BioMarin Announces Positive Results from Clinical Study of 6R-BH4 in PKU Patients

Study Demonstrates Substantial Reduction in Phenylalanine Levels in PKU Patients
Orphan Drug Designation Obtained for Phenoptin (6R-BH4) in the United States and the European Union

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BioMarin Pharmaceutical Inc. announced positive results from a pilot clinical study of 6R-BH4 in 20 patients with phenylketonuria (PKU). 6R-BH4 is the active agent in Phenoptin(TM), an investigational small molecule therapeutic for the treatment of PKU. The company also announced that it has received orphan drug designation for Phenoptin in both the United States and European Union.

"The results from this study provide us with valuable new insights that will help us design future clinical trials of Phenoptin in PKU, including a trial we expect to start later this year," said Stuart Swiedler, M.D., Ph.D., Vice President of Clinical Affairs at BioMarin. "Data from this pilot study indicate that 6R-BH4 can lower blood Phe levels and may allow many PKU patients to significantly relax or eliminate their severely restrictive protein-free diet."

6R-BH4 Pilot Study Design and Results

The open-label study enrolled 20 PKU patients at two clinical sites located in the United States. Patients were given 10 mg/kg oral doses of 6R-BH4 daily for seven days. Blood phenylalanine (Phe) levels were measured before treatment and on the first, third and seventh day of 6R-BH4 treatment. Following completion of this first dosing regimen, patients did not take 6R-BH4 for one week. The experiment was then repeated at a dose of 20 mg/kg per day for seven days. Patients were not on a strict low Phe diet prior to or during the study. Results of the study are summarized below:

* The average Phe reduction for all 20 PKU patients in the study after seven days of treatment with 6R-BH4 was 24 percent at 10 mg/kg and 36 percent for 20 mg/kg.
* The study demonstrated that nine out of 20 patients (45 percent) responded with a 30 percent or greater reduction in blood Phe levels after receiving a daily dose of 10 mg/kg of 6R-BH4 for seven days.
* The number of patients that responded with a 30 percent or greater reduction in blood Phe levels increased to 12 out of 20 patients (61 percent) with daily doses of 20 mg/kg of 6R-BH4 for seven days.
* The average blood Phe reduction in responders at the 10 mg/kg dose was 50 percent, while the average reduction in responders at the 20 mg/kg dose was 64 percent. A responder was defined as a patient who had a 30 percent or greater drop in blood Phe after the seventh day of 6R-BH4 treatment.
* The blood Phe levels in responders rose sharply seven days after discontinuing treatment with 6R-BH4, providing additional evidence that oral 6R-BH4 can reduce blood Phe levels.
* The responders experienced dose-dependent increases in tyrosine levels during the study, further suggesting that 6R-BH4 increases the normal metabolic conversion of Phe to tyrosine, which is deficient in PKU patients.
* The investigators did not report any serious side effects of 6R-BH4 during the study.

Results will be presented in detail at the Society of Inborn Errors of Metabolism 41st Annual Symposium being held in Amsterdam, the Netherlands, August 31 to September 3, 2004.

Richard Koch, M.D., Professor Emeritus of Clinical Pediatrics, University of Southern California School of Medicine, Los Angeles and investigator in the study commented, "While newborn PKU screening and the availability of a medical food diet have helped people with PKU prevent the most serious symptoms of PKU, there is still a significant need for an alternative to diet restriction." Dr. Koch continued, "Most patients become non-compliant with this highly restricted diet in adolescence, despite the known poor neurological outcomes. Results from this study suggest that a large percentage of people with PKU could potentially benefit from Phenoptin; those with the milder forms of PKU may be able to abandon the low Phe diet completely and those

with the more severe form of PKU may also benefit but to a lesser degree.

Orphan Drug Designation

BioMarin has received orphan drug designation for Phenoptin from the U.S. Food and Drug Administration (FDA). In addition, the European Medicines Evaluation Agency (EMEA) has designated Phenoptin for the treatment of PKU as an orphan medicinal product in the European Community. Orphan drug designation provides market exclusivity for seven years in the United States and 10 years in the European Union.

About Phenylketonuria (PKU)

PKU, a genetic disorder affecting at least 50,000 diagnosed patients under the age of 40 in the developed world, is caused by a deficiency of the enzyme, phenylalanine hydroxylase (PAH). PAH is required for the metabolism of Phe, an essential amino acid found in most protein-containing foods. If the active enzyme is not present in sufficient quantities, Phe accumulates to abnormally high levels in the blood and brain resulting in a variety of complications, including severe mental retardation and brain damage, seizures and tremors, and cognitive problems. As a result of global newborn screening efforts implemented in the 1960s and early 1970s, virtually all PKU patients in developed countries have been diagnosed at birth by measurement of blood Phe levels. No drugs are currently approved to treat PKU, which can only be managed through a highly restrictive and expensive medical food diet that most patients find difficult to maintain.

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 its product candidate Phenoptin; expectations related to future clinical trials of Phenoptin; the clinical efficacy of Phenoptin, particularly long term efficacy; and potential treatment protocols using Phenoptin. 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 EMEA and other regulatory authorities concerning Phenoptin; 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.

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