BioMarin Initiates Phase 3 Clinical Trial of Phenoptin for PKU

PRNewswire
NOVATO, Calif.

BioMarin Pharmaceutical Inc. (Nasdaq and SWX: BMRN) announced today that it has randomized the first patient in its Phase 3 clinical trial of Phenoptin(TM) (sapropterin hydrochloride), an investigational oral, small molecule therapeutic for the treatment of the genetic disease phenylketonuria (PKU). The company expects to announce data from this trial in the second half of 2005.

"We are pleased with the rapid pace at which we have been able to advance Phenoptin for PKU into the clinic, moving it from the initiation of our development program into a Phase 3 clinical trial in just over a year," stated Emil Kakkis, M.D., Ph.D., Senior Vice President of Business Operations at BioMarin. "During this time, we have also succeeded in forming strategic partnerships with Daiichi Suntory Pharma and Merck Eprova that provided a substantial preclinical and clinical data set and an important intellectual property position surrounding the manufacturing and formulation of sapropterin hydrochloride, the active ingredient in Phenoptin."

The Phase 3, double-blind, placebo-controlled, multi-center trial is designed to evaluate the safety and efficacy of Phenoptin for the treatment of individuals with PKU. The trial will enroll approximately 100 PKU patients and be conducted at approximately 30 sites worldwide. To qualify, patients must be over 8 years of age, have demonstrated a reduction in blood Phe levels while in the Phase 2 trial and have blood Phe levels greater than 600 umol/L at baseline. Patients enrolled in the Phase 3 trial will be randomized on a one-to-one basis into a Phenoptin treatment group (10 mg/kg daily) or a placebo

group and will be evaluated every two weeks for changes in blood Phe levels and for adverse events. The primary endpoint of the trial will be reduction in blood Phe levels compared to baseline levels, relative to placebo, after six weeks of treatment. Patients enrolled in the Phase 3 trial may be eligible to participate in a 22 week Phase 3 extension study designed primarily to evaluate long-term safety and to corroborate dose optimization and pharmacokinetics of Phenoptin.

About Phenoptin

Phenoptin is an investigational oral small molecule therapeutic for the treatment of primarily the moderate to mild forms of PKU. The active ingredient in Phenoptin, sapropterin hydrochloride, is the synthetic form of 6R-BH4, a naturally occurring enzyme cofactor. BioMarin received orphan drug designation for Phenoptin to treat PKU from both the U.S. Food and Drug Administration and European Medicines Evaluation Agency. If Phenoptin is the first drug therapy to be approved for the treatment of PKU, BioMarin would receive seven years of market exclusivity in United States and 10 years in the European Union for this indication.

About PKU

PKU, a genetic disorder affecting at least 50,000 diagnosed patients under the age of 40 in the developed world, an estimated half of whom have the moderate to mild form of the disease, 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, mental illness, 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. The only treatment currently available for PKU patients is a highly restrictive and expensive medical food diet that most patients find difficult to maintain.

About BioMarin

BioMarin develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. The company's product portfolio is comprised of two approved products, Aldurazyme(R) (laronidase) for mucopolysaccharidosis I (MPS I) and Orapred(R) (prednisolone sodium phosphate oral solution) for severe asthma, and multiple investigational product candidates including rhASB (galsulfase), a BLA-stage product candidate under review for the treatment of mucopolysaccharidosis VI (MPS VI), and Phenoptin(TM) (sapropterin hydrochloride), a Phase 3 product candidate for the treatment of phenylketonuria (PKU). For additional information, please visit www.BMRN.com. Information on BioMarin's website is not incorporated by reference into this press release.

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 current and future clinical trials of Phenoptin; the efficacy Phenoptin; and the commercialization plans for 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: slow patient enrollment rates for the Phenoptin trials; results and timing of clinical trials of Phenoptin; the content

and timing of decisions by the FDA, the EMEA and other regulatory authorities concerning Phenoptin and rhASB; the possible need to conduct additional clinical trials of 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 2004 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.

NOTE: Aldurazyme(R) is a registered trademark of BioMarin/Genzyme LLC. Orapred(R) is a registered trademark of Medicis Pediatrics, Inc. and is used under license.

CONTACT: investors, Joshua A. Grass, +1-415-506-6777, or media, Susan Ferris, +1-415-506-6701, both of BioMarin Pharmaceutical Inc.

SOURCE: BioMarin Pharmaceutical Inc.

CONTACT: investors, Joshua A. Grass, +1-415-506-6777, or media, Susan Ferris, +1-415-506-6701, both of BioMarin Pharmaceutical Inc.

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