

# BioMarin Plans Regulatory Submissions for Marketing Authorization of Vosoritide to Treat Children with Achondroplasia in 3Q 2020 in both US and Europe

**If approved, vosoritide would be the first medicine for the treatment of Achondroplasia in the US and EU**

SAN RAFAEL, Calif., April 6, 2020 [/PRNewswire/](#) -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that based on recent meetings with health authorities in the US and Europe, the Company plans to submit marketing applications to the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in the third quarter of 2020 for vosoritide. Vosoritide is an investigational, once daily injection analog of C-type Natriuretic Peptide (CNP) for achondroplasia, the most common form of disproportionate short stature in humans.

The marketing applications are based on the outcomes from the randomized, double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of vosoritide, announced in Dec 2019, and further supported by the long-term safety and efficacy from the Phase 2 study, ongoing extension studies, and extensive natural history data. If approved, vosoritide would be the first medicine for the treatment of Achondroplasia in the US and Europe.



"We have worked with the regulatory authorities throughout the design and development of our clinical program and look forward to the ongoing interactions in the evaluation of the safety and efficacy of vosoritide in children with achondroplasia," said Hank Fuchs, M.D., President Worldwide Research and Development at BioMarin. "We believe that we have a strong data package that combines the gold standard of a randomized, double-blind, placebo-controlled Phase 3 study with the long-term results in the Phase 2 open label study and extensive contemporaneous natural history data to evaluate durability. We are grateful to the children and families who have participated in these studies and are contributing to the greater body of scientific data on a potential treatment for achondroplasia."

"Vosoritide is the first potential pharmacological treatment for the underlying cause of achondroplasia. It could be a medical breakthrough in providing physicians with a new tool to treat individuals with achondroplasia," said John A. Phillips, III, M.D., Vanderbilt University Medical Center (David T Karzon Professor of Pediatrics) and investigator for the vosoritide clinical program. "To have such a possible treatment for achondroplasia on the horizon, where none existed before is significant progress."

"We are making great strides in understanding the biology of skeletal dysplasia and getting closer to a potential treatment," said Klaus Mohnike, Professor of Paediatrics at Magdeburg University Hospital in Germany and investigator for the vosoritide clinical program. "I am looking forward to therapeutic interventions that go beyond treating symptoms and have the potential to make a lasting difference for those affected children."

Vosoritide has received orphan drug designation from the FDA and EMA for the treatment of achondroplasia. The Orphan Drug Designation program is intended to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions.

## **Description of Phase 3 Study**

The global Phase 3 study was a randomized, double-blind, placebo-controlled study of vosoritide in 121 children with achondroplasia aged 5 to 14 for 52 weeks. (The enrollment age criteria were 5 to 18 per the study protocol). Vosoritide is being tested in children whose growth plates are still open. This is approximately 25% of people with achondroplasia. Children in this study have completed a minimum six-month baseline study to determine their baseline growth velocity prior to entering the Phase 3 study. The primary endpoint of the study was the change in growth velocity from baseline over one year in children treated with vosoritide compared to placebo. A wide range of secondary and exploratory endpoints included anthropometric measures such as height Z-score, body and limb proportionality and joint geometry; biochemical, biomarker and radiological assessments of bone growth and health; and evaluations of health-related quality of life (HRQoL), developmental status, and functional independence. These additional endpoints address the overall impact vosoritide has on achondroplasia and continue to be evaluated in an ongoing open-label extension study where all subjects receive active treatment.

## Description of Phase 2 Dose Finding Study

The primary objectives of the open-label, sequential cohort, dose-finding study were to evaluate the safety and tolerability of daily subcutaneous vosoritide and to determine the dose to carry forward to Phase 3. Secondary objectives were to evaluate the effects of vosoritide on change from pre-treatment baseline in annualized growth velocity (cm/year), height Z-scores, and body segment proportionality, the vosoritide pharmacokinetic (PK) profile, and biomarkers of vosoritide activity, and endochondral ossification. All children who completed the 24-month dose finding study were then eligible to continue long term follow up in the ongoing extension study which provides long term evidence of efficacy, durability of effect and safety.

## About Achondroplasia

Achondroplasia, the most common form of disproportionate short stature in humans, is characterized by slowing of endochondral ossification, which results in disproportionate short stature and disordered architecture in the long bones, spine, face and base of the skull. This condition is caused by a mutation in the fibroblast growth factor receptor 3 gene (*FGFR3*), a negative regulator of bone growth. Beyond disproportionate short stature, people with achondroplasia can experience serious health complications, including foramen magnum compression, sleep apnea, bowed legs, mid-face hypoplasia, permanent sway of the lower back, spinal stenosis and recurrent ear infections. Some of these complications can result in the need for invasive surgeries such as spinal cord decompression and straightening of bowed legs. In addition, studies show increased mortality at every age.

More than 80% of children with achondroplasia have parents of average stature and have the condition as the result of a spontaneous gene mutation. The worldwide incidence rate of achondroplasia is about one in 25,000 live births. Vosoritide is being tested in children whose growth plates are still "open," typically those under 18 years of age. This is approximately 25% of people with achondroplasia. In the U.S., Europe, Latin America, the Middle East, and most of Asia Pacific, there are currently no licensed medicines for achondroplasia.

## About BioMarin

BioMarin is a global biotechnology company that develops and commercializes innovative therapies for patients with serious and life-threatening rare genetic diseases. The company's portfolio consists of six commercialized products and multiple clinical and pre-clinical product candidates. For additional information, please visit [www.biomin.com](http://www.biomin.com). Information on such website is not incorporated by reference into this press release.

## Forward-Looking Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: BioMarin's vosoritide development program generally and specifically about the Company's planned submissions for marketing applications in the U.S. to the FDA and in Europe to the EMA, the strength of the data package to be submitted to regulatory authorities, the continued clinical development of vosoritide and the timing and conduct of such clinical program; the possible results of such studies, and the timing of the submissions of marketing applications to health authorities in the U.S. and Europe. These forward-looking statements are predictions and involve risks and uncertainties such that actual results may differ materially from these statements. These risks and uncertainties include, among others: final analysis of the Phase 3 data, results and timing of current and planned preclinical studies and clinical trials of vosoritide; our ability to successfully manufacture vosoritide; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities concerning vosoritide; and those other risks and uncertainties detailed from time to time under the caption "Risk Factors" and elsewhere in the BioMarin's Securities and Exchange Commission (SEC) filings, including, without limitation, BioMarin's Quarterly Report on Form 10-K for the year ended December 31, 2019, and future SEC filings and reports by BioMarin. BioMarin undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

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