November 2018

ACHONDROPLASIA CLINICAL DEVELOPMENT PROGRAMME

An Update for European Associations

BioMarin is a global pharmaceutical company that has 20 years of experience in medicine development for rare genetic conditions. BioMarin's investigational medicine for achondroplasia, BMN 111, is currently in the advanced stages of the medicine development process, also known as phase 3 clinical studies.

The safety and effectiveness of BMN 111 is currently being investigated in ongoing clinical studies and has not been established. BMN 111 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 BMN 111 and authorities will evaluate the safety and effectiveness data and determine whether it can be marketed in a given country.

The study sites listed below require participants to live in the country conducting the study.

Communication is very important to us, please contact us if you have any additional questions or want to provide feedback.

- *For additional information on BioMarin clinical studies:*
  - *Visit www.clinicaltrials.gov and type the study code BMN111*
  - *Email BioMarin Medical Information at medinfoeu@bmrn.com or Patient Advocacy at patientadvocacy@bmrn.com*
  - *Call BioMarin Medical Information at Toll Free 00900-742-46627*

BMN 111-901:

Observational study to collect baseline information

A study that observes how a condition changes over time is often called an observational study or a non-interventional study because participants do not receive an investigational medicine. These studies provide a comparison for effects that may be seen in a clinical study with an investigational medicine.

Since April 2012, the observational study BMN 111-901 has been collecting information to better understand and document the impact of achondroplasia.

- Open to individuals from birth to age 18
- Aims to enrol 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: https://clinicaltrials.gov/ct2/show/NCT01603095

BMN 111-202 and BMN 111-205:
Phase 2 Studies to evaluate safety, tolerability, and efficacy

BioMarin has completed the dose evaluation study BMN 111-202 and is currently following all participants in the BMN 111-205 extension study. All participants in this study are receiving BMN 111.

- Locations in Australia, France, the United Kingdom and the United States
- Data from these studies were recently presented at both the European Society for Paediatric Endocrinology (ESPE) and The Japanese Society for Pediatric Endocrinology (JSPE) meetings

For more information on BMN 111-202:
https://clinicaltrials.gov/ct2/show/NCT02055157

For more information on BMN 111-205:
https://clinicaltrials.gov/show/NCT02724228

BMN 111–206:
Phase 2 Infant and Toddler Study to evaluate safety and efficacy

The infant and toddler study began in May 2018.

- Ages 0 to 5 years old in three age groups
  - 2 to 5 years
  - 6 months to 2 years
  - 0 to 6 months
- The primary objectives of the BMN 111-206 study are to evaluate safety and growth
- Secondary outcomes include measurements of growth and health including bone health, hip function, and joint pain
- For one year, half of the participants are on placebo (inactive substance) and half are on the investigational medicine
- After one year, all participants will receive the investigational medicine in an extension study
- 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 while receiving investigational medicine
- Participants must first be enrolled in the observational study (BMN 111-901) before they can be screened to participate in the infant and toddler 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

BMN 111-301 and BMN 111-302:
Phase 3 Studies to evaluate the efficacy and safety

Phase 3 studies are the last stage of development. Enrolment of the phase 3 BMN 111-301 study is now complete.

- Ages between 5 to 18 years old
- The primary purpose of the BMN 111-301 study is to assess whether BMN 111 can help children grow at a faster rate compared to placebo over a period of 1 year (annualised growth velocity or AGV)
- Secondary outcomes include measurements of safety and health through evaluating sleep quality, major illnesses, surgeries needed, health related quality of life and change in body proportions
- For one year, half of the participants are on placebo (inactive substance) and half are on the investigational medicine
- After one year, all participants will receive the investigational medicine in the extension study BMN 111-302
- This study is blinded as well

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:
Lifetime Impact of Achondroplasia Study in Europe known as LIAISE

The LIAISE study is gathering information about:

- Types of clinical and medical interventions, such as the number of doctor visits
- Individuals' and caregivers' quality of life
- Impact on education, employment and social life

Participation in this study involves completing a questionnaire and consenting to the review of at least five years of historical clinical data.

- Open to 300 participants ages 5 to 70 years
- Caregivers may complete the questionnaire if the individual living with achondroplasia is under 18 years of age
- Locations in Germany, Italy, Spain, Denmark and Sweden

For more information, on LIAISE, please visit:
https://clinicaltrials.gov/ct2/show/NCT03449368?term=NCT03449368&rank=1