# European Commission Approves BioMarin's VOXZOGO® (vosoritide) for the Treatment of Children with Achondroplasia from Age 2 Until Growth Plates Close

***Achondroplasia is the Most Common Cause of Dwarfism***

***First Medicine Approved to Treat Children with Achondroplasia in Europe***

SAN RAFAEL, Calif., Aug. 27, 2021 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) announced today that the European Commission (EC) has granted marketing authorization for VOXZOGO® (vosoritide), a once daily injection to treat achondroplasia in children from the age of 2 until growth plates are closed, which occurs after puberty when children reach final adult height.  Voxzogo is the first medicine to be approved to treat children with achondroplasia in Europe.  Voxzogo, a modified C-type natriuretic peptide (CNP), directly targets the underlying pathophysiology of achondroplasia by down regulating fibroblast growth factor receptor 3 (FGFR3) signaling and consequently promoting endochondral bone formation.

"Today represents an important milestone for the European achondroplasia community. For the first time medical professionals in Europe can offer a meaningful targeted therapeutic treatment option for children and families affected by achondroplasia," said Klaus Mohnike, Professor of Paediatrics at Magdeburg University Hospital in Germany and investigator for the Voxzogo clinical program. "Achondroplasia is a serious, progressive, and lifelong condition, which can cause multi-system complications that in some cases require surgical intervention.  This regulatory approval is based on improved height gain, one important determinant of day-to-day function for people with achondroplasia, and is a first step to understand the potential benefits of Voxzogo beyond height over the long term."

It is estimated that over 11,000 children across Europe, Middle East, and Africa are affected by achondroplasia and could be eligible for treatment with Voxzogo. Approximately a third of this population are in countries authorized under the EMA license. Also, the French National Agency for Medicines and Health Products Safety (ANSM) granted an Autorisation Temporaire d'Utilisation de cohorte (ATU cohort), or Temporary Authorization for Use to allow access of Voxzogo to begin immediately under an authorized process. An ATU allows access to drugs not yet approved in France, when provided for rare diseases with no alternative options, and when the benefit/risk is presumed positive. The list price in France under the ATU process is 712€ per vial and constitutes flat vial pricing across the spectrum of ages and weights translating to an estimated annual per patient cost of approximately 260,000€ or $300,000, assuming 100% compliance and excluding any discounts. We expect the initial German list price to be consistent with the French ATU price. The Company expects that these list prices will be subject, in one to two years, to material discounts after reimbursement negotiations in key markets such as Germany, France and Italy.

"We are committed to advancing the care of children affected by achondroplasia and are pleased to be able to offer a genetically targeted medicine that when administered in children over the age of two only while skeletal growth plates are open but could potentially offer benefit over a lifetime," said Jean-Jacques Bienaimé, Chairman and Chief Executive Officer of BioMarin. "We are grateful to the families and study investigators and their teams, who dedicated their time to the clinical program to make this treatment option a reality for this community in the EU. Voxzogo is the most widely studied therapeutic option for achondroplasia with an ongoing robust clinical program built on more than a decade of research and development."

"Today, we applaud the European Commission for recognizing the urgent need to treat children with a progressive condition by providing parents of children

with achondroplasia with a therapeutic treatment option. We look forward to the results of ongoing studies of this treatment, which will deepen our understanding of the impact of bone growth on proportionality, quality of life, and functional independence," said Carmen Alonso Alvarez, Managing Director of Fundacion ALPE Foundation. "We appreciate all of the parties who came together to bring the first medicine to treat children with achondroplasia in Europe and to expand treatment options beyond surgical intervention."

The EC based its decision on the totality of data from the Voxzogo clinical development program including the outcomes from the randomized, double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of Voxzogo. The Phase 3 Study was further supported by the ongoing long-term safety and efficacy from the Phase 2 dose-finding study, which showed that growth rates have been sustained above participants' baseline rates and above the expected annualized growth velocity for untreated children with achondroplasia throughout the five-year observation period for which data are currently available. No acceleration of bone age was observed, suggesting that Voxzogo is not reducing the total duration of growth. The data package included results from an ongoing Phase 2 randomized double-blind study in infants and young children, including extensive pharmacokinetic and biomarker data, as well as preliminary growth data from participants in the 2 to 5-year age cohort. Data in sentinel study participants showed a positive effect on growth following two years of Voxzogo treatment in subjects aged 2 to 5 years. In addition, the data package included data from the Phase 3 extension study and extensive natural history data.

The U.S. New Drug Application (NDA) for Voxzogo is under review by the FDA with a Prescription Drug User Fee Act (PDUFA) target action date of November 20, 2021. The Company successfully closed out the in-person FDA pre-approval inspection of its manufacturing facilities for Voxzogo earlier this year.

**Voxzogo Safety**

Voxzogo was generally well tolerated at all doses, and approximately 38,000 injections have been administered to children around the world. The majority of adverse events (AEs) were mild and no serious adverse events (SAEs) were reported as study drug related. Across all doses, injection site reactions and hypotension were the most common drug-related AEs. All injection site reaction events were transient. AEs of hypotension were mild and transient with the majority being asymptomatic and reported in the context of routine blood pressure measurements with minimal clinical impact. No new safety findings were observed. There were no AEs related to disproportionate bone growth or bone pathology. There has been no evidence of accelerated bone age (as assessed by radiologists blinded to the age of the subjects) or negative changes in bone mineral density.

**Regulatory Status**

In January 2021, the Company received notice from the FDA that the NDA for Voxzogo 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 Voxzogo 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.

Voxzogo 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.

**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.  Voxzogo 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 and ultra-rare genetic diseases. The company's portfolio consists of seven 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 Statements**

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: BioMarin's Voxzogo development program generally, access of Voxzogo to begin immediately in France, an estimated annual per patient cost of approximately 260,00€ or $300,000, based on a 712€ per vial price, assuming 100% compliance and excluding any discounts, the expectation that the initial German list price will be consistent with the French ATU price, and that these list prices will be subject, in one to two years, to material discounts after reimbursement negotiations in key markets such as Germany, France and Italy, the potential benefit of vosoritide over a lifetime, the status of the FDA's review of BioMarin's Voxzogo U.S. New Drug Application (NDA) and the anticipated PDUFA Target Action Date of November 20, 2021, BioMarin's anticipation that there will be additional patient access to Voxzogo through named patient sales based on an EMA approval in countries in the Middle East and Africa, BioMarin's expectation that additional market registrations will be facilitated by an anticipated EMA license and the potential for the Voxzogo NDA to qualify for a Priority Review Voucher. 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

Voxzogo; our ability to successfully manufacture Voxzogo for the clinical trials and commercially, if approved; the content and timing of decisions by the U.S. Food and Drug Administration, the European Commission and other regulatory authorities concerning Voxzogo; 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-Q for the quarter ended June 30 , 2021, 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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