



July 2019

## ACHONDROPLASIA CLINICAL DEVELOPMENT PROGRAM

### An Update for US Associations

BioMarin is a global pharmaceutical company that has over 20 years of experience in medicine development for rare genetic conditions. The investigational medicine for achondroplasia BMN 111, known as vosoritide, is currently in the advanced stages of the medicine development process. Over the last five years more than 150 children with achondroplasia have enrolled in BioMarin clinical studies across eight countries.

The safety and effectiveness of vosoritide is currently being investigated in ongoing clinical studies and has not been established. Vosoritide has not been approved for use outside of a clinical study by any country. At the conclusion of the clinical studies, BioMarin can apply for approval of vosoritide and authorities will evaluate the safety and effectiveness data and determine whether it can be made available in a given country.

### Recent Publication

The New England Journal of Medicine (NEJM) published a peer-reviewed article based on the most recent results from the ongoing Phase 2 dose-finding and extension study. The article, "*C-type Natriuretic Peptide Analogue Therapy in Children with Achondroplasia*," discusses the 42-month findings.

### BMN 111-901:

#### Observational Study

A study that observes how a condition changes over time is often called an observational study or a non-interventional study. Participants do not receive an investigational medicine. This study aims to provide a comparison for effects that may be seen in studies that include treatment with the investigational medicine vosoritide.

- Opened April 2012
- Participants from birth to age 18
- Aimed to enroll an equal number of boys and girls
- Measurements include growth and health related quality of life (e.g. major illnesses and surgeries)
- Locations in Australia, Germany, Japan, Spain, Turkey, the United Kingdom, and the United States

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

### BMN 111-202 and BMN 111-205:

#### Dose finding and Extension Studies

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

- 35 participants, aged 5 to 14 years
- All participants are receiving the investigational medicine vosoritide



- Locations in Australia, France, the United Kingdom, and the United States

For more information on BMN 111-202, please visit: <https://clinicaltrials.gov/ct2/show/NCT02055157>

For more information on BMN 111-205, please visit: <https://clinicaltrials.gov/show/NCT02724228>

## **BMN 111–206 and BMN-208: Phase 2 Infant and Toddler Studies**

To evaluate the effect of vosoritide in children between the ages of 0 to 5 years.

- Approximately 70 children split into three groups
  - 2 to 5 years age group has completed enrollment
  - 6 months to 2 years age group continues global enrollment
  - 0 to 6 months age group is predicted to begin enrollment later this year
- The study is designed to assess the safety of vosoritide and effect on
  - Growth – measured as annualized growth velocity (AVG) or rate of growth
- In addition measurements include effects on
  - Sleep apnea
  - Requirement for surgeries
  - Growth of the skeleton including
    - Foramen magnum (in relation to health of the spinal cord)
    - Base of the skull (in relation to causes of sleep and ear health)
    - Spine (in relation to back pain and spinal cord compression)
  - Proportionality of the body segments and limbs
    - Including effects on leg bowing, elbow extension, arm span
  - Bone health
  - Hip function
  - Joint pain
  - Health-related quality of life
  - Health-related functional assessments as they relate to day to day activities
- For one year, half of the participants are on placebo (inactive medicine) and half are on the investigational medicine, allowing for the two groups to be compared
- After one year, all participants will receive the investigational medicine in a long-term extension study called BMN 111-208
- The study is blinded which means the participants and the doctors do not know whether the participant received a placebo or not
- Participants must live in the country conducting the study
- Locations in Australia, Japan, the United Kingdom and the United States

For more information on BMN 111-206, please visit: <https://clinicaltrials.gov/ct2/show/NCT03583697>

For more information on BMN 111-208, please visit: <https://clinicaltrials.gov/ct2/show/NCT03989947>

## **BMN 111-301 and BMN 111-302: Phase 3 Studies**

Enrollment of this study is now complete. Top line results will be available at the end of 2019. Additional study results will be available in the beginning of 2020.

Phase 3 studies can be the last stage of clinical development before manufacturers submit their data to authorities for evaluation of safety and efficacy.

- Participants aged between 5 to 18 years
- The study is designed to assess the safety of vosoritide and effect on
  - Growth – measured as annualized growth velocity (AVG) or rate of growth
- In addition, measurements include effects on
  - Sleep quality
  - Major illnesses
  - Number of surgeries needed (for example: ear tubes)
  - Health related quality of life
  - Health related functional assessments as they relate to day to day activities
  - Proportionality of the body segments and limbs
    - Including effects on leg bowing, elbow extension, arm span
- For one year, half of the participants are on placebo (inactive medicine) and half are on the investigational medicine, allowing for the two groups to be compared
- After one year, all participants will receive the investigational medicine in a long-term extension study called BMN 111-302
- The study is blinded which means the participants and the doctors do not know whether the participant received a placebo or not
- Participants must live in the country conducting the study
- Locations in Australia, Germany, Japan, Spain, Turkey, the United Kingdom and the United States.

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

For more information on BMN 111-302, please visit: <https://clinicaltrials.gov/ct2/show/NCT03424018>

## **BMN 111-501 and 111-502: Observational Studies on Lifetime Impact**

Identifying health trends that occur from childhood through to adulthood may result in better care. The following studies aim to better understand what it is like to live with achondroplasia. Information will be collected from past medical visits (for example: number and types of surgeries).

### *Lifetime Impact of Achondroplasia Study in Europe (LIAISE)*

- Open to 300 participants ages 5 to 70 years
- Review of at least five years of past medical information
- Locations in Germany, Italy, Spain and Sweden
- Denmark and Austria expected to open later this year

### *Lifetime Impact Study for Achondroplasia (LISA)*

- Open to 175 participants ages 3 years and older
- Review of at least three years of past medical information
- Locations in Argentina, Colombia and Brazil

There is no need to travel to the hospital or to change doctors. To participate, individuals living with achondroplasia or their caregivers would provide medical records and complete a questionnaire. The



questionnaire takes approximately one hour to complete.

For more information on LIAISE, please visit: <https://clinicaltrials.gov/ct2/show/NCT03449368>

For more information on LISA, please visit: <https://clinicaltrials.gov/ct2/show/NCT03872531>

*For additional information on BioMarin clinical studies:*

- Visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and type the study code BMN 111
- For inquiries or to provide feedback from advocacy organizations, please contact [patientadvocacy@bmrn.com](mailto:patientadvocacy@bmrn.com)
- Contact BioMarin Medical Information toll free at 1-800-983-4587, or [medinfo@bmrn.com](mailto:medinfo@bmrn.com)