BioMarin Announces Positive Phase 3 Data on Aryplase(TM) for MPS VI

Aryplase Demonstrates Statistically Significant Benefit in Primary Endpoint

Company Expects to File for Marketing Authorization in the United States and the European Union in the Fourth Quarter of 2004

Conference Call and Webcast to be Held Today at 12:00 p.m. EDT (18:00 CEST)

PRNewswire-FirstCall

NOVATO, Calif.

BioMarin Pharmaceutical Inc. today announced positive results from its Phase 3 clinical trial of Aryplase(TM), an investigational enzyme replacement therapy for the treatment of mucopolysaccharidosis VI (MPS VI). The company reported the following results:

-- The clinical trial demonstrated a statistically significant improvement in endurance (p=0.025) in patients receiving Aryplase compared to patients receiving placebo as measured by the distance walked in 12 minutes, the primary endpoint in the trial.
-- The data from the trial demonstrated a statistically significant reduction in glycosaminoglycans (GAGs) excreted in the urine (p<0.001) in patients receiving Aryplase compared to patients receiving placebo. GAG reduction was one of two secondary endpoints measured in the clinical trial.
-- The 3-minute stair climb, another measure of endurance and also a secondary endpoint, demonstrated a positive trend (p=0.053) in patients receiving Aryplase compared to patients receiving placebo.
-- The results of the clinical trial indicate that treatment with Aryplase was generally well-tolerated. Adverse events during infusions were more common in patients receiving Aryplase but were generally mild to moderate in nature. The frequency of serious adverse events (SAEs) was more common in the placebo group.

"We are pleased that this trial has confirmed the favorable safety and efficacy profile of Aryplase that we have seen in the earlier Phase 1 and Phase 2 trials," stated Stuart J. Swiedler, M.D., Ph.D., Vice President of Clinical Affairs at BioMarin. "We hope to provide MPS VI patients with the first specific treatment option for this progressive and debilitating disease in the not-too-distant future."

Dr. Swiedler continued, "Through our three clinical studies, one disease survey study, and efforts led by our commercial planning group, we have already identified more than 200 patients with MPS VI who could potentially benefit from treatment with Aryplase, if approved. Our recently acquired 66-person pediatric sales force is now planning educational campaigns targeting pediatricians and medical geneticists in the United States to raise awareness about MPS VI and other lysosomal storage diseases and metabolic disorders."

Phase 3 Trial Design

The Phase 3, multi-center, double-blind, placebo-controlled trial was designed to evaluate the safety and efficacy of Aryplase for the treatment of MPS VI. The trial enrolled 39 patients, ranging in age from 5 to 29 years, at six sites located in the United States, Brazil, the United Kingdom, Germany, France, and Portugal. Patients were randomized on a one-to-one basis into one of two groups: an Aryplase treatment group or a placebo control group. Each group received a weekly intravenous infusion of 1.0 mg/kg of either Aryplase or placebo solution for 24 consecutive weeks. During the 24-week period, 19 patients received weekly intravenous infusions of Aryplase and 20 patients received weekly placebo infusions. One patient in the placebo group dropped out of the trial for reasons unrelated to treatment. All 38 patients who completed the trial have elected to receive Aryplase in an ongoing open-label extension study.

Summary of Results

Patients were evaluated at pre-defined, six-week intervals to assess changes in primary and secondary efficacy endpoints and the safety and tolerability of weekly Aryplase infusions. Results of the trial are summarized below:

Primary Efficacy Endpoint
-- Patients receiving Aryplase demonstrated a statistically significant
improvement (p=0.025) in endurance compared to patients receiving placebo as measured by the change relative to baseline in the distance walked in 12 minutes. The mean difference between patients receiving Aryplase and patients receiving placebo after 24 weeks was 92 meters.

Secondary Efficacy Endpoints

-- Patients receiving Aryplase experienced a statistically significant reduction (p<0.001) in GAGs excreted in the urine, compared to patients receiving placebo. Patients with MPS VI experience a build-up in GAGs as a result of the underlying enzyme deficiency. A reduction in urinary GAG levels is an indication of enzyme activity in vivo. The average urinary GAG reduction in patients receiving Aryplase after 24 weeks was 75.5 percent.

