

2002

2003

2004

BIOMARIN

VISION, PRODUCTS & PIPELINE

ANNUAL REPORT 2005





Pipeline



BIOMARIN: MATCHING PROVEN SCIENCE WITH PROVEN NEEDS

On May 31, 2005, the U.S. Food and Drug Administration (FDA) approved Naglazyme™ (galsulfase), the first enzyme replacement therapy for the treatment of mucopolysaccharidosis VI (MPS VI). This was the second time in BioMarin's eight-year history that the company successfully advanced a product through the clinic and into the marketplace.

At BioMarin, we are committed to developing and commercializing innovative biopharmaceuticals for serious diseases and medical conditions. We are aggressive in this undertaking and seek product opportunities that suggest a clear development path, provide an opportunity to be first to market and, most importantly, will address unmet medical needs.



A MESSAGE FROM THE CEO

2005 was a year marked by significant growth and success for BioMarin: we increased net product sales of Aldurazyme® (laronidase); we moved Naglazyme through clinical development to market; we advanced and added to our product pipeline; and we formed a strategic partnership that will help fund our lead clinical programs. We enter 2006 with continued resolve to build a sustainable biopharmaceutical company that will satisfy the interests of our stockholders and address unmet medical needs.

Net product sales of Aldurazyme for mucopolysaccharidosis I (MPS I) by BioMarin/Genzyme LLC continued to grow in 2005, increasing 79 percent in comparison to the previous year. In line with this, our share of the profit from this 50/50 joint venture grew to \$11.8 million for the year. As we move forward in 2006, we expect to see increasing profits

from Aldurazyme as product sales continue to grow and as we reduce research and development-related spending.

Net product sales of Naglazyme for MPS VI totaled \$6.1 million in 2005. Naglazyme was approved by the FDA on May 31, 2005, and subsequently by the European Commission in late January 2006. We anticipate net product sales of Naglazyme to increase significantly in 2006 as more individuals begin receiving commercial treatment in the United States, Europe and other parts of the world.

With regard to our product pipeline, in April 2005, we initiated a Phase 3 clinical trial of Phenoptin™ (sapropterin dihydrochloride) for the treatment of phenylketonuria (PKU). Phenoptin is a synthetic form of 6R-BH4 (commonly known as tetrahydrobiopterin or BH4), an enzyme cofactor that works in combination with the enzyme needed to metabolize

EIGHT YEARS OF PROGRESS

Two approved products, a state-of-the-art manufacturing facility, commercial operations in the United States and Europe, and new product opportunities in the pipeline.

1997

BioMarin Pharmaceutical Inc. Founded

Leadership team from left to right:

Jean-Jacques Bienaimé
Chief Executive Officer

Emit Kakkis, M.D., Ph.D.
Chief Medical Officer

Jeffrey Cooper
Vice President
Chief Financial Officer

Stephen Aselage
Senior Vice President
Global Commercial Operations

Robert Baffi, Ph.D.
Senior Vice President
Technical Operations

G. Eric Davis
Vice President
General Counsel &
Secretary

Stuart Swiedler, M.D., Ph.D.
Senior Vice President
Clinical Affairs

1997

BioMarin Initiates Phase 1 Clinical Trial of Aldurazyme for MPS I

phenylalanine (Phe). We announced positive results from this trial in March 2006 that demonstrated a highly statistically significant reduction in blood Phe levels ($p < 0.0001$) following six weeks of treatment with Phenoptin versus placebo. This was the primary endpoint of the trial. Phenoptin was well tolerated and the type and incidence of adverse events was similar in the Phenoptin and placebo groups. We remain on-track to file a New Drug Application (NDA) in early 2007. Phenoptin has been designated an orphan drug in the United States and Europe and assigned Fast Track status in the United States. We are developing Phenoptin in collaboration with Serono, our corporate partner as of May 2005, which will equally share Phase 3 development costs in exchange for rights to market Phenoptin outside of the United States and Japan.

1998

BioMarin/Genzyme LLC Formed to Support the Development and Commercialization of Aldurazyme for MPS I

Pursuant to this 50/50 joint venture, BioMarin and Genzyme share all costs and profits associated with the development and commercialization of Aldurazyme. BioMarin manufactures the product and Genzyme commercializes it.

