Rhythm Pharmaceuticals Announces Positive Interim Data from Long-term Extension Study of Setmelanotide in Bardet-Biedl Syndrome (BBS)

February 16, 2022

-- Patients with BBS achieved deepened and sustained weight loss at 24 months on setmelanotide therapy --

-- Company to provide update on U.S. BBS commercial readiness during virtual event today at 4 p.m. ET --

BOSTON, Feb. 16, 2022 (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 positive interim data from its long-term extension study evaluating setmelanotide in patients with Bardet-Biedl Syndrome (BBS).

Rhythm will review these data, as well as provide an update on ongoing preparations in support of a potential U.S. commercial launch of IMCIVREE (setmelanotide) for the treatment of obesity and hyperphagia in patients with BBS, during a virtual event for investors and analysts beginning today at 4 p.m. ET. This event will also feature guest speakers, who will discuss their experience living with BBS or caring for patients and their families.

“There is a significant need for an effective therapy for patients with BBS for the hyperphagia, or pathological hunger, and severe obesity that manifests in childhood,” said Bob Haws, M.D., Director of Clinical Research Center at the Marshfield Clinic Research Institute and Director of the Center of Excellence for Bardet-Biedl Syndrome, who will present interim data from Rhythm’s long-term extension trial of setmelanotide in patients with BBS today. “With these long-term data, we are encouraged to see that the clinically meaningful weight loss and reduction of hyperphagia in patients at one year on therapy was sustained and even deepened at two years on setmelanotide, without specific dietary and exercise support.”

Of the patients enrolled in Rhythm’s long-term extension trial, 19 individuals with BBS have reached 24 months on therapy. As of a data cutoff date of October 29, 2021:

- The mean percent reduction in body mass index (BMI) from pivotal trial baseline was -14.3% (n=19);
- The mean percent reduction in body weight from pivotal trial baseline among patients 18 years of age or older was -14.9% (n=6);
- The mean reduction in BMI Z score from pivotal trial baseline among patients younger than 18 was -0.72 (n=12).[1,2]

Consistent with prior clinical observations, setmelanotide was generally well-tolerated in the long-term extension study and no new safety signals were observed. Rhythm plans to present detailed results from this study at a major medical meeting later this year.

In addition to Dr. Haws, guest speakers at Rhythm’s BBS event today include Mary Morris, parent to two people living with BBS, and Rushika Conroy, M.D., M.S., Medical Director, Pediatric Weight Management and Type 2 Diabetes programs at Baystate Children's Hospital and Associate Professor of Pediatrics at University of Massachusetts Chan Medical School – Baystate.

Also at the event, Rhythm management will provide an update on ongoing preparations in support of a U.S. commercial launch of setmelanotide for the treatment of obesity and hyperphagia in individuals with BBS, pending approval by the U.S. Food and Drug Administration (FDA). A supplemental New Drug Application (NDA) for IMCIVREE (setmelanotide) for the treatment of patients with BBS or Alström syndrome is currently under review by the U.S. Food and Drug Administration (FDA), and has been assigned a Prescription Drug User Fee Act (PDUFA) goal date of March 16, 2022. A Type II variation application has also been submitted to the European Medicines Agency (EMA) for the treatment of obesity and control of hyperphagia in adult and pediatric patients six years of age and older with BBS or Alström syndrome.

Webcast Information:
The live webcast of today’s event will be available under “Events and Presentations” in the Investors & Media section of Rhythm’s website at http://www.rhythmtx.com. A replay of the webcast will be available on Rhythm’s website for at least 30 days following the event.

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. Rhythm’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 in July and September 2021, respectively, by the European Commission (EC) and Great Britain’s Medicines & Healthcare Products Regulatory Agency (MHRA) 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- and MHRA-authorized therapy for patients with these rare genetic diseases of obesity. The Company submitted a supplemental New Drug Application (sNDA) to the FDA, which was accepted for filing in November 2021 and assigned a Prescription Drug User Fee Act (PDUFA) goal date of March 16, 2022, and submitted a Type II variation application to the European Medicines Agency in October 2021 seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hyperphagia in adult and pediatric patients 6 years of age and older with BBS or Alström syndrome in both the United States and European Union. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare genetic diseases of obesity and is leveraging the Rhythm Engine and the largest known obesity DNA database -- now with approximately 45,000 sequencing samples -- to improve the understanding, diagnosis and care

of people living with severe obesity due to certain genetic deficiencies. Rhythm's headquarters is 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, confirmed by an FDA-approved genetic test demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

In the EU and Great Britain, 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, EU SmPC and MHRA SmPC 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, including with respect to the long-term extension study, 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, 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 ability to successfully commercialize setmelanotide, 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 September 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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[1] BMI Z score measures standard deviations beyond the norm and account for weight, height, gender and age in children.

[2] For one patient who was 17 years old when enrolled and at baseline in the pivotal trial, BMI Z score could not be calculated as this patient was 20 years old at 24 months on therapy.

Source: Rhythm Pharmaceuticals, Inc.