BioMarin to Initiate a Phase 3 Clinical Trial of Phenoptin in PKU in the First Quarter of 2005

Blood Phenylalanine Level will be the Primary Efficacy Measurement

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BioMarin Pharmaceutical Inc. (Nasdaq and SWX: BMRN) announced today that it expects to initiate a six-week, multi-center, international, double-blind, placebo-controlled Phase 3 clinical trial of Phenoptin(TM) (sapropterin hydrochloride) in phenylketonuria (PKU) in the first quarter of 2005, based on its recent meeting with the U.S. Food and Drug Administration (FDA). As a primary efficacy endpoint, the trial will measure the changes in blood phenylalanine (Phe) level in patients receiving Phenoptin compared to patients receiving placebo.

"After discussing the critical components of our plan with the FDA, we can now advance Phenoptin into late-stage clinical development," stated Louis Drapeau, acting Chief Executive Officer at BioMarin. "Based on the anticipated patient enrollment schedule, we expect to announce results of the double-blind portion of the Phase 3 clinical trial in the second half of 2005." Mr. Drapeau continued, "Phenoptin represents the opportunity for BioMarin to be the first company to develop an oral therapeutic for PKU. It could also become BioMarin's fourth marketed product, and potentially the third product that the company commercializes itself in the United States."

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Overview of the Phenoptin Clinical Program

Phase 2
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BioMarin's multi-center, international Phase 2 clinical trial of Phenoptin, set to begin by the end of 2004, will screen up to 400 PKU patients 8 years of age or older with blood Phe levels greater than 600 µmoles/L for responsiveness to Phenoptin. Dosing in the Phase 2 study will be 10 mg/kg once daily for eight days.

Phase 3

Patients in the Phase 2 clinical trial of Phenoptin who respond with decreases in blood Phe levels of 30 percent or greater will be eligible to enroll into the randomized Phase 3 clinical trial to begin in the first quarter of 2005. The Phase 3 trial, which is expected to enroll approximately 100 patients, will compare changes in blood Phe levels and safety-related endpoints in patients receiving Phenoptin compared to patients receiving placebo over a six-week period. Following the placebo-controlled portion of the trial, all patients will receive Phenoptin in an extension study, which will evaluate dosing, pharmacokinetics and safety. If Phenoptin is approved, BioMarin expects to conduct several post-marketing studies with Phenoptin in PKU.

Projected Development Timeline

Depending on the rate of enrollment, BioMarin expects to release results of the double-blind portion of the Phase 3 clinical trial in the second half of 2005. BioMarin could file for approval of Phenoptin in the United States in the first half of 2006, depending on the outcomes of the clinical trials and other factors involved in the development of Phenoptin. In the first quarter of 2005, BioMarin plans to discuss its Phenoptin clinical program with the European Medicines Evaluation Agency (EMEA).

About Phenoptin

Phenoptin(TM) (sapropterin hydrochloride, also known as 6R-BH4) is an investigational oral small molecule therapeutic for the treatment of primarily the moderate to mild forms of the genetic disease phenylketonuria (PKU). BioMarin received orphan drug designation for Phenoptin to treat PKU from both the FDA and EMEA. BioMarin would receive seven years of market exclusivity in United States and 10 years in the European Union if it were first to receive approval for 6R-BH4 to treat PKU.

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 phenylalanine (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.

BioMarin Pharmaceutical Inc. develops and commercializes innovative biopharmaceuticals for serious diseases and medical 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 development of its product candidates Phenoptin and Aryplase(TM) (galsulfase); expectations related to future clinical trials of Phenoptin; the efficacy Phenoptin; expectations regarding the New Drug Application for Aryplase filed with the FDA; and the commercialization plans for Aryplase and 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 Aryplase; the possible need to conduct additional clinical trials of Phenoptin; risks associated with the commercial scale-up of the manufacturing process of Phenoptin, including cost and viability risks; 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.

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