Update for the Hemophilia Community

The European Medicines Agency Committee for Medicinal Products for Human Use issues a positive opinion on BioMarin's investigational treatment, valoctocogene roxaparvovec

BioMarin announced today that the Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion recommending conditional marketing authorization (CMA) for BioMarin's investigational gene therapy, valoctocogene roxaparvovec. A final decision is expected from the European Commission in Q3 2022. In the United States, valoctocogene roxaparvovec has not been approved for use or determined to be safe or effective.

What is the European Medicines Agency (EMA)?

The EMA is responsible for the approval and regulation of medicines across all European Union member states and the European Economic Area (EEA). The EMA's role is to ensure that all medicines available on the EU market are safe, effective, and of high quality. It is important to note that the CHMP positive opinion is not a product approval in Europe, it is a step in the review process for products in Europe. Additionally, it is not part of the FDA review process for products in the United States, which are subject to a separate review process by the FDA.

What is the Committee for Medicinal Products for Human Use (CHMP)?

The CHMP is responsible for conducting the initial assessment of EU-wide marketing authorization applications made by medicine developers and recommends whether a medicine should be granted marketing authorization. After CHMP issues an opinion, the European Commission then is responsible for making a final decision. BioMarin's investigational gene therapy for severe hemophilia A has not been approved for use in Europe, the United States, or any country. This opinion is not an approval and is not related to the FDA review process in the United States. A final decision is expected from the European Commission in Q3 2022.

In Europe, a conditional marketing authorization may be granted in the interest of public health based on less comprehensive clinical data than normally required, where the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required.

Continued

What is the US regulatory status for BioMarin's investigational gene therapy for severe hemophilia A?

In the United States, valoctocogene roxaparvovec has not been approved for use or been determined to be safe or effective. BioMarin plans to include the previously reported results from the two-year follow-up of the 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). Based on recent feedback received from the FDA related to our plans for the upcoming BLA, the Agency has requested additional information and analyses of data to be included in the BLA prior to submission. The FDA has not requested additional pre-clinical or clinical studies. Based on these new information requests, the BLA resubmission is now expected 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

BioMarin Haemophilia A Clinical Development Programme: An Update for the Haemophilia Community

BioMarin is providing an update to the community regarding our ongoing gene therapy clinical trial program in haemophilia A. BioMarin's investigational gene therapy for haemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's investigational gene therapy, valoctocogene roxaparvovec, is currently being studied in adults with severe haemophilia A.

The first Phase 1/2 study was initiated in 2015 and involved 15 individuals and two dose levels. These individuals are now in long-term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is currently being conducted in 13 countries and is fully enrolled. 134 study participants have received investigational gene therapy as part of this study.

On May 31st, 2022 BioMarin released an update on the Phase 1/2 study of valoctocogene roxaparvovec, including the most recent results based on 6 years of follow up data for participants receiving the 6E13 vg/kg dose.

BioMarin intends to present a six-year update from the Phase 1/2 study during an oral presentation at the upcoming International Society on Thrombosis and Haemostasis (ISTH) 2022 Virtual Congress taking place July 9-13.

BioMarin extends its sincere gratitude to all study participants, families and care partners who have helped make this milestone possible.

Regulatory Status

In Europe, the European Medicines Agency (EMA) continues the review of our Marketing Authorization Application (MAA) for valoctocogene roxaparvovec, and we anticipate a Committee for Medicinal Products for Human Use (CHMP) opinion mid-year 2022. BioMarin has provided the EMA with two-year follow-up safety and efficacy data from the GENEr8-1 study.

Continued

Regulatory Status (continued)

In the United States, 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). Based on recent feedback received from the FDA related to our plans for the upcoming BLA, the Agency has requested additional information and analyses of data to be included in the BLA prior to submission. The FDA has not requested additional pre-clinical or clinical studies. While at present, no requests have been made concerning evaluation of efficacy and safety three years after dosing from the GENEr8-1 study, we are aware that such data will become available during the anticipated BLA review. Based on these new information requests, the BLA resubmission is now expected 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 medinfoeu@bmrn.com

An update for the hemophilia community from BioMarin, regarding the ongoing Phase 3 BioMarin hemophilia A gene therapy study, and a serious adverse event deemed, by the Independent Data Safety Monitoring Committee, unrelated to the investigational gene therapy from the phase 1/2 study.

