BioMarin Announces Ongoing Study Demonstrates Durable Treatment Benefit from Brineura® (cerliponase alfa) for 3 Years

Reduced Rate of Decline Maintained in Children with CLN2 Disease, a Form of Batten Disease

SAN RAFAEL, Calif., Feb. 7, 2019 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) today announced that an ongoing open-label extension study treating patients with Brineura® (cerliponase alfa) continued to show a reduced rate of decline compared to a natural history cohort of CLN2 disease for three years as measured by the CLN2 Clinical Rating Scale.

The data presented today shows a durability of treatment effect in the primary efficacy endpoint where response to treatment was seen in 19 of 23 or 83% of treated patients after three years. A response is defined as the absence of an unreversed two-point decline in the motor-language (ML) scale or a score of 0, outcomes that represent clear and substantial decline in motor and language function. Natural history patients were 12 times more likely on average to have experienced an unreversed two-point decline in ML score than treated patients at three years. After three years on treatment with Brineura, treated patients' ML scores were on average 3.8 points better than natural history. After two years on treatment with Brineura, treated patients' ML scores were on average 3.3 points better than natural history.

"Every day, week, month and year of maintaining clinical function, including language and mobility, is critical to children with CLN2 disease and their families," said Angela Schulz, M.D., lead study investigator from the Department of Paediatrics, Children's Hospital, University Medical Center Hamburg-Eppendorf, Germany. "Following these children has allowed us to better understand the effect of the treatment over time, which contributes to the advancement in the standard of care."

"CLN2 disease is a destructive and rapidly progressing brain disease in children and the data has consistently shown over time that cerliponase alfa can make a big difference in slowing the progression of the disease," said Hank Fuchs, M.D., President, Worldwide Research and Development at BioMarin. "It is important to us to contribute to the body of medical knowledge of CLN2 disease with data that is useful to the medical community treating these children."

Brineura was approved in April 2017 by the U.S. Food and Drug Administration (FDA) to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency. Brineura also was approved in June 2017 by the European Commission. Brineura is the first treatment approved to treat children with CLN2 disease, a form of Batten disease.

Study Design

An open-label study was conducted from September 2013 to November 2015 at five centers (Germany, Italy, US, and two in the UK) to assess the efficacy and safety of intraventricular cerliponase alfa in children with CLN2 disease. The studies were performed in accordance with the Declaration of Helsinki; the study protocol was approved by relevant ethics boards.

Eligible patients were aged 3-16 years of age with a diagnosis of CLN2 disease and a combined score of 3-6 on the motor and language domains of a CLN2 clinical rating scale (total range 0-6, 0 representing no

function and 3 representing normal function for each of the two domains). Patients who completed the 48-week open-label study were eligible to enroll in a 240-week extension study of 300 mg administered every two weeks. Patients enrolled in the DEM-CHILD NCL natural history database and diagnosed with CLN2 disease served as the comparison group.

Twenty-four patients aged 3-8 years were enrolled in the clinical study. One patient withdrew after week 1 due to inability to continue with study procedures; 23 patients were treated with Brineura every other week for three years or more. Of 23 patients enrolled in the extension study, 21 are continuing in the extension. The discontinuation in the extension study of two patients was not due to adverse events.

About CLN2 Disease

Children with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency, typically begin experiencing seizures between the ages of two and four years old, preceded in the majority of cases by language development delay. The disease progresses rapidly with most affected children losing the ability to walk and talk by approximately 6 years of age. Initial symptoms are followed by movement disorders, motor deterioration, dementia, blindness, and death usually occurring between the ages of eight and 12 years of age. During the later stages of the disease, feeding and tending to everyday needs become very difficult. BioMarin estimates the incidence of CLN2 disease is approximately one in 200,000, with up to 1,200 to 1,600 children in the regions of the world where BioMarin operates, many of whom are undiagnosed.

The neuronal ceroid lipofuscinoses (NCLs) are a heterogeneous group of lysosomal storage disorders that includes the autosomal recessive neurodegenerative disorder CLN2 disease. CLN2 disease is caused by mutations in the TPP1 gene resulting in deficient activity of the enzyme TPP1. In the absence of TPP1, lysosomal storage materials normally metabolized by this enzyme accumulate in many organs, particularly in the brain and retina. Buildup of these storage materials in the cells of the nervous system contribute to the progressive and relentless neurodegeneration which manifests as loss of cognitive, motor, and visual functions.

