BioMarin Announces Incremental Progress on Biologics License Application (BLA) Review for Valoctocogene Roxaparvovec AAV Gene Therapy for Adults with Severe Hemophilia A Program

FDA Pre-Licensure Inspection of Gene Therapy Manufacturing Facility Scheduled

FDA Requests Submission of Upcoming 3-Year Data Analysis from Phase 3 GENEr8-1 Study

Current PDUFA Target Action Date of March 31, 2023, Could Be Extended by 3 Months, If 3-Year Data Submission Deemed a Major Amendment

SAN RAFAEL, Calif., Nov. 7, 2022 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today a progress update on its Biologics License Application (BLA) for valoctocogene roxaparvovec AAV gene therapy for adults with severe Hemophilia A that is currently under review by the U.S. Food and Drug Administration (FDA). As part of their review of the BLA, the FDA has scheduled its Pre-Licensure Inspection (PLI) of BioMarin's gene therapy manufacturing facility, located in Novato, CA. As anticipated, the FDA also has requested that the Company submit results from the upcoming three-year data analysis from the ongoing Phase 3 GENEr8-1 Study.

While the FDA did not communicate a change to the current PDUFA target action date of March 31, 2023, the Agency stated that submission of these results may qualify as a Major Amendment, which would extend the action date by 3 months. FDA will evaluate the additional data prior to making this determination.

"We appreciate the level of engagement from FDA this early in their BLA review cycle and are pleased to share that the inspection of our gene therapy manufacturing facility has now been scheduled. Additionally, with their request related to the upcoming three-year data analysis from our Phase 3 GENEr8-1 study, FDA stated that these data are expected to provide longer-term efficacy and safety information and would thus be useful to people with Hemophilia A and healthcare providers in making better and more informed decisions when considering valoctocogene roxaparvovec as a treatment choice should it be approved," said Hank Fuchs, M.D., President of Worldwide Research and Development at BioMarin. "We are encouraged by the bleed control results observed in the first cohort of patients who reached three years of observation in the Phase 3 study as shared in January, and we look forward to reviewing the three-year results from all participants

(N=134). We anticipate sharing the three-year results from all 134 participants in our Phase 3 study in early 2023."

On Oct. 12, 2022, the FDA accepted the Company's resubmission of the BLA for valoctocogene roxaparvovec. Previously, the FDA communicated plans to hold an advisory committee meeting on a date that has yet to be confirmed per their usual practice of notification in the Federal Register. Depending on the timing of this meeting, BioMarin looks forward to the opportunity to discuss the recently requested 3-year data analysis with the Advisory Committee.

About valoctocogene roxaparvovec (ROCTAVIAN™)

In addition to the RMAT Designation and Breakthrough Therapy Designation, BioMarin's valoctocogene roxaparvovec also received orphan drug designation from the EMA and FDA for the treatment of severe hemophilia A. Orphan drug designation is reserved for medicines treating rare, life-threatening or chronically debilitating diseases. The European Commission (EC) granted conditional marketing authorization to valoctocogene roxaparvovec gene therapy under the brand name ROCTAVIAN™ on August 24, 2022.

Robust Clinical Program

BioMarin has multiple clinical studies underway in its comprehensive gene therapy program for the treatment of severe hemophilia A. In addition to the global Phase 3 study GENEr8-1 and the ongoing Phase 1/2 dose escalation study, the Company is also conducting a Phase 3, single arm, open-label study to evaluate the efficacy and safety of valoctocogene roxaparvovec at a dose of 6e13 vg/kg with prophylactic corticosteroids in people with severe hemophilia A (Study 270-303). Also ongoing are a Phase 1/2 Study with the 6e13 vg/kg dose of valoctocogene roxaparvovec in people with severe hemophilia A with pre-existing AAV5 antibodies (Study 270-203) and a Phase 1/2 Study with the 6e13 vg/kg dose of valoctocogene roxaparvovec in people with severe hemophilia A with active or prior Factor VIII inhibitors (Study 270-205).

Safety Summary

Overall, to date, a single 6e13 vg/kg dose of valoctocogene roxaparvovec has been well tolerated with no delayed-onset treatment related adverse events. The most common adverse events (AE) associated with valoctocogene roxaparvovec have occurred early and included transient infusion associated reactions and mild to moderate rise in liver enzymes with no long-lasting clinical sequelae. Alanine aminotransferase (ALT) elevation, a laboratory test of liver function, has remained the most common adverse drug reaction. Other adverse reactions have included aspartate aminotransferase (AST) elevation (101

participants, 63%), nausea (55 participants, 34%), headache (54 participants, 34%), and fatigue (44 participants, 28%). No participants have developed inhibitors to Factor VIII, thromboembolic events or malignancy associated with valoctocogene roxaparvovec.

About Hemophilia A

People living with hemophilia A lack sufficient functioning Factor VIII protein to help their blood clot and are at risk for painful and/or potentially life-threatening bleeds from even modest injuries. Additionally, people with the most severe form of hemophilia A (Factor VIII levels <1%) often experience painful, spontaneous bleeds into their muscles or joints. Individuals with the most severe form of hemophilia A make up approximately 50 percent of the hemophilia A population. People with hemophilia A with moderate (Factor VIII 1-5%) or mild (Factor VIII 5-40%) disease show a much-reduced propensity to bleed. Individuals with severe hemophilia A are treated with a prophylactic regimen of intravenous Factor VIII infusions administered 2-3 times per week (100-150 infusions per year) or a bispecific monoclonal antibody that mimics the activity of Factor VIII administered 1-4 times per month (12-48 injections or shots per year). Despite these regimens, many people continue to experience breakthrough bleeds, resulting in progressive and debilitating joint damage, which can have a major impact on their quality of life.

Hemophilia A, also called Factor VIII deficiency or classic hemophilia, is an X-linked genetic disorder caused by missing or defective Factor VIII, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people have hemophilia A.

About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for people with serious and life-threatening genetic diseases and medical conditions. The Company selects product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market or offer a significant benefit over existing products. The Company's portfolio consists of seven commercial products and multiple clinical and preclinical product candidates for the treatment of various diseases. For additional information, please visit www.biomarin.com.

Forward-Looking Statements

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including without limitation, statements about: the FDA planned inspection of the valoctocogene roxaparvovec manufacturing facility, the FDA's request for the three-year data from the Phase 3 GENEr8-1 study, the possible results of such analysis and the predictability of the results based on the early cohort, the timing of the PDUFA target action date, the timing of the advisory committee meeting, the possibility of regulatory approval, BioMarin's expectations regarding the duration of the review procedure. 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 and timing of current and planned preclinical studies and clinical trials of valoctocogene roxaparvovec; additional data from the continuation of the clinical trials of valoctocogene roxaparvovec, including the 3-year results of the Phase 3 GENEr8-1 study; any potential adverse events observed in the continuing monitoring of the participants in the clinical trials; the content and timing of decisions by the FDA and other regulatory authorities particularly as related to the inspection and the determination of any additional submissions as "major amendment";; and those and those factors detailed in BioMarin's filings with the Securities and Exchange Commission (SEC), including, without limitation, the factors contained under the caption "Risk Factors" in BioMarin's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 as such factors may be updated by any subsequent reports. 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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