## BioMarin Completes Full Enrollment in Phase 2 Study of Vosoritide for Treatment of Infants and Young Children with Achondroplasia

***Topline data expected to be available in mid-2022***

SAN RAFAEL, Calif., March 3, 2021 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ:BMRN) announced today that the company has completed full enrollment in a global Phase 2 randomized, placebo-controlled study of vosoritide, an investigational, once daily injection analog of C-type Natriuretic Peptide (CNP) for children with achondroplasia, the most common form of disproportionate short stature in humans. The 52-week study consists of approximately 70 infants and young children with achondroplasia, aged zero to less than five years old (60 months). The study will be followed by a subsequent open-label extension trial where all children receive active treatment. Children in this study will have completed a minimum three- or six-month baseline study to determine their respective baseline growth prior to entering the Phase 2 study. The objectives of the study are to evaluate safety, tolerability, and the effect of vosoritide on growth. The company also plans to augment the height data with assessments including proportionality, functionality, quality of life, sleep apnea, and foramen magnum dimension, as well as the advent of major illnesses and surgeries.

There are currently no approved pharmacological treatments for achondroplasia, with existing treatments mainly limited to surgical interventions to address a variety of symptoms. This treatment gap presents a significant unmet need. Vosoritide is an investigational therapy that seeks to directly target the root cause of achondroplasia by interrupting the pathway that slows bone growth due to the causative mutation in achondroplasia. Beyond disproportionate short stature, people with achondroplasia can experience serious health complications, such as foramen magnum compression, sleep

apnea, and spinal stenosis. Some of these complications can result in the need for invasive surgeries. In addition, studies show increased mortality at every age.

"This milestone is an important building block of a comprehensive clinical program that is methodically and responsibly studying this potential first pharmacological treatment choice for achondroplasia with the goal of further understanding the safety and efficacy in the youngest children," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "In this trial, we are studying the effects of vosoritide during the most productive time of growth. We are grateful to the children and families enrolled in this placebo-controlled study and are committed to the long-term follow up of the children in these studies."

"This is an exciting milestone for children and families, who are interested in a treatment choice to address the basic cause of the irregular bone growth seen in achondroplasia. It represents a potential medical breakthrough that would be the first non-surgical treatment for children 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. "As a treating physician, I see an urgent demand from families for a treatment option that addresses bone growth and potentially the serious complications associated with achondroplasia, especially during infancy."

"This milestone is a giant step towards improving the quality of medical care and options available to individuals with achondroplasia and to their families," said Munira Shamim, co-founder of Growing Stronger. Many families are eagerly awaiting a drug treatment option that could possibly decrease the risk of health issues associated with achondroplasia and increase the quality of life. We would like to recognize the committed families and participants in the placebo-controlled studies for collaborating with dedicated scientists to further

scientific learning that can potentially change the lives of thousands of families."

**Regulatory Status**

In 2020, the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) accepted and validated the marketing authorization application for vosoritide for achondroplasia. The Committee for Medicinal Products for Human Use (CHMP) opinion is expected in Europe in June of 2021. The U.S. New Drug Application (NDA) for vosoritide is under review by the FDA with a Prescription Drug User Fee Act (PDUFA) target action date of August 20, 2021. In the United States, the Company has chosen to provide the 2-year outcomes from the Phase 3 extension study to the FDA as additional data to convey the vosoritide treatment effect and long-term durability. The Company believes that supplying this additional data could result in a major amendment, resetting the current PDUFA target action date out three months to November.

In January 2021, the Company received notice from the FDA that the NDA for vosoritide had been granted Priority Review Designation based on the serious pediatric indication it addresses, and the lack of treatment options currently available. Consistent with FDA's policy on changes to review classification for an ongoing application review, the PDUFA action date is not affected by this designation. If approved, the vosoritide NDA may qualify for a Priority Review Voucher (PRV). A PRV confers priority review to a subsequent drug application that would not otherwise qualify for that designation. The rare pediatric disease review voucher program is designed to encourage development of new drugs and biologics for the prevention or treatment of rare pediatric diseases.

Upon the acceptance of the regulatory submission for vosoritide, the Agency

reiterated a position raised during the Pediatric Advisory Committee (PAC) and Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) held on May 11, 2018 recommending two-year controlled trials in different age groups. BioMarin believes the highly persuasive outcomes from the one-year randomized, double-blind, placebo-controlled Phase 3 trial, coupled with data from the Phase 2 program with up to 5 years of long-term follow-up that has been compared to robust natural history data on growth and the updated 2-year data from the Phase 3 study, offers a rigorous and reliable method to assess whether vosoritide has a durable impact on the rate of endochondral bone growth that ultimately increases final adult height.

Vosoritide has also received orphan drug designation from the FDA and EMA for the treatment of children with 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 2 Study in Infants and Young Children Ages 0 to 5 Years**

This is a Phase 2 randomized, placebo-controlled study of vosoritide. The 52-week study consists of approximately 70 infants and young children with achondroplasia, aged zero to less than five years old (60 months). The study will be followed by a subsequent open-label extension trial when all subjects receive active treatment. Children in this study will have completed a three-to-six-month baseline study to determine their respective baseline growth prior to entering the Phase 2 study. The primary objectives of the study are to evaluate safety, tolerability, and the effect of vosoritide on height. The company also plans to augment the height data with other analyses of effects on growth and assessments including proportionality, functionality, quality of life, sleep apnea, and foramen magnum dimension, as well as the advent of major illnesses and

surgeries.

**About Achondroplasia**

Achondroplasia, the most common form of skeletal dysplasia leading to 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 change 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. Approximately 25% of people with achondroplasia fall into this category.  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 and ultra-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.biomarin.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: the development of BioMarin's vosoritide program generally; the potential benefits of vosoritide for infants and young children; the continued clinical development of vosoritide; the timing, design and conduct of the planned Phase 2 study in infants and young children and the expectation that topline results from this Phase 2 study will be released in mid-2022; the timing, design and conduct of other ongoing and possible future studies of vosoritide; the expected results of such studies, the ability to use the primary objectives of the Phase 2 study to support the use of vosoritide in infants and young children; the timing of actions by regulatory authorities including the expectation of the CHMP opinion for vosoritide in Europe in June of 2021; the potential for the vosoritide NDA, if approved, to qualify for a Priority Review Voucher; and the plan to submit the second year of Phase 3 data to the FDA and the potential that this could result in a major amendment, resetting the current PDUFA date out three months to November. 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: results and timing of current and planned preclinical studies and clinical trials of vosoritide; our ability to enroll participants into such clinical trials, 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 Company's Securities and Exchange Commission (SEC) filings, including, without limitation, BioMarin's Annual Report on Form 10-K for the year ended December 31, 2020 as such factors may be updated by any subsequent reports. 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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