BioMarin's investigational gene therapy for hemophilia A has not been approved for use; clinical trials are ongoing.

Clinical Trial Overview

BioMarin's valoctocogene roxaparvovec, is currently being studied in adults with severe hemophilia A.

On February 4th, 2022, during the European Association for Haemophilia and Allied Disorders (EAHAD) Congress, there was a presentation of the ongoing Phase 3 pivotal study of valoctocogene roxaparvovec, including the most recent data of 2 years or more of follow up for individuals enrolled in the GENEr8-1 study.

The Phase 3 study (named GENEr8-1) is currently being conducted in 13 countries. This study has been fully enrolled since November 2019 with 134 participants who received investigational gene therapy.

The first trial of valoctocogene roxaparvovec, a Phase 1/2 study with 15 participants, was initiated in 2015 and completed enrollment in 2017. These participants are now in long-term follow-up; the safety of study participants is of paramount importance to BioMarin. In November 2021, BioMarin was notified of a serious adverse event of cancer by one of this study's clinical trial investigators. 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.

The participant noticed a lump in his neck that was later diagnosed as salivary gland cancer. He then reported it to the study team. The cancer was completely removed during surgery, and the individual is being closely followed by his personal health care team. Separately, he continues his monitoring associated with the clinical trial.

BioMarin applauds this person's attention to his health and reporting to his physician, while participating in clinical research.

continued

Clinical Trial Overview (continued)

As with any serious adverse event, a committee of experts was brought together to help determine the cause of the cancer 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 (Data Monitoring Committee), as well as other medical and scientific experts. In this case, the event was deemed by the study team as well as external experts to be unrelated to the investigational gene therapy given the available information. The relevant health regulatory authorities were notified. In addition, further analyses are currently being carried out on the cancer tissue which was removed.

All clinical studies with valoctocogene roxaparvovec remain active, including study enrolment.

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.

For additional information:

- For information on BioMarin clinical studies, 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

BioMarin Hemophilia A Clinical Development Program: An Update for the Hemophilia Community

BioMarin is pleased to update the community regarding our ongoing gene therapy clinical trial program in hemophilia A. BioMarin's investigational gene therapy for hemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's valoctocogene roxaparvovec, is currently being studied in adults with severe hemophilia A.

The first Phase 1/2 study was initiated in 2015 and involved 15 individuals and two dose levels. These individuals are now in long-term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is currently being conducted in 13 countries. This study has been fully enrolled since November 2019 with 134 participants who received investigational gene therapy. Participants in the study continue to be closely followed as part of this study.

On January 9th, BioMarin released an update on the Phase 3 study of valoctocogene roxaparvovec, including the most recent topline data based on 2 years or more of follow up for individuals enrolled in the GENEr8-1 study. BioMarin intends to submit to an upcoming medical congress and discuss next steps with Heath Authorities.

BioMarin extends its sincere gratitude to our investigators and the study participants who have helped make this milestone possible.

continued

Regulatory Status:

In the United States, BioMarin intends to submit two-year follow-up safety and efficacy data on all study participants from the Phase 3 GENEr8-1 study to support the benefit/risk assessment of valoctocogene roxaparvovec, as previously requested by the Food and Drug Administration (FDA). Based on these results, BioMarin is planning to meet with FDA to discuss the resubmission of a Biologics License Application (BLA) targeted for the second quarter of 2022, followed by an expected six-month review by the FDA.

Valoctocogene roxaparvovec has received both Regenerative Medicine Advanced Therapy (RMAT) designation and Breakthrough Therapy Designation from FDA, which are intended to expedite development of drugs for serious or life-threatening diseases and conditions. In addition to the RMAT Designation and Breakthrough Therapy Designation, valoctocogene roxaparvovec also has received Orphan Drug Designation from the FDA and EMA for the treatment of severe hemophilia A.

For additional information:

- For information on BioMarin clinical studies, 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

BioMarin Hemophilia A Clinical Development Program: An Update for the Hemophilia Community

BioMarin is pleased to update the community regarding our ongoing gene therapy clinical trial program in hemophilia A. BioMarin's investigational gene therapy for hemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's investigational gene therapy valoctocogene roxaparvovec, is currently being studied in adults with severe hemophilia A.

The first Phase 1/2 study was initiated in 2015 and involved 15 individuals and two dose levels. These individuals are now in long- term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is currently being conducted in 13 countries and is fully enrolled. 134 patients have received investigational gene therapy as part of this study.

