BioMarin Highlights Breadth of Innovative Development Pipeline at R&D Day on November 7th in New York

Vosoritide for Achondroplasia: Demonstrates Continued Increased Growth through 42 months in Phase 2; Global Phase 3 Fully Enrolled
Elements of Possible 2H 2019 BLA for valoctocogene Roxaparvovec for Hemophilia A Outlined
PKU Gene Therapy Planned IND for 2H 2019
Brineura® (cerliponase alfa) Demonstrates Continued Stabilization to 3 Years in Clinical Study Patients with CLN2 Batten Disease

SAN RAFAEL, Calif., Nov. 7, 2018 /PRNewswire/ -- BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) updated the investment community on the Company's research and development portfolio, which is focused on innovative therapies to treat rare and ultra-rare diseases.

"BioMarin is poised to deliver multiple research, development and regulatory milestones in 2019 driven by the tremendous productivity of our R&D organization. We continue to tap into our deep experience and knowledge in rare genetic diseases to advance our pipeline programs, while also demonstrating the long-term benefit to patients of our recently approved therapies like Palynziq and Brineura," said Hank Fuchs, M.D., President Worldwide Research and Development of BioMarin. "By concentrating on the underlying pathology of disease, we're able to increase our odds of demonstrating meaningful and sustained outcomes. Our next potential commercial prospects include vosoritide, valoctocogene roxaparvovec and European regulatory approval for Palynziq."

Vosoritide Data Update

BioMarin provided an update on its clinical program for vosoritide, an analog of C-type Natriuretic Peptide (CNP), in children with achondroplasia, the most common form of disproportionate short stature in humans.

An ongoing open-label, Phase 2 study of vosoritide for achondroplasia demonstrated sustained increase in cumulative height gained over 42 months of treatment in children in cohort 3 at a dose of 15 µg/kg/day. The cohort gained a mean of 5.7 cm of cumulative height over what the participants' baseline would have predicted. At 30 months, the same cohort experienced a 4 cm increase over what the participants' baseline growth velocity would have predicted.

BioMarin announced today that the Phase 3 study of vosoritide in children is now fully enrolled and top line results are planned for the end of 2019. BioMarin has also initiated a global Phase 2 study in infants and young children up to age 5 with achondroplasia. See "About Vosoritide Phase 3 Study" below for more information on this study.

In addition to clinical studies of vosoritide, in collaboration with the leading skeletal dysplasia centers in the United States (U.S.), BioMarin is conducting a multi-center, natural history study in 1,377 people with achondroplasia. This natural history study will make it possible to compare the final adult height of people treated with vosoritide in our clinical studies and those not treated. These data will support the assessment of efficacy of vosoritide.

Vosoritide has been granted orphan drug designation in both the U.S. and Europe.

Valoctocogene Roxaparvovec, Investigational Gene Therapy for Severe Hemophilia A

Based on the recently released Food and Drug Administration (FDA) Draft Guidance for Human Gene Therapy for Hemophilia, BioMarin expects that data available in 2019 could potentially allow submission of a marketing application for valoctocogene roxaparvovec through an accelerated approval pathway in the second half of 2019. The key elements necessary to enable this plan include an agreed upon Factor VIII assay, targeted Factor VIII levels in the normal range, preliminary Annualized Bleed Rate data to evaluate that this level of Factor VIII activity is reasonable likely to predict clinical benefit, longer term efficacy and safety data from our Phase 1/2 study, and a comprehensive Chemistry, Manufacturing and Controls package. BioMarin expects to have 3.5 years of data from its Phase 1/2 study at the time of potential submission.

If the FDA feedback and interim results from ongoing clinical trials support an accelerated review for valoctocogene roxaparvovec, BioMarin would target the second half of 2019 to submit a Biologic License Application (BLA) for accelerated approval.

"We are meeting with the FDA regularly, consistent with valoctocogene roxaparvovec's status as a breakthrough therapy, and our most recent interactions with the FDA have given us increased confidence and alignment on our development and accelerated regulatory strategy," said Fuchs.

Valoctocogene roxaparvovec has Orphan Drug designation from the FDA and the European Medicines Agency (EMA).

Valoctocogene roxaparvovec has also been accepted for Priority Medicines (PRIME) scheme from the EMA. Additionally, the FDA has granted valoctocogene roxaparvovec Breakthrough Therapy designation.

Gene Therapy Manufacturing

BioMarin has constructed one of the largest gene therapy manufacturing facilities of its kind, which is located in Novato, California. Good Manufacturing Practices (GMP) production of valoctocogene roxaparvovec has commenced and will support clinical development activities and anticipated commercial demand. This facility is capable of supporting approximately 4,000 doses per year, and the production process was developed in accordance with International Conference on Harmonisation guidance for Pharmaceuticals for Human Use facilitating worldwide registration with health authorities.