About Brineura

Brineura is a recombinant form of human TPP1, the enzyme deficient in patients with CLN2 disease. It is an enzyme replacement therapy designed to restore TPP1 enzyme activity and break down the storage materials that cause CLN2 disease. In order to reach the cells of the brain and central nervous system, the treatment is delivered directly into the fluid surrounding the brain (cerebrospinal fluid) using BioMarin's patented technology.

For additional information regarding this product, please contact BioMarin Medical Information at medinfo@bmrn.com.

Indication

Brineura® (cerliponase alfa) is a prescription medication used to slow loss of ability to walk or crawl (ambulation) in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

Important Safety Information

Brineura is a prescription medicine. Before treatment with Brineura, it is important to discuss your child's medical history with their doctor. Tell the doctor if they are sick or taking any medication and if they are

allergic to any medicines. Your child's doctor will decide if Brineura is right for them. If you have questions or would like more information about Brineura, contact your child's doctor.

Brineura is only given by infusion into the fluid of the brain (known as an intraventricular injection) and using sterile technique to reduce the risk of infection. An intraventricular access device or port must be in place at least 5 to 7 days prior to the first infusion. Intraventricular access device-related infections, including meningitis, were observed with Brineura treatment. If any signs of infection or meningitis occur, contact your child's doctor immediately. The signs and symptoms of infections may not be readily apparent in patients with CLN2 disease. Your doctor should vigilantly be looking for signs and symptoms of infection, including meningitis, during treatment with Brineura.

Your child's intraventricular access device should be replaced prior to 4 years of single-puncture administration of Brineura, because the device may deteriorate due to repeated use.

Brineura should not be used in patients with active intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection, including meningitis), symptom of acute, unresolved localized infection around the device insertion site (e.g. cellulitis or abscess), or with shunts used to drain extra fluid around the brain. Your child's doctor should inspect the scalp and collect samples of your child's cerebrospinal fluid (CSF) prior to each infusion of Brineura, to check that there is no device failure or infections present.

Low blood pressure and/or slow heart rate may occur during and following the Brineura infusion. Contact your child's doctor immediately if these reactions occur.

Undesirable or hypersensitivity reactions related to Brineura treatment, including fever, vomiting, and irritability, may occur during treatment and as late as 24 hours after infusion. Your child may receive medication such as antihistamines before Brineura infusions to reduce the risk of reactions. Serious and severe allergic reactions (anaphylaxis) may occur. If a reaction occurs, the infusion will be stopped and your child may be given additional medication. If a severe reaction occurs, the infusion will be stopped and your child will receive appropriate medical treatment. If any signs of anaphylaxis occur, immediately seek medical care.

Safety and effectiveness in pediatric patients below 3 years of age have not been established.

The most common side effects reported during Brineura infusions included fever, problems with the electrical activity of the heart, decreased or increased protein in the fluid of the brain, vomiting, seizures, hypersensitivity, collection of blood outside of blood vessels (hematoma), headache, irritability, and increased white blood cell count in the fluid of the brain, device-related infection, slow heart rate, feeling jittery, and low blood pressure. Intraventricular device-related side effects included infection, delivery system-related complications, and increased white blood cell count in fluid of the brain.

These are not all of the possible side effects with Brineura. Talk to your child's doctor if they have any symptoms that bother them or that do not go away.

Call your doctor for medical advice about side effects. You may report side effects to BioMarin Pharmaceutical Inc. at 1-866-906-6100, or the FDA at 1-800-FDA-1088 or go to www.fda.gov/medwatch.

Please see accompanying full Prescribing Information, or visit www.Brineura.com.

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 Statement

This press release contains forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: BioMarin's product Brineura, and specifically about persistent treatment benefit after three years, and expectations regarding its potential to change the course of CLN2 disease. 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: the continued clinical development and commercialization of BioMarin's commercial products and product candidates; actions by regulatory authorities, our ability to manufacture sufficient quantities of Brineura for commercial use; and those factors detailed in BioMarin's filings with the Securities and Exchange Commission, including, without limitation, the factors contained under the caption "Risk Factors" and elsewhere in the Company's Securities and Exchange Commission (SEC) filings, including the Company's 10Q for the quarter ended September 30, 2018, as such factors may be updated by any subsequent reports. Stockholders are urged not to place undue reliance on forward-looking statements, which speak only as of the date hereof. BioMarin is under no obligation to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

Contacts:

Investors	Media
Traci McCarty	*Debra Charlesworth*
BioMarin Pharmaceutical Inc.	*BioMarin Pharmaceutical Inc.*
(415) 455-7558	*(415) 455-7451*

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