On July 19, 2021 BioMarin provided an oral presentation on the ongoing Phase 3 pivotal study of valoctocogene roxaparvovec, including the most recent data of 1 year or more of follow up for individuals enrolled in the GENEr8-1 study. This update was provided at the International Society on Thrombosis and Haemostasis (ISTH) 2021 Virtual Congress.

BioMarin intends to present a five-year update from the Phase 1/2 study during an oral presentation at International Society on Thrombosis and Haemostasis (ISTH) 2021 Virtual Congress on Wednesday, July 21st, 2021.

BioMarin extends its sincere gratitude to all study participants who have helped make this milestone possible.

Regulatory Status:

In the United States, BioMarin plans to submit two-year follow-up safety and efficacy data on all study participants from the GENEr8-1 study to support the benefit/risk assessment of valoctocogene roxaparvovec. BioMarin is targeting a Biologics License Application (BLA) submission in the second quarter of 2022 assuming favorable study results, followed by an expected six-month review procedure by the FDA

In Europe, BioMarin resubmitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) on June 28, 2021. In May 2021, the EMA granted the company's request for accelerated assessment. Accelerated assessment reduces the time frame for the EMA Committee for Medicinal Products for Human Use (CHMP) and Committee for Advanced Therapies (CAT) to review a MAA for an Advanced Therapy Medicinal Product (ATMP). A CHMP opinion is anticipated in the first half of 2022.

For additional information:

- For information on BioMarin clinical studies, visit www.clinicaltrials.gov and type in the study code "BMN 270"
- For inquiries or to provide feedback from advocacy organisations, please contact patientadvocacy@bmrn.com
- Contact BioMarin Medical Information at medinfoeu@bmrn.com

Update for Hemophilia Associations

BioMarin is pleased to update the community regarding our gene therapy clinical trial program in hemophilia A. BioMarin's investigational gene therapy for hemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's investigational gene therapy valoctocogene roxaparvovec, is currently being studied in adults with severe hemophilia A. The first Phase 1/2 study was initiated in 2015 and involved 15 individuals and two dose levels. These individuals are now in long- term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is currently being conducted in 13 countries and is fully enrolled. 134 patients have received investigational gene therapy as part of this study.

On May 19, 2021 BioMarin released a high-level update on the Phase 1 / 2 study of valoctocogene roxaparvovec, including the most recent results based on 5 years of follow up data for individuals receiving the 6E13 vg/kg dose.

BioMarin intends to present more detail on the five-year update from the ongoing Phase 1 / 2 study during an oral presentation at the upcoming International Society on Thrombosis and Haemostasis (ISTH) 2021 Virtual Congress taking place July 17-21.

BioMarin extends its sincere gratitude to all study participants who have helped make this milestone possible.

Regulatory Status

In the United States, BioMarin plans to submit two-year follow-up safety and efficacy data on all study participants from the GENEr8-1 study to support the benefit/risk assessment of valoctocogene roxaparvovec. BioMarin is targeting a Biologics License Application (BLA) submission in the second quarter of 2022 assuming favorable study results, followed by an expected six-month review procedure by the FDA.

In Europe, BioMarin plans to submit a Marketing Authorization Application (MAA) for valoctocogene roxaparvovec for the treatment of severe hemophilia A with one-year results from the Phase 3 GENEr8-1 study to the European Medicines Agency (EMA) in June 2021.

For More 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 1-800-983-4587 or medinfo@bmrn.com

BioMarin Hemophilia A Clinical Development Program: An Update for the Hemophilia Community

BioMarin is committed to updating the community regarding our ongoing gene therapy clinical trial program in hemophilia A.

Clinical Trial Overview

BioMarin's investigational gene therapy valoctocogene roxaparvovec is currently being studied in adults with severe hemophilia A. It has not been approved for use or determined to be safe or effective.

The first Phase 1/2 study was initiated in 2015 and consists of 15 individuals in long- term follow-up, following treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is being conducted in 13 countries; it is fully enrolled with 134 patients having received investigational gene therapy.

Regulatory Status

On 21st November 2019, BioMarin submitted a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for valoctocogene roxaparvovec in adult males with severe hemophilia A. The EMA designated valoctocogene roxaparvovec a Priority Medicines (PRIME) Investigational Product, recognising the potential benefit to address an unmet medical need, while supporting the review of a validated MAA under Accelerated Assessment.

