BioMarin Announces FDA Regenerative Medicine Advanced Therapy (RMAT) Designation Granted to Valoctocogene Roxaparvovec, Investigational Gene Therapy for Hemophilia A

RMAT Designation Granted by FDA During Bleeding Disorders Awareness Month

SAN RAFAEL, Calif., March 8, 2021 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that the U.S. Food and Drug Administration (FDA) granted Regenerative Medicine Advanced Therapy (RMAT) designation to valoctocogene roxaparvovec, an investigational gene therapy for the treatment of adults with severe hemophilia A. The FDA granted RMAT designation based on the potential of the valoctocogene roxaparvovec clinical data to address the unmet medical need within this population.

RMAT is an expedited program intended to facilitate development and review of regenerative medicine therapies, such as valoctocogene roxaparvovec, that are intended to address an unmet medical need in patients with serious conditions. The RMAT designation is complementary to Breakthrough Therapy Designation, which the Company received in 2017, allowing early, close, and frequent interactions with the FDA. One additional feature of the RMAT program is that sponsors of products that have been granted RMAT designation and which receive accelerated approval may be able to fulfill the post-approval requirements from clinical evidence obtained from sources other than the traditional confirmatory clinical trials.

The RMAT designation comes coincidently during Bleeding Disorders Awareness Month initiated by the National Hemophilia Foundation to celebrate and honor the bleeding disorders community.

"We are encouraged that the FDA granted RMAT Designation to valoctocogene

roxaparvovec. This designation confirms our belief in this treatment's potential to address unmet medical needs for people with hemophilia A at this time," said Hank Fuchs, M.D., President of Worldwide Research and Development at BioMarin. "We look forward to continuing a productive dialogue with the FDA around the RMAT designation, which provides options for the Agency to leverage data post approval, while also recognizing the agency's initial request to see two years of data from the Phase 3 study to evaluate the safety and efficacy of this investigational treatment option that could potentially provide a transformational treatment choice for the hemophilia community."

"During Bleeding Disorders Awareness Month, we applaud the FDA for its efforts to recognize the potential of cell and gene therapies to help people with hemophilia who have medical needs not currently addressed," said Leonard A. Valentino, MD, President & CEO of the National Hemophilia Foundation (NHF). "Established under the 21st Century Cures Act, RMAT designation has the potential to provide more treatment choices to people with bleeding disorders at a faster pace, which benefits the whole community."

"The FDA's RMAT designation is a critical program to advance the efficient development and regulatory review of regenerative medicine products that have the potential to address unmet needs," said the Alliance for Regenerative Medicine (ARM). "As the global voice of the regenerative medicine sector, ARM played a critical role in the creation of this pathway. The FDA has granted more than 50 RMAT designations to investigational products and in February approved an RMAT-designated product for the first time, illustrating the agency's commitment to advancing the development of regenerative medicines."

Regulatory Status

In the Complete Response Letter of August 18, 2020 to the Company's Biologics License Application (BLA) for valoctocogene roxaparvovec, the FDA recommended that the Company complete the Phase 3 GENEr8-1 study and submit two-year follow-up safety and efficacy data on all study participants. The Company plans to meet with FDA to review the two-year data request and share the Phase 3 GENEr8-1 results announced on January 10, 2021. In the EU, BioMarin is targeting submission of the Marketing Authorization Application (MAA) with these results to the EMA in the second quarter of 2021 pending confirmation in planned pre-submission meetings.

In addition to the RMAT Designation and Breakthrough Therapy Designation, BioMarin's valoctocogene roxaparvovec also has received orphan drug designation from the FDA and EMA for the treatment of severe hemophilia A. The Orphan Drug Designation program is intended to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.

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 recently began enrolling participants in a Phase 3b, 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 hemophilia A. The Company is running a Phase 1/2 Study with the 6e13kg/vg dose of valoctocogene roxaparvovec in approximately 10 participants with pre-existing AAV5 antibodies, as well as another Phase 1/2 Study with the 6e13 vg/kg dose of valoctocogene roxaparvovec in people with hemophilia A with active or prior FVIII inhibitors.

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 (FVIII 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 (FVIII 1-5%) or mild (FVIII 5-40%) disease show a much-reduced propensity to bleed. The standard of care for individuals with severe hemophilia A is a prophylactic regimen of replacement Factor VIII infusions administered intravenously up to two to three times per week or 100 to 150 infusions 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 serious and life-threatening rare and ultra-rare genetic diseases. The Company's portfolio consists of six commercialized products and multiple clinical and pre-clinical product candidates. For additional information, please visit www.biomarin.com. Information on BioMarin's website is not incorporated by reference into this press release.

Forward Looking Statements

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc., including without limitation, statements about the development of BioMarin's valoctocogene roxaparvovec program generally, the RMAT designation, the Company's plans to meet with the FDA to review the 2-year data request and share the Phase 3 GENEr8-1 results announced on January 10, 2021, BioMarin targeting submission of the MAA with these results to the EMA in the second quarter of 2021; the potential of valoctocogene roxaparvovec to address the unmet medical need within this hemophilia A population. 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, including final analysis of data from the continuation of these trials; any potential adverse events observed in the continuing monitoring of the patients in the clinical trials; the content and timing of decisions by the FDA, the EMA and other regulatory authorities; the content and timing of decisions by local and central ethics committees regarding the clinical trials; our ability to successfully manufacture the product candidate for the preclinical and clinical trials; and those other risks detailed from time to time under the caption "Risk Factors" and elsewhere in BioMarin's Securities and Exchange Commission (SEC) filings, including without limitation, BioMarin's Annual Report on Form 10-K for the year ended December 31, 2020 as such factors may be updated by any subsequent reports. BioMarin 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.BioMarin® is a registered trademark of BioMarin Pharmaceutical Inc.

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