MEDIA RELEASE

BioMarin's VOXZOGO® (vosoritide) Approved in Australia for the Treatment of Achondroplasia[1], the Most Common Form of Dwarfism

Registered by the Therapeutic Goods Administration (TGA) for the Treatment of Children with Achondroplasia from Age 2 Until Growth Plates Close[1]

First and Only Medicine Approved in Australia to Treat Children with this Rare Genetic Condition[1]

SYDNEY, Australia; 6 July 2022 -- BioMarin Pharmaceutical Australia Pty Ltd (BioMarin Australia) today announced that VOXZOGO (vosoritide) is registered in the Australian Register of Therapeutic Goods (ARTG) (AUST R 376616, AUST R 376617, AUST R 376618). VOXZOGO (vosoritide) is a once-daily subcutaneous injection for the treatment of children diagnosed with achondroplasia,[1] the most common form of disproportionate short stature or dwarfism.[2] Voxzogo was granted an Orphan Drug Designation by the TGA and is the first and only medicine to be listed in the ARTG in Australia for this condition.[3]

Achondroplasia affects around 1 in 20,000 live births in Australia, with an estimated 1,100 people currently thought to be living with this rare, progressive and lifelong genetic condition.[4] The local approval means Voxzogo will now be included in the ARTG to treat children from the age of 2 years until growth plates are closed[1], which typically occurs after puberty when children reach final adult height.[5]

"As a doctor who looks after children with achondroplasia, the lack of effective therapeutic options has been an urgent unmet medical need in this area," said Professor Ravi Savarirayan, Clinical Geneticist and global lead trial investigator from the Murdoch Children's Research Institute (MCRI) and Royal Children's Hospital (RCH) in Melbourne, Victoria. "Until now, available treatment options were very limited and were predominantly focused on managing the symptoms, rather than treating the underlying condition. Voxzogo represents a world-first pharmacological advance that addresses the underlying cause of achondroplasia in children."

Achondroplasia is caused by a spontaneous change in the fibroblast growth factor receptor 3 (FGFR3) gene, which inhibits the development and maintenance of bone.[2,5] As a modified C-type natriuretic peptide (CNP), a natural substance that exists in the body, Voxzogo directly targets the underlying pathophysiology of achondroplasia by supplementing the body's existing CNP to promote endochondral bone formation and increase bone growth velocity.[2,5,6]

Voxzogo is delivered as a dose-dependent (15.0 micrograms/kg/day), once-daily, subcutaneous (under the skin) injection in children, until growth plates are closed.[7]

Australia plays a leading role in the global Voxzogo clinical research program, with the Melbourne trial site located at the MCRI and RCH, led by Professor Savarirayan, representing the largest Voxzogo clinical trial site in the world.

"While today's TGA registration announcement is a significant milestone for Australian families impacted by achondroplasia, this is just the first step. I won't rest until all families have the option to receive

subsidised and affordable access to this treatment," said Professor Savarirayan. "I urge the Pharmaceutical Benefits Advisory Committee, the Department of Health and Aged Care and the Australian Government to list Voxzogo on the Pharmaceutical Benefits Scheme as quickly as possible."

While most people diagnosed with achondroplasia can live a full and productive life, the condition can often lead to a range of serious medical complications that significantly increase the risk of morbidity and mortality over the person's lifetime.[8] These include delayed motor function and speech development in children; respiratory dysfunction, including obstructive sleep apnoea; spinal stenosis and compression; and ongoing neurological, ear, nose and throat (ENT), orthopaedic and dental issues.[8] These medical complications can cause significant pain, and diminish both their physical function and quality of life.[8]

Mortality rates are elevated in individuals with achondroplasia at all ages.[8] In young children, an increased risk of sudden death can occur as a result of brainstem compression from spinal stenosis, with the incidence of sudden infant death syndrome (SIDS) during the first five years of life 50 times greater in children with achondroplasia, than those without the condition.[8] In adulthood, mortality risk is increased due to cardiovascular disease, neurological complications and accidents.[8]

"BioMarin is committed to advancing the care of achondroplasia and improving outcomes for children living with the condition," said Dr Kathryn Evans, Managing Director of BioMarin Australia. "Voxzogo's approval in Australia is the result of more than a decade of research and development and an ongoing robust clinical trial program, making it the most widely studied therapeutic option for achondroplasia."

"We extend our deepest gratitude to the community, clinical investigators and the children and their families, who have been involved in our comprehensive clinical research program as we continue to investigate the full potential of Voxzogo in treating achondroplasia."

The approval of Voxzogo was based on the totality of data from the clinical development program, including the outcomes from the global Phase 3 randomised, double-blind, placebo-controlled 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.

The Australian registration of Voxzogo follows approvals in the United States, Europe, Brazil and Japan. Marketing applications have been submitted in several other countries.

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About Achondroplasia
Achondroplasia, the most common form of skeletal dysplasia leading to disproportionate short stature, is characterised 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.[9] This condition is caused by a change in the fibroblast growth factor receptor 3 gene (FGFR3), a negative regulator of bone growth.[2,5] Beyond disproportionate short stature, people with achondroplasia can experience serious health complications, including spinal cord compression, sleep apnoea, bowed legs, mid-face hypoplasia, permanent sway of the lower back, spinal stenosis and recurrent ear infections.[8] 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.[8]

More than 80 per cent of children with achondroplasia have parents of average stature and have the condition as the result of a spontaneous change in the FGFR3 gene.[8] Voxzogo is being tested in children whose growth

plates are still "open", typically those under 18 years of age,[5] representing approximately 25 per cent of all people living with achondroplasia.

About VOXZOGO

In patients with achondroplasia, endochondral bone growth, an essential process by which bone tissue is created, is negatively regulated due to a spontaneous change in the *FGFR3* gene.[2,5] Voxzogo, a C-type natriuretic peptide (CNP) analog, represents a new class of therapy, which acts as a positive regulator of the signalling pathway downstream of FGFR3 to promote endochondral bone growth.[2,5,6] Voxzogo continues to be studied in a broad clinical development program in achondroplasia, and safety and efficacy are being further evaluated across different ages and over time. To date, 250 children with achondroplasia from eight countries, including Australia, have been enrolled in seven BioMarin clinical studies evaluating the safety and efficacy of Voxzogo.[10]

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.

About BioMarin

BioMarin is a global biotechnology company that develops and commercialises innovative therapies for patients with serious and life-threatening rare and ultra-rare genetic diseases. The company's portfolio consists of seven commercialised 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.

About BioMarin Australia

Established in 2012, BioMarin Pharmaceutical Australia Pty Ltd brings first- or best-in-class therapies for patients living with rare genetic diseases. The company's culture is focused on transforming lives through genetic discovery, giving hope to patients, their families, and their caregivers for first-in-class or best-in-class therapies. For further information, please visit www.biomarin.com.au.

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[1] Therapeutic Goods Administration. Australian Register of Therapeutic Goods (ARTG). Available at: https://www.tga.gov.au/australian-register-therapeutic-goods.
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