The regulatory review process for new Marketing Authorisations at the EMA follows a pre-determined and specific timeline. The MAA submission included updated 3-year data from BioMarin's Phase 1/2 study in 15 patients and an interim analysis of the initial 16 patients enrolled in the Phase 3 study.

Recently, as part of the MAA review process, BioMarin was asked to provide1-year data on all 134 patients participating in the Phase 3 study. The EMA has not requested any new studies.

Given the depth and breadth of data expected from the Phase 3 results, together with the current regulatory timelines, BioMarin plans to withdraw the current MAA and resubmit the application once the full dataset is available. It is expected that this new submission will be made in the second quarter of 2021.

BioMarin remains committed to our gene therapy programme in Hemophilia A. There are currently five ongoing clinical trials evaluating the safety and efficacy of valoctocogene roxaparvovec.

BioMarin's investigational gene therapy for hemophilia A has not been approved for use.

We are extremely grateful to all study participants for their ongoing and long-term commitment to this clinical program.

For More 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 1-800-983-4587 or medinfo@bmrn.com

BioMarin Hemophilia A Clinical Development Program: An Update for the Hemophilia Community

BioMarin is committed to updating the community regarding our ongoing gene therapy clinical trial program in hemophilia A. BioMarin's investigational gene therapy for hemophilia A is in ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's investigational gene therapy valoctocogene roxaparvovec is currently being studied in adults with severe hemophilia A.

The first Phase 1/2 study was initiated in 2015 and consists of 15 individuals in long- term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is fully enrolled and currently being conducted in 13 countries with 134 patients that have received investigational gene therapy.

Regulatory Status

On December 23, 2019, BioMarin submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for its investigational gene therapy, valoctocogene roxaparvovec, for adults with hemophilia A.

On August 18, 2020, BioMarin received a Complete Response Letter from the FDA. The FDA issues Complete Response Letters to indicate that the review cycle for an application is complete and that the application is not ready for approval in its present form. The FDA did not identify any new safety concerns but recommended that BioMarin complete the Phase 3 Study and submit two-year follow-up safety and efficacy data on all study participants.

BioMarin remains committed to collaborating with the FDA to address points raised during the BLA review and generating additional data to support the FDA's benefit-risk evaluation of valoctocogene roxaparvovec.

The FDA granted valoctocogene roxaparvovec Breakthrough Therapy and orphan drug designations.

The European Medicines Agency (EMA) review of the company's marketing authorization (MAA) for valoctocogene roxaparvovec is ongoing.

(continued)

Regulatory Status (continued)

BioMarin extends sincere gratitude to our investigators and the study participants who have contributed to the investigational study thus far.

A patient's medical team remains the best source of information regarding any health effects of hemophilia A.

For additional information on BioMarin clinical studies:

- 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

Update for Hemophilia Associations

BioMarin is a global pharmaceutical company with more than 20 years of experience in developing medicines for rare genetic conditions.

BioMarin is pleased to update the community regarding our ongoing gene therapy clinical trial program in hemophilia A. BioMarin's investigational gene therapy for hemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

Clinical Trial Overview

BioMarin's investigational gene therapy valoctocogene roxaparvovec, is currently being studied in adults with severe hemophilia A.

The first Phase 1/2 study was initiated in 2015 and involved 15 individuals and two dose levels. These individuals are now in long- term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study (named GENEr8-1) is currently being conducted in 13 countries and is fully enrolled. 134 patients have received investigational gene therapy as part of this study.

On May 31st 2020 BioMarin released an update on the Phase 1 / 2 study of valoctocogene roxaparvovec, including the most recent results based on 4 years of follow up data for individuals receiving the 6E13 vg/kg dose.

BioMarin intends to present a four-year update from the ongoing Phase 2 study in a late breaking oral presentation at World Federation of Hemophilia Virtual Summit on June 17, 2020.

BioMarin extends its sincere gratitude to all study participants who have helped make this milestone possible.

Regulatory Status

The Food and Drug Administration (FDA) is reviewing the biologics license application, under Priority Review, for valoctocogene roxaparvovec with a PDUFA action date of August 21, 2020. The FDA priority review designation is granted to drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of a serious condition.