In March 2018, the International Society for Pharmaceutical Engineering (ISPE) named BioMarin's gene therapy manufacturing facility the 2018 Facility of the Year Category Winner for Project Execution. The recognition highlighted the company's successful construction of the facility in Novato, California, which took less than a year to transform basic infrastructure into one of the first gene manufacturing facilities of its kind in the world. ISPE's Facility of the Year program is the premier global awards program, recognizing innovation and creativity in the pharmaceutical and biotechnology manufacturing industries. Projects selected for recognition set the standard by demonstrating excellence in facility design, construction and operations.

Phenlyketonuria (PKU) Portfolio: BMN 307, Pre-Clinical Gene Therapy for PKU, and Palynziq®(pegvaliase-pqpz) Injection

BMN 307 Program Update

BioMarin shared pre-clinical data of its investigational gene therapy program for PKU using an AAV5 PAH vector, which demonstrated lifetime Phe corrections in mouse models. Mouse coat color is a readily detectable biomarker of therapeutic response, and the coat color of all of the mice treated with BMN 307 changed from light brown, evidence of high Phe levels, to black, evidence of therapeutic activity. Treated mice showed normalized Phe levels sustained through 80 weeks, associated with normalization of circulating neurotransmitter levels, which are involved in neurological characteristics of human PKU.

BioMarin plans to file an investigational new drug application (IND) for BMN 307 with the FDA in the second half of 2019.

Palynziq Data at 36 Months

In an ongoing open-label extension study at 36 months, patients being treated with Palynziq® (pegvaliase-pqpz) Injection showed durability and an increase in participants reaching blood Phe thresholds of physiologically normal (<120 µmol/L), as well as thresholds recommended in the U.S. (<360 µmol/L) and the European Union (E.U.) (<600 µmol/L). At 36 months, 59% of the participants reached physiologically normal, 67% reached Phe levels as recommended in the U.S. and 74% reached Phe levels as recommended in the E.U.

BioMarin is also committed to bringing Palynziq to adult PKU patients outside of the U.S. In March 2018, the EMA accepted BioMarin's submission of a Marketing Authorization Application (MAA) for Palynziq. The company expects to learn the status of this application in the first half of 2019.

Palynziq, a PEGylated recombinant phenylalanine ammonia lyase enzyme, is the first approved enzyme substitution therapy to target the underlying cause of PKU by helping the body to break down Phe and BioMarin's second approved treatment for this important condition.

Brineura® (cerliponase alfa) Data at Three or More Years

BioMarin announced today that twenty-three patients in the ongoing open-label extension study treated with Brineura® (cerliponase alfa) showed continued maintenance of stabilization of disease for three years or more as measured by the CLN2 Clinical Rating Scale as compared to untreated patients from a natural history cohort.

Patients were assessed for decline in the motor domain of the CLN2 Clinical Rating Scale. The scale measures performance of mobility with normal function being a score of 3 and no function being a score of 0. Decline was defined as having a sustained 2-point decline or an unreversed score of 0 in the motor domain of the CLN2 Clinical Rating Scale.

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. Two Brineura treated patients, who at study initiation had a maximum score, were excluded from the analyses; they maintained that score throughout the study period. Both children had motor scores of 3 after three years of treatment.

About BioMarin and Disease Information

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.

About Achondroplasia

Achondroplasia, the most common form of disproportionate short stature in humans, is characterized by failure of normal conversion of cartilage into bone, which results in disproportionate short stature. 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 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 and the Middle East, there is currently no licensed medicines for achondroplasia.

About Vosoritide Phase 3 Study

The global Phase 3 study is a randomized, placebo-controlled study of vosoritide in approximately 110 children with achondroplasia ages 5-18 for 52 weeks. The study will be followed by a subsequent open-label extension. Children in this study will have completed a minimum six-month baseline study to determine their respective baseline growth velocity prior to entering the Phase 3 study. Vosoritide is being tested in children whose growth plates are still open. This is approximately 25% of people with achondroplasia.

The primary endpoint of the study is the change in growth velocity from baseline over one year in children treated compared to placebo. The company also plans to augment the growth velocity data with assessments of proportionality and functionality.

