BioMarin Presents Positive Long-Term Results from Ongoing Phase 1 and Phase 2 Clinical Studies of Aryplase for MPS VI

BioMarin on Track to File for US and EU Marketing Authorization in 2004 Pending Positive Results from the Ongoing Phase 3 Study

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BioMarin Pharmaceutical Inc. announced positive long-term results from Phase 1 and Phase 2 clinical studies of Aryplase(TM), an investigational enzyme replacement therapy for the treatment of mucopolysaccharidosis VI (MPS VI). Long-term data from both studies indicate that Aryplase is generally well-tolerated and that patients continue to benefit from Aryplase treatment.

Data from the Phase 1 and Phase 2 studies are being presented by John Hopwood, Ph.D., of Brigham and Women's Hospital, Adelaide, Australia, and by Paul Harmatz, M.D., of Children's Hospital Research Institute, Oakland, California, respectively, at the 53rd Annual Meeting of the American Society of Human Genetics in Los Angeles, California, November 4-8, 2003.

"We are pleased to see the clinical improvements these patients experienced, especially those observed beyond the initial six months of treatment and well into the second year of weekly Aryplase infusions," stated Stuart Swiedler, M.D., Ph.D., Vice President, Clinical Affairs of BioMarin. "Already, well in advance of a potential NDA filing, we have enrolled approximately 170 MPS VI patients in clinical and disease survey studies, whom someday may benefit from Aryplase treatment."

Phase 2 Study

The Phase 2 open-label study enrolled 10 patients with MPS VI at a dose of 1.0 mg/kg, the higher of two doses investigated in the Phase 1 dose-ranging study. The study enrolled patients at two sites, one in the United States (US) and one in Australia. Results after 48 weeks of treatment with Aryplase are summarized below:

- Endurance as measured by distance walked in 12 minutes improved by an average of 139 percent (211 meters) over the baseline distance. This represents an average incremental improvement of 56 meters over the improvement observed after 24 weeks of Aryplase treatment. The 12-minute walk test is the primary endpoint in the current Phase 3 clinical study of Aryplase.
- Endurance as measured by the number of stairs climbed in three minutes increased by an average of 147 percent (61 stairs) over the baseline number. This represents an average incremental improvement of an additional 13 stairs over the improvement observed after 24 weeks of Aryplase treatment. The 3-minute stair climb is a secondary endpoint in the current Phase 3 study.
- Urinary glycosaminoglycan (GAG) level, another secondary endpoint in the current Phase 3 study, was reduced by 76 percent on average after 48 weeks of treatment with Aryplase. Urinary GAG level was reduced by 71 percent on average after 24 weeks of treatment with Aryplase. GAG, the carbohydrate residue that accumulates in tissues of patients and causes MPS VI disease, is a biomarker for enzyme activity in vivo.
- Sustained improvements were also observed in joint pain and stiffness, and variable improvements were observed in joint range of motion. Reduction in liver and spleen size was observed in all five patients presenting with hepatosplenomegally at baseline, and four of the five now have liver volumes in the normal range. Pulmonary function improvements were observed in several patients, primarily between 24 and 48 weeks.

Phase 1 Study

The randomized, double-blind, Phase 1 study initially investigated two doses of Aryplase (0.2 mg/kg and 1.0 mg/kg) in two groups of three patients each. Following positive results after 24 weeks of treatment, all six patients continued to receive treatment at 1.0 mg/kg in an open-label extension study. Results after 96 weeks of treatment are summarized below:

- Endurance as measured by the distance walked in six minutes improved by an average of 96 percent (120 meters) over baseline after 96 weeks

of therapy. Gains in the 6-minute walk test were maintained or improved from week 48 to week 96 for the four evaluable patients in the study at the 96-week time point.

-- Urinary GAG level was reduced by 75 percent on average after 96 weeks of treatment. Patients who initially received the lower of the two doses experienced an incremental decrease in GAG level after receiving treatment with the higher dose.

Phase 1 and Phase 2 Safety

Aryplase was generally well-tolerated during both clinical studies. In the Phase 1 study, after nearly two years of treatment during which patients underwent 508 infusions, there was one serious adverse event (SAE) that the investigator attributed as related to drug. This patient experienced urticaria (rash) approximately three hours after the start of the week 76 infusion. After the rate of infusion was decreased, the patient recovered. There were 46 mild, four moderate, and no severe drug-related adverse events (AE). Fever and dermatitis were most commonly observed. In the Phase 2 study, out of 475 infusions, there was one SAE, an asthma attack, which the investigator attributed as possibly related to drug. A total of 31 infusion-related AEs were attributable to the drug, 18 of which were mild skin hypersensitivity reactions in one patient, and four similar incidences in a second patient. Most patients in both studies developed antibodies to Aryplase although antibody presence did not correlate with clinical safety or efficacy. Additionally, approximately 1.5 years after initiating treatment, relative antibody levels for all patients involved in the Phase 1 study fell to levels slightly above background.

BioMarin has received orphan drug and fast track designations for Aryplase from the US Food and Drug Administration (FDA). In addition, the European Commission has designated Aryplase for the treatment of MPS VI as an orphan medicinal product in the European Union (EU). BioMarin is currently conducting a multinational, placebo-controlled, double-blind, Phase 3 study of Aryplase in patients with MPS VI. The company expects to announce data from this study in the second quarter of 2004, and pending positive data, to file for

marketing authorization in the US and EU in the fourth quarter of 2004.

About MPS VI

MPS VI (also known as Maroteaux-Lamy Syndrome) is a debilitating, life-threatening genetic disease for which no drug therapies are currently available. MPS VI is caused by a deficiency of the enzyme arylsulfatase B. The deficiency leads to the accumulation of GAG in the lysosomes, the digestive organelles of the cell, giving rise to progressive cellular, tissue and organ system dysfunction. Debilitating symptoms can include impaired cardiac and pulmonary function, delayed physical development, skeletal and joint deformities, impaired vision and hearing, sleep apnea, and reduced endurance. The majority of subjects die from disease-related complications between childhood and early adulthood, depending on the severity of the disease.

To date, BioMarin has enrolled approximately 170 patients in its Phase 1, Phase 2, Phase 3 and disease survey studies. BioMarin estimates that there are approximately 1,100 MPS VI patients in the developed world, an estimate based on published epidemiological data.

BioMarin Pharmaceutical Inc. specializes in the development and commercialization of enzyme therapies for serious, life-threatening diseases and conditions.

Forward-Looking Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc., including without limitation, statements about: the presentations about clinical data related to Aryplase; expected timing of ongoing clinical trials for Aryplase; patient registry activities; and actions by regulatory authorities. These forward-looking statements are

predictions and involve risks and uncertainties such that actual results may differ materially from these statements. These risks and uncertainties include, among others: results and timing of current extension studies and clinical trials; the content and timing of decisions by the FDA, the European Commissionand other regulatory authorities concerning Aryplase; and those factors detailed in BioMarin's filings with the Securities and Exchange Commission, including, without limitation, the factors contained under the caption "Factors That May Affect Future Results" in BioMarin's 2002 Annual Report on Form 10-K and the factors contained in BioMarin's reports on Forms 10-Q and 8-K. Stockholders are urged not to place undue reliance on forward-looking statements, which speak only as of the date hereof. BioMarin is under no obligation, and expressly disclaims any obligation, to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

BioMarin's press releases and other company information are available online at http://www.bmrn.com/ . Information on our website is not incorporated by reference into this press release.

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