(continued)

Regulatory Status (continued)

The European Medicines Agency (EMA) validated the Company's Marketing Authorization Application (MAA) for valoctocogene roxaparvovec which has been in review under accelerated assessment since January. Although the MAA remains under accelerated assessment at this time, the Company expects the review procedure to be extended by at least three months due to COVID-19 delays. Further, the Company believes there is a high possibility that the MAA will revert to the standard review procedure, as is the case with most filings that initially receive accelerated assessment. Because of the combination of these events, the Company expects an opinion from the Committee for Medicinal Products for Human Use (CHMP) in late 2020/early 2021.

The company believes that both submissions represent the first time a gene therapy product for any type of hemophilia indication is under review for marketing authorization by health authorities.

No gene therapies for hemophilia have been determined to be safe or effective or approved for use.

For additional information on BioMarin clinical studies:

- 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 toll free at 1-800-983-4587 or medinfo@bmrn.com

Update for North American Hemophilia Associations

Impact of the COVID-19 pandemic

This statement is to provide general information about BioMarin's ongoing clinical trials for its investigational gene therapy (valoctocogene roxaparvovec) in the context of the COVID-19 pandemic.

As more cases of COVID-19 are confirmed, we recognize the increased challenges and concerns faced by participants in the BioMarin Gene Therapy clinical studies. The safety and well-being of patients, healthcare providers, and our communities is paramount as the ongoing COVID-19 pandemic impacts the health and livelihoods of many worldwide.

Many regulatory bodies, health authorities, and government departments have issued directives and guidance to help sponsors safely and appropriately manage clinical trials during this pandemic. BioMarin continues to conduct our trials according to this guidance. BioMarin is in regular contact with and providing study-related guidance to investigators and trial site staff in all countries and to all sites.

The current pandemic and the burden being placed on hospitals is dramatically affecting the way in which many sponsor companies can conduct clinical studies. In many cases, study participants are having difficulty attending their study site for assessments and company study support staff are also experiencing restricted access.

For the BioMarin Gene Therapy Clinical Trial program, where possible, and without putting study participants and site staff at risk, study visits are continuing. Where this is not possible, some parts of sample collection and some assessments are being performed in a manner that is in-line with local, regional, and/or national directives and with the utmost attention paid to maintaining appropriate safety precautions for study participants who may have an alternative option to the usual study visits available to them.

Study participants who are in self-isolation are encouraged to maintain communications remotely with their trial site staff.

This is a rapidly evolving situation and all efforts are being made to continue the BioMarin Gene Therapy Clinical Trial program while remaining acutely aware of the safety of study participants and site staff alike.

We acknowledge and are extremely grateful for all participants and study staff for their contribution and commitment to this program especially during this pandemic.
For any study participant directly affected by the current pandemic, the best source of information about ongoing participation and care is their study doctor and site staff.
Information about more general concerns regarding COVID-19 and hemophilia may be available through patient association websites.

For More Information:

- Visit www.clinicaltrials.gov and type in the study code BMN 270
- Contact BioMarin Medical Information toll free at 1-800-983-4587 or by email at: medinfo@bmrn.com

November 2019

BioMarin Hemophilia A Clinical Development Program: An Update for the Hemophilia Community

BioMarin is pleased to update the community regarding our gene therapy clinical trial program in Hemophilia A.

Clinical Trial Update

BioMarin's investigational gene therapy valoctocogene roxaparvovec, is currently being studied in adults with severe Hemophilia A.

The first Phase 1/2 study was initiated in 2015 and consists of 15 individuals in long- term follow-up, post treatment with valoctocogene roxaparvovec.

The Phase 3 study is currently being conducted in 13 countries and 130 patients have been enrolled and have received investigational gene therapy.

Regulatory Status

The EMA recently granted BioMarin's accelerated assessment of valoctocogene roxaparvovec, for adults with severe Hemophilia A. Additionally, the FDA has granted valoctocogene roxaparvovec Breakthrough Therapy designation. Valoctocogene roxaparvovec has Orphan Drug designation from the Food and Drug Administration (FDA) and the European Medicines Agency (EMA).

BioMarin plans to submit marketing applications in United States and Europe before the end of 2019 which will allow regulators to evaluate the safety and efficacy of valoctocogene roxaparvovec.

BioMarin's investigational gene therapy for Hemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

A patient's medical team remains the best source of information regarding any health effects of hemophilia.