About Vosoritide Phase 2 Infant and Young Children Study

The Phase 2 vosoritide study is a randomized, placebo-controlled study of vosoritide in approximately 70 infants and young children with achondroplasia ages zero to less than 60 months for 52 weeks. The study will be followed by a subsequent open-label extension. Children in this study will have completed a minimum three-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 Z-scores, which is the number of standard deviations in relation to the mean height of age-matched, average stature children. The company also plans to augment the height Z-score 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.

Vosoritide Safety

Vosoritide, administered in over 28,000 injections, was generally well tolerated at all doses. 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, transient and resolved without medical intervention, and the majority were asymptomatic and reported in context of routine blood pressure measurements. No new safety findings were observed at the 30 µg/kg/day dose.

About Hemophilia A

Hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation, a new mutation that was not inherited. Approximately 1 in 10,000 people is born with Hemophilia A. People living with the disease are not able to form blood clots efficiently and are at risk for excessive bleeding from modest injuries, potentially endangering their lives. People with severe hemophilia often bleed spontaneously into their muscles or joints. The standard of care for the 43% of individuals with hemophilia A who are severely affected is a prophylactic regimen of Factor VIII infusions two to three times per week. Even with prophylactic regimens, many people still experience spontaneous bleeding events that result in progressive and debilitating joint damage.

Valoctocogene Roxaparvovec Phase 1/2 Study Safety

Overall, valoctocogene roxaparvovec has been well-tolerated by patients across all doses, including the two patients that received the lowest doses of 6e12 and 2e13 vg/kg, respectively. No patients developed inhibitors to Factor VIII and no patients withdrew from the study. The most common AEs across all dose cohorts were alanine

aminotransferase (ALT) elevation (11 patients, 73%); arthralgia, aspartate aminotransferase elevation, and headache (7 patients each, 47%); back pain and fatigue (5 patients each, 33%). Two patients reported SAEs during the study. One patient was hospitalized for observation after developing Grade 2 pyrexia with myalgia and headache within 24 hours of receiving valoctocogene roxaparvovec. The event resolved within 48 hours following treatment with paracetamol, an over-the-counter treatment for pain and fever. The event was assessed as related to valoctocogene roxaparvovec. The other AE was assessed as not related to the therapy, attributed to a planned knee surgery to treat hemophilic arthropathy, and Grade 1 in severity. No complications were reported.

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 2 and 4 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 8 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 CLN2 disease, also known as 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 were observed with Brineura treatment. If any signs of infection occur, contact your child's doctor immediately. Your child's intraventricular access device may need to be replaced over time.

Brineura should not be used in patients with active intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) and with shunts used to drain extra fluid around the brain.

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 FDA at 1-800-FDA-1088.

Please see accompanying full Prescribing Information, or visit www.Brineura.com. Information on such website is not incorporated by reference into this press release.

About Phenylketonuria

PKU, or PAH deficiency, is a genetic disorder affecting approximately 50,000 diagnosed patients in the regions of the world where BioMarin operates and is caused by a deficiency of the enzyme PAH. This enzyme is required for the metabolism of Phe, an essential amino acid found in most protein-containing foods. If the active enzyme is not present in sufficient quantities, Phe accumulates to abnormally high levels in the blood and becomes toxic to the brain, resulting in a variety of complications including severe intellectual disability, seizures, tremors, behavioral problems and psychiatric symptoms. As a result of newborn screening efforts implemented in the 1960s and early 1970s, virtually all individuals with PKU under the age of 40 in countries with newborn screening programs are diagnosed at birth and treatment is implemented soon after. PKU can be managed with a Phe-restricted diet, which is supplemented by low-protein modified foods and Phe-free medical foods; however, the strict diet is difficult for most adult patients to adhere to the extent needed for achieving adequate control of blood Phe levels.

To learn more about PKU and PAH deficiency, please visit www.PKU.com. Information on such website is not incorporated by reference into this press release.

About Palynziq

Palynziq substitutes the deficient phenylalanine hydroxylase (PAH) enzyme in PKU with the PEGylated version of the enzyme phenylalanine ammonia lyase to break down Phe. **Palynziq** is administered using a dosing regimen designed to facilitate tolerability; Palynziq's safety profile consists primarily of immune-mediated responses, including anaphylaxis, for which robust risk management measures effective in clinical trials are in place.

The dosing and administration of Palynziq follows an induction, titration, and maintenance paradigm. Treatment is individualized to the lowest effective and tolerated dosage. Prescribers may consider increasing to a maximum of 40 mg once daily in patients who have not achieved a response with 20 mg once daily for at least 24 weeks. Prescribers are instructed to discontinue treatment in patients who have not responded after 16 weeks of continuous treatment with the maximum dosage of 40 mg once daily. Periodic blood Phe monitoring is recommended, and patients should be counseled on how to adjust their dietary intake, as needed, based on blood Phe concentrations.

