European Medicines Agency (EMA) Accepts BioMarin's Marketing Application for Pegvaliase MAA for Treatment of Phenylketonuria (PKU)

FDA PDUFA Action Date for Pegvaliase is May 25, 2018

SAN RAFAEL, Calif., March 28, 2018 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (Nasdaq:BMRN) announced today that the European Medicines Agency (EMA) has accepted BioMarin's submission of a Marketing Authorization Application (MAA) for pegvaliase, a PEGylated recombinant phenylalanine ammonia lyase enzyme product, for the treatment of adults with phenylketonuria (PKU) who have inadequate blood phenylalanine control (blood phenylalanine levels greater than 600 micromol/l) despite prior management with available treatment options including sapropterin. The U.S. Food and Drug Administration accepted the Biologics License Application (BLA) for pegvaliase and granted priority review status in August 2017, with the Prescription Drug User Fee Act (PDUFA) Action Goal Date of May 25, 2018.

"The acceptance of the pegvaliase application for review by the EMA signifies a milestone in our journey to bring this important treatment to patients and families worldwide, offering a new option with the potential to alter the course of lifelong PKU management," said Hank Fuchs, M.D., President Worldwide Research and Development at BioMarin. "For more than 10 years, we have been committed to advancing the development of therapies for the PKU community, and we look forward to working with European regulatory authorities on the pegvaliase application."

Medical Guidelines Support Lifelong Therapy to Manage PKU

Medical guidelines in both the United States and Europe support the need for lifelong management of phenylalanine (Phe) levels in patients with phenylketonuria or PKU. In Europe in 2017, The *Lancet Diabetes & Endocrinology* published shortened medical guidelines, and the *Orphanet Journal of Rare Diseases* published a full version of the Guidelines. Both publications can be accessed from a page on the website of the European Society for Phenylketonuria (ESPKU). The guidelines state that untreated blood Phe concentrations greater than 600 µmol/l should be treated.

In the U.S., the American College of Medical Genetics and Genomics (ACMG) issued guidelines in 2014, which state that treatment of PKU should be initiated as early as possible and must be continued throughout adulthood and "lifelong," with a goal of maintaining blood levels of Phe for all patients between 120-360 umol/L. 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."

About Pegvaliase

Pegvaliase is an investigational study drug that substitutes the deficient PAH enzyme in PKU with the PEGylated version of the enzyme phenylalanine ammonia lyase, to break down Phe. It is being developed as a potential treatment for adults with inadequately controlled blood Phe levels in the study. 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

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 under the age of 40 in developed countries are diagnosed at birth and treatment is implemented soon after. PKU 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, please visit www.PKU.com. Information on this website is not incorporated by reference into this press release.

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. (BioMarin), including, without limitation, statements about: BioMarin's product candidate pegvaliase, and specifically about expectations regarding the MAA filing for pegvaliase with the EMA and the BLA filing for pegvaliase with the FDA; the potential outcome of the review of such filings, including the expected FDA action on the pegvaliase BLA at the end of May 2018; and the possible approval of pegvaliase by the FDA and EMA. 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 of current and planned clinical trials of pegvaliase; the content and timing of decisions by the FDA, the EMA and other regulatory authorities; our ability to manufacture sufficient quantities of pegvaliase for clinical trials, commercial launch and other preapproval requirements; 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" and elsewhere in the Company's Securities and Exchange Commission (SEC) filings, including the Company's Annual Report on Form 10-K for the year ended December 31, 2017, and future filings and reports by the Company. 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 to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

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