For inquiries from Patient Advocacy Organizations please contact patientadvocacy@bmrn.com. For further information on BioMarin Hemophilia A studies please visit www.clinicaltrials.gov or contact BioMarin Medical Information at medinfo@bmrn.com.

May 2019

BioMarin's valoctocogene roxaparvovec Hemophilia A Clinical Development Program: An Update for the Hemophilia Community

BioMarin is pleased to update the community regarding our gene therapy clinical trial program in hemophilia A. BioMarin's investigational gene therapy for hemophilia A has not been approved for use; it is in ongoing clinical trials evaluating its safety and efficacy.

Ongoing Clinical Studies

BioMarin's valoctocogene roxaparvovec, previously known as BMN 270, is currently being investigated in adults with severe hemophilia A. There are six studies that are part of the program.

- The first Phase 1/2 study was initiated in 2015 and consists of 15 individuals in long-term follow-up, post treatment with valoctocogene roxaparvovec
- A global seroprevalence study seeks to determine the frequency of individuals who have a pre-existing antibody against different serotypes of adeno-associated virus (AAV)
- A non-interventional study seeks to evaluate the rates of bleeding episodes and FVIII use, as well as health-related quality of life, in participants receiving FVIII prophylaxis
- The Phase 3 program consists of two global studies (named GENEr8-1 and GENEr8-2) to evaluate two dose levels, 6E13 and 4E13 vg/kg, respectively of valoctocogene roxaparvovec
    - The GENEr8-1 study is currently being investigated in 12 countries to include 130 participants and is expected to be fully enrolled in the third quarter of 2019
- In addition, a Phase 1/2 study evaluating the safety of valoctocogene roxaparvovec in participants who have a pre-existing antibody against AAV serotype 5, the vector used in valoctocogene roxaparvovec, is open for enrollment at a limited number of sites in the UK

On May 28, 2019, BioMarin released an update on the Phase 1/2 study of valoctocogene roxaparvovec**,** including the most recent results based on 3 years of follow-up data for individuals who received the 6E13 vg/kg dose. Additionally our BioMarin medical team will inform Principal Investigators and Key Opinion Leaders within the community, including those that represent your organization, about this development.

Regulatory Status

The U.S. Food and Drug Administration (FDA) has granted valoctocogene roxaparvovec Breakthrough Therapy Designation, and it has also been given access to the Priority Medicines (PRIME) regulatory initiative from the European Medicines Agency (EMA). Valoctocogene roxaparvovec has previously received orphan drug designation from the FDA and European Commission. This designation is intended to facilitate and expedite development and review of new therapies for patients with serious conditions for which there is still unmet need, allowing them to benefit as early as possible.

For general inquiries from advocacy organizations, please contact patientadvocacy@bmrn.com. For further information on BioMarin clinical studies, please visit www.clinicaltrials.gov or contact BioMarin Medical Information at medinfo@bmrn.com or by phone: Toll Free 1-800-983- 4587; Local (651) 523-0310. Your medical team remains the best source of information for you about any health effects of hemophilia A.

SEPTEMBER 2018

BioMarin BMN 270 Hemophilia A Program Update

On September 6, 2018, BioMarin presented an update to our investigational therapy program for Hemophilia A at the Citi Biotech Conference. Being transparent and communicating updates on our clinical program with the Advocacy community is very important to us. Equally as important is fielding any questions you may have on these announcements. For this reason, our BioMarin medical team has informed all of our Principal Investigators and Key Opinion Leaders within the community, including NHF, HFA and WFH (Dr Pipe and Glenn Pierce); EHC (Flora Peyvandi). Should you have any scientific questions, please feel free to reach out to them or, should you wish to schedule a call with BioMarin medical personnel, we can arrange that as well.

Key Program updates:

BMRN Positioning for Accelerated Approval

BioMarin plans to file for accelerated approval for its investigational gene therapy for hemophilia, valoctocogene roxaparvovec, in H2 2019 (~1 year ahead of our previous H2 2020 expectation). The company arrived at this decision based on careful evaluation of the recent hemophilia gene therapy FDA guidance.

