November 2017

BIOMARIN ACHONDROPLASIA CLINICAL DEVELOPMENT PROGRAMME

An Update for Associations and Families

BioMarin Pharmaceutical Inc. (BioMarin) is a global biotechnology company that has two decades of experience in addressing the complex needs of people, often children, with rare diseases. We are focused on families and children affected by the conditions in which we work and aim to communicate with the communities in which we serve on a regular basis. As such, the current status of the achondroplasia clinical programme is described in the document below. BioMarin's investigational therapy for achondroplasia, BMN 111, is currently under investigation and has not been approved for use in any country.

111-901:

A multinational observational trial open from birth to 17 years of age. The ongoing observational trial is collecting growth measurements, health related quality of life scores and other details including associated symptoms, major illnesses and surgeries for up to 7 years. This baseline information can then be compared to information from BioMarin's trial that includes an investigational therapy (both for individual children and for all children in total). The trial aims to enroll an equal number of boys and girls and has been ongoing since April of 2012; therefore, some children have been in the trial for several years. In this trial, participants do not receive the investigational therapy.

This trial is ongoing in many countries, including the US, Australia, France, Germany, Spain, Turkey and the UK. For more detailed eligibility criteria and current information about the sites, please visit: https://clinicaltrials.gov/show/NCT01603095

111-202:

An open-label dose-escalation study of BioMarin's investigational therapy, now complete. The term open-label means that both the clinical team and participant know which treatment is being administered. Approximately 30 participants between the ages of 5 to 14 years of age received one of three different dosing regimens of BMN 111. This trial was held in the US, France, Australia and the UK. For additional information please visit: https://clinicaltrials.gov/ct2/show/NCT02055157

111-205:

An extension study for participants who have completed two years of treatment in the 111-202 study. The primary objective is to evaluate the long-term safety and tolerability of daily subcutaneous injections of BMN 111, BioMarin's investigational therapy for achondroplasia. This trial has been fully enrolled as of October 2017. For more information please visit:

https://clinicaltrials.gov/show/NCT02724228

111-301:

The third ongoing trial is our Phase 3, placebo-controlled trial. This trial is open for patient ages 5 to 17 years of age and includes approximately 110 participants. In this trial, participants have a randomized and equal chance of receiving either placebo or BMN 111. The primary outcome of the trial is to evaluate change in the rate of growth or change in height. Secondary outcomes include measurements of health through evaluating health related quality of life scores, other associated symptoms, sleep quality as well as major illnesses and surgeries. This trial lasts for 52 weeks and participants will have to have to complete a minimum of 6 months in the observational trial (111-901) before they can be screened for the Phase 3 (111-301) trial. Participants on placebo can receive the investigational therapy after the one year trial period is complete. For more information, please visit: https://clinicaltrials.gov/show/NCT03197766

111-501:

The Lifetime Impact of Achondroplasia Study in Europe (LIAISE) is an observational study looking at the impact on quality of life, healthcare resource use, clinical, socio-economic and psychosocial state of individuals living with achondroplasia. Most of the studies performed in the past have only looked at children living with achondroplasia, however, we believe it is important to understand the lifetime impact of the condition. This study is recruiting up to 300 participants between 5 and 70 years of age and will be opening in the following countries between now and early 2018: Germany, Spain, Italy, Sweden and Denmark. Participation in the study will include a 5 year review of historical clinical data as well as data obtained using questionnaires.

In addition to the studies listed above, BioMarin is planning a separate Phase 2 study evaluating the effect of BMN 111 in infants and toddlers. More information regarding this study will be available in early 2018.

Please know that BioMarin values your experience and knowledge of achondroplasia. For 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 medinfoeu@bmrn.com or by phone: Toll Free: 00800 742 46627