Update for the Hemophilia Community

An update for the hemophilia community from BioMarin regarding a serious adverse event in the ongoing hemophilia A gene therapy [valoctocogene roxaparvovec, BMN 270] Phase 3 study that was deemed, by the Independent Data Safety Monitoring Committee and the company, very unlikely to be related to the investigational therapy.

BioMarin is providing an update to the community regarding their ongoing gene therapy clinical trial program in hemophilia A. The safety of patients and study participants is BioMarin's top priority. BioMarin's investigational gene therapy for hemophilia A has not been approved for use in the United States and is currently ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's BMN 270, is currently being studied in adults with severe hemophilia A.

On August 19, 2022, BioMarin was notified that a participant in the BMN 270 Phase 3 study (named GENEr8-1) was diagnosed with leukemia approximately 3 years after he received the dose of BMN 270. The specific type was B-cell acute lymphoblastic leukemia (B-ALL). This leukemia is cancer of the bone marrow and blood affecting the type of white blood cells known as B-lymphocytes.

A serious adverse event (SAE) is the term used to describe the occurrence of a serious health issue in a study participant, regardless of whether it was caused by the treatment under investigation. As with any serious adverse event, a committee of experts was brought together to help determine the cause of the leukemia and whether it may be related to the therapy being studied in the trial. The committee was composed of the BioMarin study team, the study investigator, an independent committee of experts that routinely monitors the study (Independent Data Safety Monitoring Committee), as well as other medical and scientific experts.

The study team as well as external experts concluded that, based on the results of initial molecular analysis, it is very unlikely BMN 270 played any role in the development of B-ALL in this study participant. This initial finding is based on test results for this participant which were consistent with findings typically seen in patients who are diagnosed with B-ALL. In addition, tests of the participant's leukemic cells for genetic material (DNA) from BMN270 showed that it was found in extremely low levels.

This participant remains in the study and is currently receiving standard-of-care treatment for ALL. BioMarin continues to follow their health for five years after initial treatment, and for another decade as a participant in a long-term follow-up study.

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The relevant health regulatory authorities were notified. At this time, trials of BMN 270 are ongoing and BioMarin does not expect to make any modifications in the future due to this event. The overall rate of all cancers observed in all BMN 270 trial participants (2 in approximately 400 patient years of observation) appears consistent with expected rates of cancer in persons with Hemophilia.

The safety of patients and study participants is BioMarin's top priority. Although the evidence so far points to the conclusion that it is very unlikely that BMN 270 played a role in the development of B-ALL in this participant, patients should speak with their physicians about any questions they have about gene therapy.

BioMarin supports the shared decision-making framework to enable a personalized dialogue between an individual patient, his physician and care team and we remain committed to informing & educating physicians, patients, advocacy groups & the Hemophilia community as we learn more about this case.

We acknowledge and thank the members of this community for their continued commitment and for the huge contribution that they have made to research in hemophilia.

Regulatory Status

In the United States, BMN 270 (valoctocogene raxoparvovec) has not been approved for use or determined to be safe or effective. BioMarin plans to include the previously reported results from the two-year follow-up safety and efficacy data from the Phase 3 GENEr8-1 study in a Biologics Licensing Application (BLA) resubmission for valoctocogene roxaparvovec to the Food and Drug Administration (FDA). The company remains on track to resubmit a BLA by the end of September.

For additional information:

- Visit www.clinicaltrials.gov and type in the study code "BMN 270"
- For inquiries or to provide feedback from advocacy organizations, please contact: patientadvocacy@bmrn.com
- Contact BioMarin Medical Information at medinfo@bmrn.com or toll free at 1 –800-983-4587