To reach a BioMarin RareConnections® case manager, please call, toll-free, 1-866-906-6100 or e-mail support@biomarin-rareconnections.com. For more information about Palynziq, please visit www.palynziq.com. Information on such website is not incorporated by reference into this press release. For additional information regarding this product, please contact BioMarin Medical Information at medinfo@bmrn.com.

Indication

Palynziq (pegvaliase-pqpz) Injection is a phenylalanine-metabolizing enzyme indicated to reduce blood phenylalanine concentrations in adult patients with PKUwho have uncontrolled blood phenylalanine concentrations greater than 600 µmol/L on existing management.

Important Safety Information

BOXED WARNING: RISK OF ANAPHYLAXIS

- **Anaphylaxis has been reported after administration of PALYNZIQ and may occur at any time during treatment with PALYNZIQ.**
- **Administer the initial dose of PALYNZIQ under the supervision of a healthcare provider equipped to manage anaphylaxis, and closely observe patients for at least 60 minutes following injection. Prior to self-injection, confirm patient competency with self-administration, and patient's and observer's (if applicable) ability to recognize signs and symptoms of anaphylaxis and to administer auto-injectable epinephrine, if needed.**
- **Prescribe auto-injectable epinephrine to all patients treated with PALYNZIQ. Prior to the first dose, instruct the patient and observer (if applicable) on its appropriate use. Instruct the patient to seek immediate medical care upon its use. Instruct patients to carry auto-injectable epinephrine with them at all times during treatment with PALYNZIQ.**

- **PALYNZIQ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the PALYNZIQ REMS.** Further information, including a list of qualified pharmacies, is available at www.PALYNZIQREMS.com (site will be live within 24 hours) or by telephone 1-855-758-REMS (1-855-758-7367).

WARNINGS AND PRECAUTIONS

Anaphylaxis

- Signs and symptoms of anaphylaxis reported include syncope, hypotension, hypoxia, dyspnea, wheezing, chest discomfort/chest tightness, tachycardia, angioedema (swelling of face, lips, eyes, tongue), throat tightness, skin flushing, rash, urticaria, pruritus, and gastrointestinal symptoms (vomiting, nausea, diarrhea).
- Anaphylaxis generally occurred within 1 hour after injection; however, delayed episodes occurred up to 48 hours after PALYNZIQ administration.
- Consider having an adult observer for patients who may need assistance in recognizing and managing anaphylaxis during treatment with PALYNZIQ. If an adult observer is needed, the observer should be present during and for at least 60 minutes after administration of PALYNZIQ, and should be able to administer auto-injectable epinephrine and call for emergency medical support upon its use
- Anaphylaxis requires immediate treatment with auto-injectable epinephrine. Prescribe auto-injectable epinephrine to all patients receiving PALYNZIQ and instruct patients to carry auto-injectable epinephrine with them at all times during treatment with PALYNZIQ. Prior to the first dose, instruct the patient and observer (if applicable) on how to recognize the signs and symptoms of anaphylaxis, on how to properly administer auto-injectable epinephrine, and to seek immediate medical care upon its use. Consider the risks associated with auto-injectable epinephrine use when prescribing Palynziq. Refer to the auto-injectable epinephrine prescribing information for complete information.
- Consider the risks and benefits of readministering PALYNZIQ following an episode of anaphylaxis. If the decision is made to readminister PALYNZIQ, administer the first dose under the supervision of a healthcare provider equipped to manage anaphylaxis and closely observe the patient for at least 60 minutes following the dose. Subsequent dose titration of PALYNZIQ should be based on patient tolerability and therapeutic response.
- Consider premedication with an H_1-receptor antagonist, H_2-receptor antagonist, and/or antipyretic prior to administration of PALYNZIQ based upon individual patient tolerability.

Other hypersensitivity reactions

- Hypersensitivity reactions other than anaphylaxis have been reported in 196 of 285 (69%) patients treated with PALYNZIQ.
- Consider premedication with an H_1-receptor antagonist, and/or antipyretic prior to PALYNZIQ administration based upon individual patient tolerability.
- Management of hypersensitivity reactions should be based on the severity of the reaction, recurrence of the reaction, and the clinical judgment of the healthcare provider, and may include dosage adjustment, temporary drug interruption, drug discontinuation, or treatment with antihistamines, antipyretics, and/or corticosteroids.

