Results From Phase 1 Clinical Study of PEG-PAL in PKU and Update on Phase 2 Clinical Study

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BioMarin Pharmaceutical Inc. today announced results from the Phase 1 clinical study of PEG-PAL (PEGylated recombinant phenylalanine ammonia lyase) for the treatment of phenylketonuria (PKU). The company expects to initiate the Phase 2 clinical study in late June or early July, pending institutional review board (IRB) approval from the clinical trial sites. The U.S. Food and Drug Administration (FDA) has reviewed the Phase II clinical trial protocol.

Key findings from the Phase 1 study:

- Substantial blood Phe level reductions in the range of 36% to 97% (mean of 62%) were observed in all patients in the fifth dosing cohort (0.1 mg/kg) with a mean baseline blood Phe level of 1113 umol/L. No notable blood Phe level reductions were observed in the first four dosing cohorts (0.001 to 0.03 mg/kg).
- No serious immune reactions, including hives or anaphylactoid reactions, were observed.
- Seven out of 25 patients developed late mild to moderate injection-site reactions, of which two also developed skin rashes without other symptoms and two patients developed reactions to Depo-Provera (medroxyprogesterone acetate).

Click here for graph: Correlation between blood Phe level and plasma concentration of PEG-PAL in Cohort 5.

"We are encouraged to see significant reductions in blood Phe levels in all patients in the fifth dosing cohort of the Phase 1 trial. Importantly, there were no serious reactions, and both the number and severity of the mild to moderate reactions were in-line with expectations of an enzyme of this nature," said Hank

Fuchs, M.D., Chief Medical Officer of BioMarin. "The Phase 2 study will answer the critical questions of optimal dose, dosing regimen and tolerability."

Phase 1 Study Design

The Phase 1 clinical trial was an open-label, multi-center study conducted in 25 PKU patients in a series of five dose-escalating cohorts ranging from 0.001 to 0.1 mg/kg, with each cohort receiving a single dose, and a 6-week follow-up period.

The primary objective of the study was to assess the safety and tolerability of single, subcutaneous injections of PEG-PAL in subjects with PKU. The secondary objectives of the study were to evaluate the pharmacokinetics of single, subcutaneous injections of PEG-PAL administered at escalating doses and to evaluate the effect of PEG-PAL on blood Phe concentrations in subjects with PKU.

Phase 2 Study Design

The Phase 2 clinical trial is an open-label, multi-center study to be conducted in up to 35 patients in a series of dose-escalating cohorts from 0.001 mg/kg. The primary treatment period of eight once weekly injections at a fixed dose will be followed by eight weeks of dose and frequency optimization and an extension period where doses can be increased up to 2.0 mg/kg/week.

The primary objective is to evaluate the effect of PEG-PAL on blood Phe concentrations in subjects with PKU. The secondary objectives are to evaluate the safety and tolerability, immune response and steady state PK of subcutaneous injections of multiple dose levels of PEG-PAL.

About PEG-PAL

PEG-PAL (PEGylated recombinant phenylalanine ammonia lyase) is an investigational enzyme substitution therapy for the treatment of PKU. Pharmacology studies conducted in the PKU mouse model demonstrated that weekly subcutaneous administrations of PEG-PAL resulted in a significant and stable decrease of plasma phenylalanine. BioMarin estimates that PEG-PAL could be a potential treatment option for a significant portion of the PKU population.

About BioMarin

BioMarin develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. The company's product portfolio comprises three approved products and multiple clinical and pre-clinical product candidates. Approved products include Naglazyme(R) (galsulfase) for mucopolysaccharidosis VI (MPS VI), a product wholly developed and commercialized by BioMarin; Aldurazyme(R) (laronidase) for mucopolysaccharidosis I (MPS I), a product which BioMarin developed through a 50/50 joint venture with Genzyme Corporation; and Kuvan(R) (sapropterin dihydrochloride) Tablets, for phenylketonuria (PKU), developed in partnership with Merck Serono, a division of Merck KGaA of Darmstadt, Germany. Other product candidates include PEG-PAL (PEGylated recombinant phenylalanine ammonia lyase), which is in clinical development for the treatment of PKU and GALNS (N-acetylgalactosamine 6-sulfatase), which is currently in Phase 1/2 clinical development for the treatment of MPS IVA. 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 PEG-PAL, the timing, design, conduct and expectations related to the PEG-PAL clinical trials, and expectations regarding filings with regulatory agencies. 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: the results of current and planned clinical trials related to PEG-PAL; the content and timing of decisions by the U.S. Food and Drug Administration and other regulatory agencies, particularly with respect to PEG-PAL, and those factors detailed in BioMarin's filings with the Securities and Exchange Commission, including, without limitation, the factors contained under the caption "Risk Factors" in BioMarin's 2008 Annual Report on Form 10-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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