-- Patients receiving Aryplase demonstrated an improvement in endurance compared to patients receiving placebo as measured by the change relative to baseline in the number of stairs climbed per minute (p=0.053). Although not statistically significant, after 24 weeks, the average total improvement in the number of stairs climbed per minute in patients receiving Aryplase was approximately six compared to patients receiving placebo.

Safety Data

Aryplase was generally safe and well-tolerated. All 38 patients who completed the trial have elected to receive Aryplase in an open-label extension study. There were more study drug-related adverse events in the Aryplase group compared to placebo (92 versus 14), which largely reflected a higher incidence of adverse events during infusion in the Aryplase group (74 versus 13). Of the drug-related adverse events that occurred in the Aryplase group, 49 were considered mild, 39 were considered moderate, and four were considered to be severe. There were three SAEs in the Aryplase group compared to 12 in the placebo group.

Paul Harmatz, M.D., Associate Director of the Pediatric Clinical Research Center at Children's Hospital & Research Center at Oakland, California, who served as Principal Investigator of the Phase 3 trial stated, "It is encouraging to see the functional benefits MPS VI patients experience with Aryplase -- benefits that can greatly contribute to an improved quality of life. We are grateful to the patients and their families who have participated in this clinical trial and those who participated in the earlier trials."

Ongoing Assessments

Following the 24-week double-blind trial, all patients began receiving weekly infusions of Aryplase in an open-label extension study with continued assessment of primary and secondary efficacy variables as well as assessments related to safety and tolerability. The company expects to submit an electronic common technical document to the U.S. Food and Drug Administration and the European Medicines Agency in the fourth quarter of 2004.

Data at Upcoming Medical Conferences

Summary data from the Aryplase Phase 3 clinical trial will be presented at the following medical conferences later this month:

8th International Symposium on MPS and Related Diseases, June 10 - 13, 2004, Mainz, Germany:

-- Update on Phase 1, 2, and 3 Clinical Trial Results of Aryplase in MPS VI
-- A Threshold Effect of Urinary Glycosaminoglycans and the Walk Test as Indicators of Disease Progression in a Survey of Subjects with Mucopolysaccharidosis VI (Maroteaux-Lamy Syndrome)
-- Long-Term Combined Therapy with Recombinant Human Nacetylgalactosamine-4-Sulfatase for Degenerative Joint Disease in Mucopolysaccharidosis VI Cats
-- Flexible Endoscopy in a 13-Year-Old Boy with MPS VI and Tracheostomy Because of Upper Airway Obstruction: Changes After 91 and 146 Weeks of a Phase I/II Enzyme Replacement Therapy with Recombinant Human Arylsulfatase B

36th European Human Genetics Conference, June 12 - 15, 2004, Munich, Germany:

-- Update on Phase 1, 2, and 3 Clinical Trial Results of Aryplase in MPS VI
-- A Threshold Effect of Urinary Glycosaminoglycans and the Walk Test as
Indicators of Disease Progression in a Survey of Subjects with Mucopolysaccharidosis VI (Maroteaux-Lamy Syndrome)

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 human N-acetylgalactosamine 4-sulfatase, also known as 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.

BioMarin will host a conference call and webcast to discuss data from the Phase 3 trial of Aryplase today at 12:00 PM EDT (18:00 CEST). This event can be accessed on the BioMarin website at:

Date: June 3, 2004
Time: 12:00 PM EDT (18:00 CEST)
U.S. & Canada Toll-free Dial in #: 1-800-915-4836
International Dial in #: 973-317-5319
Replay Toll-free Dial in #: 1-800-428-6051
Replay International Dial in #: 973-709-2089
Replay Code #: 358780

BioMarin Pharmaceutical Inc. develops innovative biopharmaceutical products and commercializes therapeutics for serious pediatric diseases.

Forward-Looking Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc., including, without limitation, statements about: the development of Aryplase; expectations related to extension arms of clinical trials of Aryplase; and filings with 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 clinical trials; the content and timing of decisions by the FDA, the European Commission and 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 2003 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 www.BMRN.com. Information on BioMarin's website is not incorporated by reference into this press release.

CONTACT:
Joshua A. Grass                      Susan Ferris
Sr. Manager, Investor and Financial Relations  Manager, Corporate Communications
415-506-6777                         415-506-6701

SOURCE: BioMarin Pharmaceutical, Inc.


Web site: http://www.bmrn.com/