ADVERSE REACTIONS

- The most common adverse reactions (at least 20% of patients in either treatment phase) were injection site reactions, arthralgia, hypersensitivity reactions, headache, generalized skin reaction lasting at least 14 days, pruritus, nausea, abdominal pain, oropharyngeal pain, vomiting, cough, diarrhea, and fatigue.
- Of the 285 patients exposed to PALYNZIQ in an induction/titration/maintenance regimen in clinical trials, 31 (11%) patients discontinued treatment due to adverse reactions. The most common adverse reactions leading to treatment discontinuation were hypersensitivity reactions (6% of patients)—including anaphylaxis (3% of patients) and angioedema (1% of patients)—arthralgia (4% of patients), generalized skin reactions lasting at least 14 days (2% of patients), and injection site reactions (1% of patients)
- The most common adverse reactions leading to dosage reduction were arthralgia (14% of patients), hypersensitivity reactions (9% of patients), injection site reactions (4% of patients), alopecia (3% of patients), and generalized skin reactions lasting at least 14 days (2% of patients)
- The most common adverse reactions leading to temporary drug interruption were arthralgia (13% of patients), hypersensitivity reactions (13% of patients), anaphylaxis (4% of patients), and injection site reactions (4% of patients)

Blood Phenylalanine Monitoring and Diet

- Obtain blood phenylalanine concentrations every 4 weeks until a maintenance dosage is established.

- After a maintenance dosage is established, periodically monitor blood phenylalanine concentrations.
- Counsel patients to monitor dietary protein and phenylalanine intake, and adjust as directed by their healthcare provider.

DRUG INTERACTIONS

Effect of PALYNZIQ on other PEGylated products

- In a single dose study of PALYNZIQ in adult patients with PKU, 2 patients receiving concomitant injections of medroxyprogesterone acetate suspension (a formulation containing PEG 3350) experienced hypersensitivity reactions, and 1 of the 2 patients also experienced anaphylaxis.
- The clinical effects of concomitant treatment with different PEGylated products is unknown. Monitor patients treated with PALYNZIQ and concomitantly with other PEGylated products for hypersensitivity reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy and Lactation

- PALYNZIQ may cause fetal harm when administered to a pregnant woman.
- If PALYNZIQ is administered during pregnancy, or if a patient becomes pregnant while receiving PALYNZIQ or within 1 month following the last dose of PALYNZIQ, healthcare providers should report PALYNZIQ exposure by calling 1-866-906-6100.
- Monitor blood phenylalanine concentrations in breastfeeding women treated with PALYNZIQ.

Pediatric use

- The safety and efficacy of PALYNZIQ in pediatric patients have not been established.

Geriatric Use

- Clinical studies of PALYNZIQ did not include patients aged 65 years and older.

You are encouraged to report side effects to report suspected adverse events to BioMarin at 1-877-695-8826 and the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**.**

Please see full Prescribing Information, including Boxed Warning, at PALYNZIQ.com/hcp, which will be available in 24 hours.

About ISPE

The ISPE is the world's largest not-for-profit association serving its members through leading scientific, technical, and regulatory advancement across the entire pharmaceutical lifecycle. The 18,000 members of ISPE are building solutions in the development and manufacture of safe, effective pharmaceutical and biologic medicines, and medical delivery devices in more than 90 countries around the world. Founded in 1980, ISPE has its worldwide headquarters in Bethesda, Maryland USA, and an operations and training center in Tampa, Florida USA. Visit ispe.org for more information. 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., including, without limitation, statements about its development programs and regulatory actions related to these programs, including the timing of (i) decisions by regulators, including the EMA's decision regarding BioMarin's MAA for Palynziq, (ii) BioMarin's preclinical studies and clinical studies and trials, (iii) completion of enrollment of those studies and trials, and (iv) announcements of data from those studies and trials; the production capacity of BioMarin's gene therapy manufacturing facility; the continued clinical development and commercialization of BioMarin's commercial products and product candidates, including BioMarins plans to potentially submit a BLA for valoctocogene roxaparvovec for accelerated approval in the second half of 2019, to file an IND with the FDA for BMN 307 in the second half of 2019 and make Palynziq commercially available to adult PKU patients outside of the U.S.; and the possible approval and commercialization of BioMarin's product candidates. 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 our product candidates, the continued clinical experiences of the patients in the current clinical studies; the content and timing of decisions by the FDA, the European Commission and other regulatory authorities; our ability to successfully manufacture our product candidates for the preclinical and clinical trials; and those factors detailed in BioMarin's filings with the Securities and Exchange Commission (SEC), including, without limitation, the factors contained under the caption "Risk Factors" in BioMarin's Quarterly Report on Form 10-Q 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,

and expressly disclaims any obligation to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

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