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 Post Effective Amendment No.2 to Registration Statement on form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Novato, State of California, this 15th day of August, 2001.

BIOMARIN PHARMACEUTICAL INC.

By: /s/ Fredric D. Price

Fredric D. Price
Chairman, Chief Executive Officer and Director
(Principal Executive Officer)

Pursuant to the requirements of the Securities Act of 1933, this Post effective Amendment No. 2 to Registration Statement on Form S-3 has been signed

by the following persons in the capacities and on the dates indicated:

Signature	Title
/s/ Fredric D. Price Fredric D. Price	Chairman, Chief Executive Officer and Director (Principal Executive Officer)
/s/ Raymond W. Anderson Raymond W. Anderson	Chief Financial Officer, Chief Operating Officer, Secretary, and Vice President Finance and Administration (Principal Financial and Accounting Officer)
/s/ * Grant W. Denison, Jr.	Director
/s/ * Ansbert S. Gadicke, M.D.	Director
/s/ * Erich Sager	Director
/s/ * Gwynn R. Williams	Director

*By: /s/ Raymond W. Anderson
Raymond W. Anderson
as Attorney-In-Fact

INDEX TO EXHIBITS

EXHIBIT NO.	DESCRIPTION OF DOCUMENT
1.1*	Engagement Letter between BioMarin Pharmaceutical Inc. and Reedland Capital Partners, an Institutional Division of Financial West Group, dated August 15, 2001
1.2*	Common Stock Purchase Agreement between BioMarin Pharmaceutical Inc. and Acqua Wellington North American Equities Fund, Ltd., dated August 15, 2001
5.1	Opinion of Paul, Hastings, Janofsky & Walker, LLP
10.1*	Letter Agreement between BioMarin Pharmaceutical Inc. and Acqua Wellington North American Equities Fund, Ltd., dated August 15, 2001 regarding Termination of the Common Stock Purchase Agreement dated January 26, 2001
23.1*	Consent of Paul, Hastings, Janofsky & Walker LLP.
23.2*	Consent of Arthur Andersen LLP
24.1	Power of Attorney

* Filed herewith. All other Exhibits filed previously.