BioMarin Presents Interim Data of Phase 1/2 Study of BMN 250 for Treatment of Sanfilippo B Syndrome (MPS IIIB) at 13th International Congress of Inborn Errors of Metabolism (ICIEM) 2017

Preliminary biomarker and liver size data show marked decreases; early cognitive effects encouraging, pending more mature data

SAN RAFAEL, Calif., Sept. 6, 2017 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ:BMRN) announced today that it presented interim data from the dose escalation arm of a Phase 1/2 trial for BMN 250, an investigational enzyme replacement therapy using a novel fusion of recombinant human alpha-N-acetylglucosaminidase (NAGLU) with a peptide derived from insulin-like growth factor 2 (IGF2), for the treatment of Sanfilippo B syndrome or mucopolysaccharidosis IIIB (MPS IIIB) at the 13th International Congress of Inborn Errors of Metabolism (ICIEM) 2017. Discovered by BioMarin, BMN 250 is being studied in a multicenter, international clinical trial evaluating safety and tolerability, as well as cognitive function of patients with Sanfilippo B receiving BMN 250. Designed to restore functional NAGLU activity in the brain, BMN 250 is administered via intracerebroventricular (ICV) infusion.

In the completed dose escalation portion of the study (Part 1), which was primarily designed to determine safety and pharmacodynamic activity of BMN 250, three patients received escalating doses (30mg, 100mg, 300mg) of BMN 250 over 9 to12 months. Cerebrospinal fluid (CSF) heparan sulfate (HS) levels, which were markedly elevated at baseline, were reduced to the non-affected or normal range in all three patients, whether assessed as total or disease-specific HS. Sanfilippo B patients are missing one of four enzymes for HS degradation.

In those same patients, abdominal MRI scans showed significantly enlarged liver size at baseline followed by rapid decreases in liver size into the normal range for age with BMN 250 treatment, suggesting that ICV-administered BMN 250 reaches the peripheral circulation and may have activity in somatic organs. In contrast, most Sanfilippo B patients enrolled in BioMarin's concurrently-running observational study (250-901) had increased liver size at baseline and experienced further increases in liver size over time.

Two of the three treated patients from the dose escalation arm showed stabilization or some improvement compared to their pre-dose baselines in cognitive Development Quotient (DQ), a measure of cognitive function normalized to age. Patients with untreated Sanfilippo B usually show progressive decline in DQ.

Interim trial data indicates that ICV-administered BMN 250 was well-tolerated by Sanfilippo B patients. In the completed dose escalation portion (Part 1) of the study, the most common device-related adverse events (AEs) were ICV infection prior to first BMN 250 infusion, site erythema, CSF pleocytosis and blood clot in CSF. The most common AEs related to BMN 250 were pyrexia/fever and bradycardia. There were no serious treatment emergent AEs. In the ongoing stable dose portion (Part 2) of the study, there have been no serious device-related AEs reported to date. Dose-related AEs and serious adverse events (SAEs) have included vomiting, headache, fever, alteration of consciousness and CSF pleocytosis; however, all of these events were self-limited, and all Part 2 patients are currently receiving 300 mg weekly of BMN 250. In both Part 1 and Part 2, the AE profile is generally consistent with that seen with other ERTs and the ICV mode of administration.

For a limited time, the slides presented at ICIEM can be accessed here.

"We are pleased with the preliminary data from the three patients in the dose escalation stage of the study. Our experience in ICV administration of an enzyme replacement therapy combined with more than two decades of experience in developing MPS treatments has allowed us to reach this important step," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "We are grateful to the children and the families who are participating in this early clinical study."

BMN 250 has been granted orphan drug designation by the European Commission and the U.S. Food and Drug Administration. BioMarin has three approved therapies to treat different forms of MPS. BMN 250 is a potential fourth therapy in development for the treatment of an MPS disorder. BioMarin also has a recently approved enzyme replacement therapy for CLN2 delivered through intraventricular administration.

Study Design

The BMN 250 development program consists of three independent and complementary, multicenter,

international studies. BMN 250-901 is an observational study of the progression of Sanfilippo B over time in children 1-10 years of age with relatively preserved cognitive function. BMN 250-201 is a Phase 1/2 treatment study conducted in two parts, with Part 1 focused on safety and pharmacodynamic activity with dose escalation. Part 2 consists of eligible patients rolling over from the BMN 250-901 observational study, in addition to continued treatment of the patients from Part 1 of the study, treated at the highest dose. Efficacy will be assessed by comparing changes in disease progression in the observational BMN 250-901 study vs. changes observed in Part 2 of the BMN 250-201 Phase 1/2 treatment study. A companion study, BMN 250 -902, is a natural history study of the progression of Sanfilippo B over time in children 0-18 years of age with all levels of cognitive function.

About BMN 250

BMN 250 is an investigational enzyme replacement therapy using a novel fusion of recombinant human alpha-N-acetyglucosaminidase (NAGLU) with a peptide derived from insulin-like growth factor 2 (IGF2) for the treatment of Sanfilippo B syndrome or mucopolysaccharidosis IIIB (MPS IIIB). Designed to restore functional NAGLU activity in the brain, BMN 250 is delivered directly to the fluid surrounding the brain (cerebrospinal fluid) by an intracerebroventricular infusion.

For additional information regarding the investigational product BMN 250, please contact BioMarin Medical Information at medinfo@bmrn.com.

About Sanfilippo B

Sanfilippo B, a lysosomal storage disease, is caused by deficiency in the enzyme alpha-N-acetyglucosaminidase (NAGLU), one of the four enzymes required for heparan sulfate (HS) degradation. There are an estimated 2,000-3,000 patients in existing BioMarin territories who are living with Sanfilippo B syndrome.

The first symptoms generally appear between the ages of two and six years old, with behavior disorders, intellectual deterioration, sleep disorders, and in some cases, very mild dysmorphism. The neurological involvement becomes more prominent with progressive loss of motor milestones and communication problems. The prognosis is poor with death occurring in most cases in the late teens or early 20s.

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 the development plans for BMN 250 and expectations regarding the clinical trials for this product candidate. 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; final analysis of the clinical trial data collected to date, 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 BMN 250 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 June 30, 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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