BioMarin Provides Update on FDA Review of ROCTAVIAN™ (Valoctocogene Roxaparvovec) Gene Therapy for Adults with Severe Hemophilia A

FDA Extends PDUFA Target Action Date to June 30, 2023

SAN RAFAEL, Calif., March 6, 2023 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (Nasdaq: BMRN), a global biotechnology company dedicated to transforming lives through genetic discovery, today announced that it received notice this afternoon from the U.S. Food and Drug Administration (FDA) that the agency has extended review of the company's Biologics License Application (BLA) for ROCTAVIAN™ (valoctocogene roxaparvovec) gene therapy for adults with severe hemophilia A.

The FDA determined that the submission of the three-year data analysis from the ongoing Phase 3 GENEr8-1 study constituted a Major Amendment due to the substantial amount of additional data and set a new PDUFA Target Action Date of June 30, 2023. The company had previously communicated that this data submission could be qualified as a Major Amendment.

The Phase 3 study, which included 134 participants, is the longest and largest to date for a gene therapy in hemophilia.

"We are continuing to work closely with FDA and appreciate the agency's active engagement as we seek to deliver this important therapy to patients with severe hemophilia A," said Hank Fuchs, M.D., president of Worldwide Research and Development of BioMarin. "The three-year data enhance our application and further reinforce our belief that ROCTAVIAN has the potential to fundamentally transform care for people with hemophilia A."

Global Regulatory Status

The FDA completed a Pre-License Inspection of the manufacturing facility in early December 2022.

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, which 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 European Medicines Agency (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).

About Hemophilia A

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 one-third of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people have 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% 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.

About BioMarin

Founded in 1997, BioMarin is a global biotechnology company dedicated to transforming lives through genetic discovery. The company develops and commercializes targeted therapies that address the root cause of the genetic conditions. BioMarin's unparalleled research and development capabilities have resulted in eight transformational commercial therapies for patients with rare genetic disorders. The company's distinctive approach to drug discovery has produced a diverse pipeline of commercial, clinical, and pre-clinical candidates that address a significant unmet medical need, have well-understood biology, and provide an opportunity to be first-to-market or offer a substantial benefit over existing treatment options. 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 expectations regarding the FDA review of the company's BLA for valoctocogene roxaparvovec and the PDUFA target action date for such application. 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 preclinical studies and clinical trials of valoctocogene roxaparvovec; the content and timing of decisions by the FDA, including the possibility that the FDA does not act on the valoctocogene roxaparvovec BLA on or before the target action date; 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 Annual Report on Form 10-K for the quarter year ended December 31, 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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