Update for Achondroplasia Associations

Clinical Trial Update

111-209: Phase 2 Study for Children at Risk of Requiring Cervicomedullary Decompression Surgery

111-209 is open for enrollment. It is designed to study vosoritide's safety and effectiveness in children who are at risk of needing cervicomedullary decompression surgery.

- 20 children, ages 0 to 12 months
- For 2 years, half the participants will receive standard of care and half will receive standard care plus the investigational medicine
- After 2 years, all participants will receive the investigational medicine in an extension study lasting for an additional 3 years
- The study is open-label, which means that participants and the doctors know if the participant is receiving the investigational medicine
- Locations in Australia and the United Kingdom (participants must live near the trial location)

For more information on 111-209, please visit:
https://clinicaltrials.gov/ct2/show/NCT04554940

Publications and Presentations

111-301: Phase 3 Clinical Study

The most recent results from BMN 111-301, the phase 3 clinical study, have been shared recently.

- *The Lancet* published a peer-reviewed article, "Once-Daily, Subcutaneous Vosoritide Therapy in Children with Achondroplasia." Authors included Dr. Ravi Savarirayan, MD, of Murdoch Children's Research Institute, and Dr. Melita Irving, MD, of Evelina Children's Hospital.
- Presentations were given at the American Society of Bone and Mineral Research (ASBMR) 2020 Virtual Congress and the Pediatric Endocrine Society (PES) Symposium.

For more information on 111-301, please visit:
https://clinicaltrials.gov/ct2/show/NCT03197766

Update for Achondroplasia Associations

For additional information on BioMarin clinical studies:

- Visit www.clinicaltrials.gov and type in the study code "BMN 111"
- 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 Achondroplasia Associations

New Drug Application Submitted for Vosoritide

BioMarin has announced the submission of a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for vosoritide, an investigational medicine for achondroplasia. An investigational medicine is a drug that is being studied to see if it is safe and effective to treat a particular condition. Vosoritide has not been approved for use or determined to be safe or effective. BioMarin has submitted data that will now be reviewed by regulators who decide whether to approve the drug to be marketed in the United States.

Over 500 children with achondroplasia from 8 countries have enrolled in BioMarin clinical studies. These children and their families have been crucial to the ongoing research into achondroplasia and the safety and efficacy of vosoritide. We are incredibly grateful to everyone who participates in our clinical studies.

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Update for Achondroplasia Associations

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

BioMarin has announced the submission of a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for vosoritide, an investigational medicine for achondroplasia. An investigational medicine is a drug that is being studied to see if it is safe and effective to treat a particular condition. Vosoritide has not been approved for use or determined to be safe or effective. BioMarin has submitted data that will now be reviewed by regulators who will decide whether to approve the drug to be marketed in Europe.

Over 500 children with achondroplasia from 8 countries have enrolled in BioMarin clinical studies. These children and their families have been crucial to the ongoing research into achondroplasia and the safety and efficacy of vosoritide. We are incredibly grateful to everyone who participates in our clinical studies.

Ongoing Studies, Enrollment Open

111-901: an observational study

111-901 is open for enrollment by invitation. The study does not involve an investigational medicine. Data from this study will be compared to data from BioMarin studies that treat participants with vosoritide to better understand the investigational medicine's effects.

For more information on 111-901, please visit:
https://clinicaltrials.gov/ct2/show/NCT01603095

111–206 and 111-208: clinical studies

111–206 and 111–208 will be open for enrollment through 2020. These clinical studies are designed to study vosoritide's safety and effect on participants' growth, need for surgeries, bone health and quality of life.

- Ages 0 to 5 years old, in three age groups (0 to 6 months, 6 months to 2 years, 2 to 5 years)
- Enrollment into the 111-206 study is currently open for newborns around 3 months old and younger
- For one year, half of the participants are on placebo (inactive substance) and half are on the investigational medicine
- During the first year, the study is blinded which means the participants and the doctors do not know whether the participant received a placebo or not
- After one year, all participants will receive the investigational medicine in the extension study BMN 111-208

For more information on 111-206, please visit:
https://clinicaltrials.gov/ct2/show/NCT03583697
For more information on 111-208, please visit:
https://clinicaltrials.gov/ct2/show/NCT03989947

111-501 and 111-502: observational studies on lifetime impact

111-501 (LIAISE) is closed for enrollment, and 111-502 (LISA) is open for enrollment until December 2020. The study will take less than a day and does not involve an investigational medicine. These studies aim to better understand what it is like to live with achondroplasia by finding health trends from childhood through to adulthood. This information may eventually result in better care.

For more information on 111-501 (LIAISE), please visit:
https://clinicaltrials.gov/ct2/show/NCT03449368
For more information on 111-502 (LISA), please visit:
https://clinicaltrials.gov/ct2/show/NCT03872531

Ongoing Studies, Enrollment Complete

111-301 and 111-302: clinical studies

Enrollment for the phase 3 safety and efficacy study 111-301 is now complete, and BioMarin has announced primary endpoint results. Currently all participants are being followed in the long-term extension study called 111-302.

For more information on 111-301, please visit:
https://clinicaltrials.gov/show/NCT03197766
For more information on 111-302, please visit:
https://clinicaltrials.gov/ct2/show/NCT03424018

111-202 and 111-205: dose finding and extension studies

BioMarin has completed the dose evaluation study 111-202 and is currently following all participants in the long-term extension study called 111-205.

For more information on 111-202, please visit:
https://clinicaltrials.gov/ct2/show/NCT02055157
For more information on 111-205, please visit:
https://clinicaltrials.gov/ct2/show/NCT02724228

Publications and Events

Webinar

On June 4, BioMarin sponsored an educational webinar hosted by the MAGIC Foundation that discussed achondroplasia and shared an overview of the clinical program for vosoritide. A recording of the webinar is now available to view at: https://bit.ly/3jTweLF

In the Know About Achondroplasia

A new website for caregivers is now live in the United States. The website provides information about achondroplasia, its management, and resources that are available to caregivers. To learn more, please visit:
https://www.achondroplasia.com/

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Update for Achondroplasia Associations

Impact of the COVID-19 pandemic

We are providing this statement to provide general information about the BioMarin clinical development program for achondroplasia in the context of the COVID-19 (Coronavirus) pandemic.

As more cases of COVID-19 are confirmed, we recognize the increased challenges and concerns faced by participants in the BioMarin clinical studies. The safety and well-being of study participants, 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 now issued directives and guidance to help sponsors safely and appropriately manage clinical studies during this pandemic. BioMarin continues to conduct our studies according to this guidance. BioMarin plans regulatory submissions of Vosoritide in 3Q 2020 in both US and Europe. Those regulatory submissions will be reviewed by regulators over many months to allow them to evaluate Vosoritide's safety and efficacy in order to determine whether it can be made available.

BioMarin is in regular contact with investigators and study site staff at sites in all countries and is providing guidance to local study teams regarding study conduct. We acknowledge and are extremely grateful for all study participants and staff for their contribution and commitment to this program, especially during this pandemic.

> For more information: Individuals enrolled in any BioMarin clinical study should contact their trial site staff for the latest updates and to answer any specific questions they might have.

This is a rapidly evolving situation and all efforts are being made to continue the BioMarin clinical program while remaining acutely aware of the safety for all individuals. We are committed to partnering with the community to continually reassess, find solutions and provide necessary updates.

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