In May 2005, we licensed expanded intellectual property rights to 6R-BH₄ for cardiovascular indications—an investigational product candidate that could provide us with an opportunity to break into markets with substantial commercial potential. In addition to the possible application of 6R-BH₄ in treating PKU, researchers have established that a deficiency of 6R-BH₄ contributes to endothelial dysfunction and, in academic studies, they have demonstrated that administration of 6R-BH₄ improves vascular endothelial function in animal models and individuals with diabetes and cardiovascular disease. In 2006, we plan to initiate two Phase 2 clinical trials of 6R-BH₄, beginning with one in poorly controlled hypertension.

1999

BioMarin Becomes a Publicly Traded Company
(NASDAQ/SWX: BMRN)



Our 6R-BH₄ program provides us with the opportunity to expand beyond orphan drug markets into new markets that may offer substantial commercial potential.



2000

BioMarin Initiates Phase 1/2 Clinical Trial of Naglazyme for MPS VI

We are excited about what we have accomplished in 2005 and the opportunities that are ahead of us. The key to our continued success lies in our ability to strike a balance between improving our financial performance and investing in new product opportunities. To this end, we remain focused on accelerating the growth and profitability of Naglazyme and Aldurazyme, leveraging our manufacturing and commercial infrastructure, and identifying new opportunities that will help to further strengthen our company.

I would like to extend my sincere appreciation to our board of directors and our scientific advisory boards, especially those formed to guide our PKU and cardiovascular programs, for sharing with us their leadership and scientific expertise. To our employees, I gratefully acknowledge their hard

work and dedication toward meeting our aggressive corporate goals and making new therapies a reality. Finally, I extend my appreciation to our stockholders for placing their confidence in us at BioMarin and for investing in our future.

Sincerely,

Jean-Jacques Bienaimé
Chief Executive Officer

2003

Aldurazyme for MPS I Approved and Launched in the United States and Europe

The key to our continued success lies in our ability to strike a balance between improving our financial performance and investing in new product opportunities.

2004

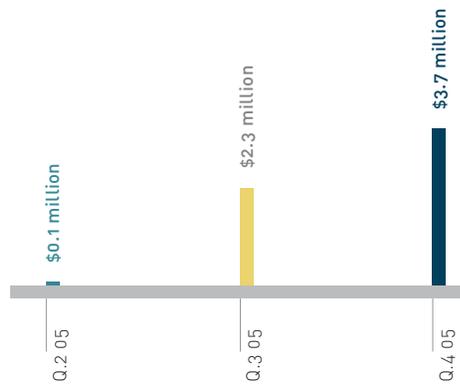
BioMarin Files Investigational New Drug Application for Phenoptin for PKU



ALDURAZYME NET PRODUCT SALES

As recorded by BioMarin/Genzyme LLC.
All profits/losses are shared equally between BioMarin and Genzyme Corporation.

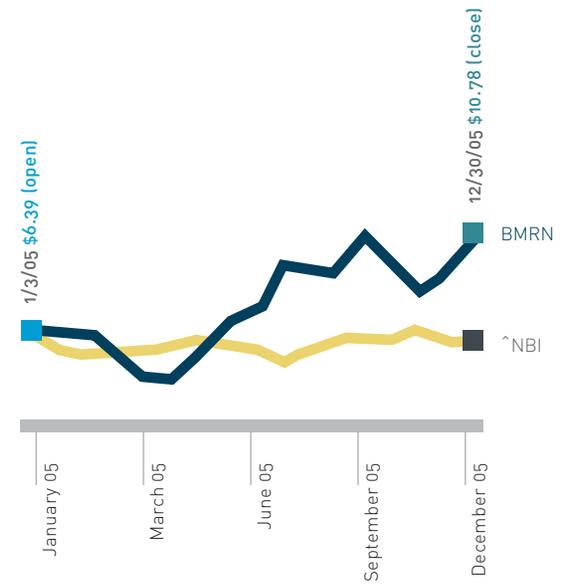
Aldurazyme was approved in the United States and Europe in April and June 2003, respectively.



NAGLAZYME NET PRODUCT SALES

Naglazyme was approved in the United States and Europe in May 2005 and January 2006, respectively.

