American College of Medical Genetics and Genomics Practice Guidelines Support Lifelong Therapy to Manage Phenylketonuria (PKU)

Recommend Drug Therapy, Such as Kuvan(R) (Sapropterin Dihydrochloride), for Appropriate Patients

SAN RAFAEL, Calif., Jan. 13, 2014 (GLOBE NEWSWIRE) -- BioMarin Pharmaceutical Inc. (Nasdaq:BMRN) announced today that new practice guidelines issued by the American College of Medical Genetics and Genomics (ACMG) support the need for lifelong management of PHE levels in patients with phenylketonuria or PKU. The new diagnosis and management guidelines were published online in Genetics In Medicine's Advance Online Publication (AOP) service and provide the first update to recommendations for therapy of PKU since the 2001 National Institutes of Health Consensus statement.

The new guidelines state that treatment of PKU should be initiated as early as possible and must be continued throughout adulthood and "lifelong," with a goal of maintaining blood levels of phenylalanine (PHE) for all patients between 120-360 umol/L. Patients treated from the early weeks of life with initial good metabolic control, but who lose that control in later childhood or adult life, may experience both reversible and irreversible neuropsychiatric consequences. The guidelines also recommend changing the name of the disease from PKU to phenylalanine hydroxylase deficiency (PAH deficiency), a unifying nomenclature that reflects the continuous spectrum of disease severity. The guidelines specifically note that for, appropriate patients, use of Kuvan® (sapropterin dihydrochloride) should be considered to help lower PHE.

According to the new guidelines, "The primary goal of therapy is to lower blood PHE, and any interventions, including medications, or combination of therapies that help to achieve that goal in an individual, without other negative consequences, should be considered appropriate therapy."

Kuvan, the first and only prescription medication that helps patients lower blood PHE levels, is recognized for its potential benefits with 25-50 percent of PKU or PAH deficient patients cited as responsive to treatment with Kuvan. PEG PAL is an experimental therapy in Phase 3 of clinical development with a primary endpoint of PHE lowering, and a secondary endpoint of neurocognitive benefit. The guidelines state that "an improvement in neuropsychiatric symptoms or increase in PHE tolerance, without a decrease in blood PHE levels in any patient, constitutes sufficient justification to continue therapy."

"We have made great strides in recent years in the understanding and management of PKU. Thanks to the American College of Medical Genetics and Genomics, we now know just how important it is for patients with PAH deficiency to continue lifelong management of their condition," said Hank Fuchs, M.D., Chief Medical Officer of BioMarin. "BioMarin is committed to the PKU community and is developing PEG PAL, a potential treatment option for patients age 16 and older who are struggling to achieve and maintain blood PHE levels within the recommended ranges. Treatments like Kuvan and the development of new therapies are critical to helping patients with PKU or PAH deficiency lead long, fulfilling lives."

Evidence for the new guidelines are drawn from two previous independent review processes from the National Institutes of Health (2001) and the Agency for Health Research and Quality (2012). The guidelines can be accessed online at:

https://www.acmg.net/docs/Phenylalanine_Hydrosylase_Deficiency_Practice_Guideline_AOP_Jan_2013.pdf

About PKU or PAH Deficiency

Phenylketonuria (PKU) or phenylalanine hydroxylase (PAH) deficiency is a genetic disorder affecting approximately 50,000 diagnosed patients in the developed world and is caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH), this enzyme is required for the metabolism of phenylalanine (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 or PAH deficiency under the age of 40 in developed countries are diagnosed at birth and treatment is implemented soon after. PAH deficiency 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 patients to adhere to the extent needed for achieving adequate control of blood PHE levels. Kuvan, the first and only prescription medicine of its kind, may help individuals with PAH deficiency lower

blood PHE levels when used in conjunction with a PHE-restricted diet, more than the use of diet alone. To learn more about PAH deficiency, please visit www.PKU.com. Information on this website is not incorporated by reference into this press release. Some of the signs and symptoms of high blood PHE include:

- For infants and children: severe intellectual disability and developmental delay, skin rash (eczema), light-colored skin, eyes and hair (hypopigmentation)
- For teens and adults: lower intelligence, psychological and psychiatric symptoms like anxiety, depression and phobias, problems with memory and performing tasks (executive function), poor concentration and irritable mood among other things.
- For pregnant women: increased risk for the baby's growing brain, including risk of intellectual disability, increased risk for a small head (microcephaly) and other problems such as a heart malformation (congenital heart defect) and poor overall growth (intrauterine growth retardation). This teratogenic effect of PHE on the developing fetus is called Maternal PKU syndrome.

About BioMarin

BioMarin develops and commercializes innovative biopharmaceuticals for serious diseases and medical conditions. The company's product portfolio comprises four approved products and multiple clinical and pre-clinical product candidates. Approved products include Naglazyme® (galsulfase) for MPS VI, a product wholly developed and commercialized by BioMarin; Aldurazyme® (laronidase) for MPS I, a product which BioMarin developed through a 50/50 joint venture with Genzyme Corporation; Kuvan® (sapropterin dihydrochloride) Tablets, for phenylketonuria (PKU), developed in partnership with Merck Serono, a division of Merck KGaA of Darmstadt, Germany; and Firdapse® (amifampridine), which has been approved by the European Commission for the treatment of Lambert Eaton Myasthenic Syndrome (LEMS). Product candidates include VIMIZIM™ (N-acetylgalactosamine 6-sulfatase), formally referred to as GALNS, which successfully completed Phase 3 clinical development for the treatment of MPS IVA, PEG PAL (PEGylated recombinant phenylalanine ammonia lyase), which is currently in Phase 3 clinical development for the treatment of PKU, BMN 673, a poly ADP-ribose polymerase (PARP) inhibitor, which is currently in Phase 3 clinical development for the treatment of germline BRCA breast cancer, BMN 701, a novel fusion of acid alpha glucosidase (GAA) with a peptide derived from insulin like growth factor 2, which is currently in Phase 1/2 clinical development for the treatment of Pompe disease, BMN 111, a modified C-natriuretic peptide, which is currently in Phase 1 clinical development for the treatment of achondroplasia and BMN 190, a recombinant human tripeptidyl peptidase-1 (rhTPP1) for the treatment of late-infantile neuronal ceroid lipofuscinosis (CLN2), a form of Batten Disease. For additional information, please visit www.BMRN.com. Information on BioMarin's 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: the development of PEG PAL, an experimental therapy, for the management of phenylketonuria or PKU. 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 clinical trials of PEG PAL; our ability to successfully manufacture PEG PAL; the content and timing of decisions by the U.S. Food and Drug Administration and other regulatory authorities concerning PEG PAL; and those risks that are discussed in BioMarin's filings with the Securities and Exchange Commission, including, without limitation, BioMarin's 2012 Annual Report on Form 10-K, and our periodic reports on Form 10-Q and Form 8-K. 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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