Rhythm Pharmaceuticals to Present at the 59th Annual ESPE Meeting

August 12, 2021

Company announces acceptance of seven abstracts with data from multiple clinical trials evaluating setmelanotide for rare genetic diseases of obesity

BOSTON, Aug. 12, 2021 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company committed to transforming the care of people living with rare genetic diseases of obesity, today announced that it will present data from multiple clinical trials at the 59th Annual European Society for Paediatric Endocrinology (ESPE) Meeting to be held virtually September 22-26, 2021.

In total, Rhythm and its clinical collaborators will present seven abstracts. This includes three oral presentations detailing results from a pivotal Phase 3 clinical trial evaluating setmelanotide in Bardet-Biedl Syndrome and results from the Company's Phase 2 basket trial evaluating setmelanotide in obesity due to SRC1 variants or SH2B1 variants. Four additional abstracts have been accepted for poster presentation.

In addition to the company's accepted abstracts, a principal investigator for Phase 3 clinical trials that evaluated setmelanotide in obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency, Peter Kühnen, M.D., University of Duisburg-Essen, Berlin, Germany, will participate in an ESPE-organized symposium, "Management of Rare Obesity," on Wednesday, September 22nd from 2:45-3:45pm CET with a presentation titled, "Setmelanotide in the treatment of rare obesity syndromes."

Full details on the oral presentations are as follows.

Oral presentations on Wednesday, September 22nd
4:05-5:05pm CET
Free Communications 2 - Fat, Metabolism and Obesity

- **4:05pm CET: Efficacy and Safety Results of a Phase 2 Trial of Setmelanotide in Obesity Due to SH2B1 Variants and 16p11.2 Deletion Syndrome**
  Cecilia Scimia, Medical Director, Rhythm Pharmaceuticals

- **4:15pm CET: Phase 3 Trial of Setmelanotide in Participants with Bardet-Biedl Syndrome: Placebo-Controlled Results**
  Jesús Argente, Department of Pediatrics and Pediatric Endocrinology, Universidad Autónoma de Madrid, University Hospital Niño Jesús, CIBER "Fisiopatología de la obesidad y nutrición" (CIBEROBN), Instituto de Salud Carlos III, IMDEA Institute, Madrid, Spain

- **4:25pm CET: A Phase 2 Trial of the Melanocortin-4 Receptor Agonist Setmelanotide in Obesity Due to SRC1 Insufficiency: Body Weight, Body Mass Index Z Score, and Safety Results**
  Sadaf Farooqi, Wellcome-MRC Institute of Metabolic Science and NIHR Cambridge Biomedical Research Centre, University of Cambridge, Cambridge, UK

Poster presentations

- Efficacy and Safety of Setmelanotide in Individuals with Obesity Due to POMC or LEPR Deficiency: Phase 3 Results from Pivotal and Supplemental Cohorts
  Jennifer Miller, Division of Pediatric Endocrinology, University of Florida

- Design of a Phase 2, Double-Blind, Placebo-Controlled Trial of Setmelanotide in Patients with Genetic Variants in the Melanocortin-4 Receptor Pathway
  Cecilia Scimia, Medical Director, Rhythm Pharmaceuticals

- An Evidence-based Framework to Evaluate Melanocortin-4 Receptor (MC4R) Pathway Relevance for Obesity-associated Genes
  Bhavik Shah, Senior Director Translational Research and Nonclinical Development, Rhythm Pharmaceuticals

- Frequency of MC4R Pathway Variants in a Large US Cohort of Pediatric and Adult Patients with Severe Obesity
  Ida Moeller, Director of Biomedical Informatics, Rhythm Pharmaceuticals

Details on the poster presentations will be announced at a later date.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the treatment paradigm for people living with rare genetic diseases of obesity. The Company's precision medicine, IMCIVREE (setmelanotide), was approved in November 2020 by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency confirmed by genetic testing and by the European Commission (EC) in July 2021 for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. IMCIVREE is the first-ever FDA-approved and EC-authorized therapy for these rare genetic diseases of obesity. Rhythm is advancing a broad clinical development program for setmelanotide in other rare genetic diseases of obesity. The Company is leveraging the Rhythm Engine and the largest known obesity DNA database - now with approximately 37,500 sequencing samples - to improve the understanding, diagnosis and care of people living with severe obesity due to certain genetic deficiencies. The company is based in Boston, MA.

IMCIVREE® (setmelanotide) Indication
In the United States, IMCIVREE is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency. The condition must be confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

In the EU, IMCIVREE is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. IMCIVREE should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

Limitations of Use
IMCIVREE is not indicated for the treatment of patients with the following conditions as IMCIVREE would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1, or LEPR deficiency with *POMC*, *PCSK1*, or *LEPR* variants classified as benign or likely benign;
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Important Safety Information

WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Sexual adverse reactions may occur in patients treated with IMCIVREE. Spontaneous penile erections in males and sexual adverse reactions in females occurred in clinical studies with IMCIVREE. Instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Depression and Suicidal Ideation: Some drugs that target the central nervous system, such as IMCIVREE, may cause depression or suicidal ideation. Monitor patients for new onset or worsening of depression. Consider discontinuing IMCIVREE if patients experience suicidal thoughts or behaviors.

Skin Pigmentation and Darkening of Pre-Existing Nevi: IMCIVREE may cause generalized increased skin pigmentation and darkening of pre-existing nevi due to its pharmacologic effect. This effect is reversible upon discontinuation of the drug. Perform a full body skin examination prior to initiation and periodically during treatment with IMCIVREE to monitor pre-existing and new skin pigmentary lesions**.**

Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants: IMCIVREE is not approved for use in neonates or infants.

ADVERSE REACTIONS

- The most common adverse reactions (incidence ≥23%) were injection site reactions, skin hyperpigmentation, nausea, headache, diarrhea, abdominal pain, back pain, fatigue, vomiting, depression, upper respiratory tract infection, and spontaneous penile erection.

USE IN SPECIFIC POPULATIONS
Discontinue IMCIVREE when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

Treatment with IMCIVREE is not recommended for use while breastfeeding.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See Full Prescribing Information for IMCIVREE.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy, and regulatory and clinical progress of setmelanotide, our expectations surrounding potential regulatory submissions, approvals and timing thereof, our business strategy and plans, including regarding commercialization of setmelanotide, and our participation in upcoming events and presentations. Statements using word such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, the impact of our management transition, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, the impact of competition, the ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, our liquidity and

expenses, the impact of the COVID-19 pandemic on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and general economic conditions, and the other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2021 and our other filings with the Securities and Exchange Commission. Except as required by law, we undertake no obligations to make any revisions to the forward-looking statements contained in this release or to update them to reflect events or circumstances occurring after the date of this release, whether as a result of new information, future developments or otherwise.

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