2005 sales: \$6.1 million



2005 STOCK CHART

2004

BioMarin Files Marketing Applications for Naglazyme in the United States and Europe

2004

BioMarin Initiates Phase 2 Clinical Trial of Phenoptin for PKU

IMPROVING FINANCIAL PROFILE

For the third year in a row, net product sales of Aldurazyme through BioMarin/Genzyme LLC increased substantially in comparison to the previous year. This continued growth led the joint venture to profitability in 2005—a first since the partnership was formed. We expect net product sales of Aldurazyme to continue to increase in 2006.

Within three weeks of approval, we launched Naglazyme in the United States and, before it was approved in Europe, we were selling it on a named-patient basis. Each quarter we transitioned more individuals onto commercial therapy, resulting in \$6.1 million of net product sales for 2005. Commercializing Naglazyme on our own in both the United States and Europe positions us to realize a profit from the product more quickly than had we outsourced it to a third party. We expect net product sales of Naglazyme to continue to

grow in 2006 as it is approved in additional countries and more individuals begin treatment.

The partnership we formed with Serono in May 2005 helped us to advance Phenoptin into Phase 3 development and contributed to our decrease in net loss in 2005 in comparison to the previous year. In 2005, pursuant to our agreement, we received a \$25 million upfront payment and equally shared Phase 3 development costs associated with Phenoptin. Looking ahead, we expect this partnership to continue to help us advance our PKU and cardiovascular programs and support our effort to reduce our net cash use.

2005

BioMarin Initiates Phase 3 Clinical Trial of Phenoptin for PKU

2005

BioMarin Acquires Rights to 6R-BH4 for the Treatment of Cardiovascular Indications

2005

BioMarin Forms Strategic Alliance with Serono for the Development and Commercialization of Phenoptin, Phenylase and 6R-BH4 for Cardiovascular Indications

This agreement helps fund late-stage development of BioMarin's PKU and 6R-BH4 programs. BioMarin and Serono will equally share Phase 3 development costs of Phenoptin and Phenylase for PKU and 6R-BH4 for the treatment of cardiovascular indications. Additionally, Serono will provide BioMarin up to \$232 million in milestone payments in exchange for ex-U.S. commercialization rights (excluding Japan).

2005

Naglazyme for MPS VI Approved and Launched in the United States

Less than 30 days after approval, BioMarin commenced its first product launch, marking a significant event in the company's growth into a fully integrated biopharmaceutical company.

In 2005, our stock price increased over 68 percent—a reflection of the progress we made throughout the year.

2005

BioMarin Files New Drug Application for Crapred ODT

2006

BioMarin Europe Ltd. Established

2006

Naglazyme for MPS VI Approved in Europe



PRODUCTS ON THE MARKET

ALDURAZYME FOR MPS I

Aldurazyme is now available in over 30 countries worldwide and remains the only drug therapy for the treatment of MPS I. MPS I is a progressive, life-threatening genetic disease characterized by a deficiency of alpha-L-iduronidase, a lysosomal enzyme. Aldurazyme is an enzyme replacement therapy that provides MPS I patients with a recombinant version of this enzyme. Today over 400 individuals are receiving treatment with Aldurazyme, and we expect this number to increase as more patients are identified and approvals are attained in additional countries.

We developed Aldurazyme in partnership with Genzyme and received FDA approval in just over five and a half years after filing the Investigational New Drug Application (IND). Aldurazyme is manufactured by BioMarin and commercialized by Genzyme.

NAGLAZYME FOR MPS VI

Naglazyme is the first enzyme replacement therapy for the treatment of MPS VI. Similar to MPS I, MPS VI is a progressive, life-threatening genetic disease characterized by a deficiency of a lysosomal enzyme. Naglazyme provides patients with a recombinant version of this enzyme, arylsulfatase B. We believe that early diagnosis is crucial to preventing irreversible multisystemic damage caused by MPS VI. To this end, we are working to educate pediatricians about the signs and symptoms of the disease so that individuals can be promptly referred to genetic specialists for diagnosis and treatment.

We independently developed Naglazyme and received FDA approval in just over five years after filing the IND. Naglazyme is manufactured and commercialized by BioMarin.