Valrox Protocol Updates

BioMarin expects to dose all patients in GENEr8-1 (dose 6E13 vg/kg) by Q2 2019, an adjustment from previously disclosed Q1 2019. The increase in enrollment numbers to 130 from 70 and the global nature of the clinical trials are the reasons for this adjustment. In addition, BioMarin is slightly restricting the enrollment criteria for the GENEr8 studies, to match the enrollment criteria from the Phase 2. Moving forward, the trial will not include patients that have HIV or mild liver disease. This change was the result of two patients having higher liver function test (LFT) elevations than what were seen in the Phase 2. The Valrox registration program continues to manage LFT elevations on demand and there is no inclusion or addition of steroid prophylaxis to the protocol as a result. Ultimately, these LFT elevations aren't unexpected given data across other gene therapy studies and we highlight that both patients are asymptomatic and the LFT elevations are resolving.

For further information on BioMarin clinical studies, please visit www.clinicaltrials.gov or contact BioMarin Medical Information at medinfo@bmrn.com or by phone: Toll Free 1-800-983- 4587; Local (651) 523-0310.

In closing, we would like to remind you of our commitment to transparency. Should you have any questions, please do not hesitate to reach out to us and we would be happy to field them.

BIOMARIN

May 2018

BioMarin BMN 270 Hemophilia A Program Update

BioMarin is continuing clinical development of an investigational gene therapy for the treatment of hemophilia A, known as valoctocogene roxaparvovec. The therapy is designed to use a carrier (known as a "vector") to deliver a functional Factor VIII (FVIII) gene to a patient's cells. Research is ongoing to determine whether once inside cells, the body can use this new DNA to produce normal functioning FVIII protein. The safety and efficacy of valoctocogene roxaparvovec has not been established.

Phase 1/2 Study update (BMN 270-201)

On May 22, 2018, BioMarin presented an update on the Phase 1/2 study of valoctocogene roxaparvovec. The most recent results based on 2 years of data were presented at the World Federation of Hemophilia (WFH) Meeting by John Pasi M.B., Ch.B., Ph.D from Barts and the London School of Medicine and Dentistry, who is the primary investigator for this Phase 1/2 study.

Phase 3 Studies (GENEr8-1 and GENEr8-2)

In December of 2017, we opened two global Phase 3 studies for valoctocogene roxaparvovec. GENEr8-1 will evaluate a 6e13 vg/kg dose and GENEr8-2 will evaluate a 4e13 vg/kg dose. Both Phase 3 GENEr8 studies will assess the efficacy and safety of valoctocogene roxaparvovec in men over 18 with severe hemophilia A.

Both GENEr8-1 and GENEr8-2 have enrolled patients and are actively recruiting. For further information on our Phase 3 studies, please visit www.clinicaltrials.gov, GENEr8-1 study number: **NCT03370913** and GENEr8-2 study number: **NCT03392974.**

Gene Therapy Manufacturing Facility Recognized with Industry Award

We have previously shared that BioMarin constructed the largest gene therapy manufacturing facility in the world, which is located in Novato, California. We are proud to announce that on Tuesday, March 20th, during the 2018 Europe Annual Conference in Rome, Italy, the International Society for Pharmaceutical Engineering (ISPE) selected the company's gene therapy manufacturing facility as the 2018 Facility of the Year Category Winner for Project Execution. With the company's hemophilia A investigational treatment valoctocogene roxaparvovec in global Phase 3 development and a need to produce material for the clinical studies and potentially for commercial demand, BioMarin converted an office building into an 18,000 square foot gene therapy facility in less than a year. As a result of this new gene therapy manufacturing capability, the company is well positioned with the necessary resources and capacity to continue with the development program for valoctocogene roxaparvovec in severe hemophilia A.

Regulatory Status

The U.S. Food and Drug Administration (FDA) has granted valoctocogene roxaparvovec Breakthrough Therapy Designation and it has also been given access to the Priority Medicines (PRIME) regulatory initiative from the European Medicines Agency (EMA). Valoctocogene

roxaparvovec has previously received orphan drug designation from the U.S. Food and Drug Administration (FDA) and European Commission. This designation is intended to facilitate and expedite development and review of new therapies for patients with serious conditions for which there is still unmet need allowing them to benefit as early as possible.

For inquiries from advocacy organizations, please contact patientadvocacy@bmrn.com. For further information on future BioMarin clinical studies, please visit www.clinicaltrials.gov or contact BioMarin Medical Information at medinfo@bmrn.com or by phone: Toll Free 1-800-983-4587; Local (651) 523-0310. Your medical team remains the best source of information for you about any health effects of hemophilia A.