BioMarin Announces Advancements in FDA Review of ROCTAVIAN™ (Valoctocogene Roxaparvovec) for Adults with Severe Hemophilia A

FDA No Longer Plans to Hold an Advisory Committee Meeting, as Previously Planned, to Discuss the Biologics License Application (BLA)

BioMarin Remains on Track to Host Scheduled Manufacturing Inspections by FDA in the Coming Weeks

SAN RAFAEL, Calif., Nov. 23, 2022 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced advancements in the U.S. Food and Drug Administration (FDA) review of the Biologics License Application (BLA) of ROCTAVIAN™ (valoctocogene roxaparvovec AAV gene therapy) for adults with severe hemophilia A. The Company was recently notified by the FDA that after further consideration, at this time, the Agency no longer plans to hold an advisory committee meeting to discuss the BLA for ROCTAVIAN that is currently under review. Previously, the FDA communicated to the Company that it did intend to hold an advisory committee meeting but did not specify a date. The Company also remains on track to host the scheduled FDA Pre-Licensure Inspection (PLI) of BioMarin's gene therapy manufacturing facility located in Novato, CA.

"The review of a BLA is a dynamic process, and we appreciate FDA's ongoing engagement as we work toward delivering a potentially transformative treatment choice to those patients with severe hemophilia A," said Hank Fuchs, M.D., President of Worldwide Research and Development at BioMarin. "We look forward to further dialogue with the Agency as it reviews our application."

About valoctocogene roxaparvovec (ROCTAVIAN™)

The FDA granted Regenerative Medicine Advanced Therapy (RMAT) designation to valoctocogene roxaparvovec in March 2021. RMAT is an expedited program intended to facilitate development and review of regenerative medicine therapies, such as valoctocogene roxaparvovec, that are expected to address an unmet medical need in patients with serious conditions. The RMAT designation is complementary to Breakthrough Therapy Designation, which the Company received for valoctocogene roxaparvovec in 2017.

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 is 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 eight 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 plans for an advisory committee meeting, and the possibility of regulatory approval. 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"; the possibility of the FDA requiring an advisory committee meeting, particularly after receipt of requested additional data; 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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