BioMarin Submits Pegvaliase Biologics License Application (BLA) to the U.S. FDA for Treatment of Phenylketonuria (PKU)

SAN RAFAEL, Calif., June 30, 2017 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced that the company submitted a Biologics License Application (BLA) on Friday, June 30, 2017 to the U.S. Food and Drug Administration (FDA) for pegvaliase, a PEGylated recombinant phenylalanine ammonia lyase enzyme product, to reduce blood phenylalanine (Phe) levels in adult patients with PKU who have uncontrolled blood Phe levels on existing management. Following receipt of the BLA, the FDA conducts an initial assessment of the application to determine its fileability. The FDA typically notifies the applicant of their filing decision and planned Prescription Drug User Fee Act (PDUFA) action date within 60 to 74 days after receipt of the application. The company also intends to submit an application for registration in the European Union (EU) by year end 2017.

"We believe that pegvaliase offers the promise of an important new treatment option for those adult patients with PKU unable to manage their condition with existing treatments. Pegvaliase has been shown to lower blood Phe levels, which was the primary endpoint for registration of the only therapy currently approved to treat PKU," said Hank Fuchs, M.D., President Worldwide Research and Development. "The current medical guidelines highlight that the primary goal of therapy is to lower Phe, and pegvaliase represents an important advance in achieving that goal for adult PKU patients. We look forward to working with the FDA to bring this treatment to patients."

"Not all PKU patients experience the same symptoms, but we know that these symptoms improve with a reduction in blood Phe levels," said Nicola Longo, M.D., Ph.D., Professor at the University of Utah School of Medicine and investigator for the pegvaliase Phase 3 studies. "For those adult patients who cannot control Phe levels on existing management, pegvaliase can reduce Phe levels and produce meaningful benefits. I look forward to working with the FDA to convey my enthusiasm for a therapy that can improve upon what's currently available."

About Pegvaliase

Pegvaliase is an investigational study drug that substitutes the deficient PAH enzyme in PKU with the PEGylated version of the enzyme phenylalanine lyase, to break down Phe. It is being developed as a potential treatment for adults with inadequately controlled blood Phe levels. In clinical studies, treatment with subcutaneous pegvaliase substantially reduced blood Phe compared to placebo using a randomized withdrawal study design, and led to long-term maintenance of Phe reduction in the majority of adult patients with PKU. Pegvaliase was administered using a dosing regimen that achieved a manageable safety profile, consisting primarily of immune-mediated responses, including anaphylaxis, for which robust risk management measures effective in clinical trials will be proposed.

For additional information regarding the investigational product pegvaliase, please contact BioMarin Medical Information at medinfo@bmrn.com.

About Phenylketonuria or Phenylalanine Hydroxylase Deficiency

Phenylketonuria (PKU) or phenylalanine hydroxylase (PAH) deficiency is a genetic disorder affecting approximately 50,000 diagnosed patients in the developed world and is caused by a deficiency of the enzyme PAH. This enzyme 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 becomes toxic to the brain, resulting in a variety of complications including severe intellectual disability, seizures, tremors, behavioral problems and psychiatric symptoms. As a result of newborn screening efforts implemented in the 1960s and early 1970s, virtually all individuals with PKU or PAH deficiency under the age of 40 in developed countries are diagnosed at birth and treatment is implemented soon after. PAH deficiency can be managed with a Phe-restricted diet, which is supplemented by low-protein modified foods and Phe-free medical foods; however, the strict diet is difficult for most patients to adhere to the extent needed for achieving adequate control of blood Phe levels.

To learn more about PKU and PAH deficiency, please visit www.PKU.com. Information on this website is not incorporated by reference into this press release.

About ACMG Guidelines

Practice guidelines issued by the American College of Medical Genetics and Genomics (ACMG) support the need for lifelong management of Phe levels in patients with phenylketonuria or PKU. The new diagnosis and management guidelines were published online in Genetics In Medicine's Advance Online Publication (AOP) service and provide the first update to recommendations for therapy of PKU since the 2001 National Institutes of Health Consensus statement.

The guidelines state that treatment of PKU should be initiated as early as possible and must be continued throughout adulthood with a goal of maintaining blood levels of Phe for all patients between 120-360 umol/L. Patients treated from the early weeks of life with initial good metabolic control, but who lose that control in later childhood or adult life, may

experience both reversible and irreversible neuropsychiatric consequences.

According to the guidelines "the primary goal of therapy is to lower blood Phe, and any interventions, including medications, or combination of therapies that help to achieve that goal in an individual, without other negative consequences, should be considered appropriate therapy."

Evidence for the guidelines are drawn from two previous independent review processes from the National Institutes of Health (2001) and the Agency for Health Research and Quality (2012). The guidelines can be accessed online at:

https://www.acmg.net/docs/Phenylalanine_Hydrosylase_Deficiency_Practice_Guideline_AOP_Jan_2013.pdf

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for people with serious and life-threatening rare disorders. The company's portfolio consists of six commercialized products and multiple clinical and pre-clinical product candidates.

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: BioMarin's development programs for pegvaliase generally, and specifically about expectations regarding the BLA filing for pegvaliase with the FDA and EMA; the potential outcome of the review of such filings; and the possible approval of such product candidates. 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 of current and planned clinical trials of its product candidates; the content and timing of decisions by the FDA, the EMA and other regulatory authorities concerning its product candidates; our ability to manufacture sufficient quantities of pegvaliase for clinical trials, commercial launch and other preapproval requirements; and those other risks detailed from time to time under the caption "Risk Factors" and elsewhere in the Company's Securities and Exchange Commission (SEC) filings, including the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, and future filings and reports by the Company. The Company undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

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