Regulatory authorities in the United States and Europe have granted Aldurazyme for MPS I and Naglazyme for MPS VI orphan drug status, conferring seven years of market exclusivity in the United States and 10 years in the European Union.



PRODUCTS IN DEVELOPMENT

PHENOPTIN FOR PKU

Phenoptin is an investigational small-molecule oral therapeutic for the treatment of PKU. The active ingredient in Phenoptin is a synthetic form of 6R-BH₄, an enzyme cofactor that plays a key role in metabolizing phenylalanine (Phe). Phe is found in most protein-containing foods and if not sufficiently metabolized, it accumulates in the blood. Sustained elevated blood Phe levels can lead to serious neurological complications, including mental illness, loss of IQ and cognitive problems. We are developing Phenoptin with the aim of providing BH₄-responsive phenylketonurics with a simple and effective way to manage their disease. Currently, the only way to manage PKU is through a restricted diet that is difficult for most to adhere to. We plan to file an NDA in early 2007.

6R-BH₄ FOR CARDIOVASCULAR INDICATIONS

6R-BH₄ is an investigational small-molecule oral therapeutic for the treatment of cardiovascular indications. In addition to playing a role in metabolizing Phe, BH₄ is required for the production of nitric oxide in the endothelium. Researchers have established that a deficiency of BH₄ contributes to endothelial dysfunction and, in academic studies, have demonstrated that administration of 6R-BH₄ improves vascular endothelial function in animal models and individuals with diabetes and cardiovascular disease. In 2006, we plan to initiate a Phase 2 clinical trial of 6R-BH₄ in poorly controlled hypertension followed by a Phase 2 clinical trial in a second indication with endothelial dysfunction. Additionally, we expect two investigator-sponsored studies to be initiated in 2006, one in pulmonary arterial hypertension and the other in coronary artery disease.



- 6R-BH₄, commonly known as tetrahydrobiopterin (BH₄), is a naturally occurring enzyme cofactor. BioMarin is evaluating its application in treating PKU as well as endothelial dysfunction seen in diabetes and cardiovascular indications.

PROJECTED MILESTONES

Quarter 2-3 2006

BioMarin to Initiate Phase 2 Clinical Trial of 6R-BH₄ in Poorly Controlled Hypertension

Early 2007

BioMarin to File New Drug Application for Phenoptin for PKU

This Annual Report contains 'forward-looking statements' as defined under securities laws. These statements can generally be identified by the use of terminology such as 'believes', 'expects', 'anticipates', 'plans', 'intends', 'may', 'will', 'projects', 'continues', 'estimates', 'potential', 'opportunity', and so on. Our actual results or experience could differ significantly from the forward-looking statement. Factors that could cause or contribute to these differences include the results of our current clinical trials, our ability to obtain regulatory approval for our product candidates, our ability to successfully market our products and the other factors discussed in the enclosed Form 10-K and the section entitled 'Risk Factors' therein.

You should not place undue influence on these forward-looking statements which speak only as of the date that they were made. These cautionary statements should be considered in connection with any written or oral forward-looking statements that we may issue in the future. We do not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the distribution of this Annual Report to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

Aldurazyme is a registered trademark of BioMarin/Genzyme LLC.

EXECUTIVES

We strengthened our management team in 2005, adding key individuals to support the continued growth of our commercial and manufacturing operations.

Jean-Jacques Bienaimé
Chief Executive Officer

Emil Kakkis, M.D., Ph.D.
Chief Medical Officer

Jeffrey Cooper
Vice President
Chief Financial Officer

Stephen Aselage
Senior Vice President
Global Commercial Operations

Jeff Ajer
Vice President
Sales & Marketing Operations

William Aliski
Vice President & General Manager
European Operations

Robert Baffi, Ph.D.
Senior Vice President
Technical Operations

G. Eric Davis
Vice President
General Counsel & Secretary

Steven Jungles
Vice President
Supply Chain

Daniel Maher
Vice President
Product Development

Victoria Sluzky, Ph.D.
Vice President
Quality & Analytical Chemistry

Stuart Swiedler, M.D., Ph.D.
Senior Vice President
Clinical Affairs

Amy Waterhouse
Vice President
Regulatory & Government Affairs

1997

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1999

2000

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