Rhythm Pharmaceuticals Presents New Data from Long-term Extension Trial Evaluating Setmelanotide in Bardet-Biedl Syndrome or POMC or LEPR Deficiency Obesity at ENDO 2022

June 13, 2022

-- Sustained weight loss observed following 18 to 36 months on therapy --

-- Setmelanotide shown to be well-tolerated for up to three years of treatment --

-- Data support continued efficacy and long-term use of setmelanotide in patients with BBS or POMC or LEPR deficiency obesity --

BOSTON, June 13, 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 new data from the Company's long-term extension (LTE) trial, which show continued body mass index (BMI) and weight reductions in patients with Bardet-Biedl syndrome (BBS) or POMC or LEPR deficiency obesity (biallelic) receiving between 18 months and three years of setmelanotide therapy. Rhythm and its collaborators delivered these data in poster presentations at the Endocrine Society Annual Meeting & Expo (ENDO), being held June 11-14, 2022 in Atlanta.

"These presentations build on our strong pivotal trial data and further illustrate setmelanotide's ability to safely deliver sustained, clinically meaningful weight loss for individuals living with severe obesity caused by BBS, or by POMC or LEPR deficiency," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "Responses to our precision therapy are shown to be durable, with both adult and pediatric patients experiencing continued reductions in body weight-related measures throughout the long-term extension. This supports our belief in setmelanotide as a chronic therapy across our approved or registration-stage indications. As we approach the June 16 PDUFA goal date for BBS, we are eager to deliver setmelanotide to the waiting community, and we look forward to offering patients and their families a safe, effective medicine that can provide lasting benefit."

Bardet-Biedl Syndrome
A total of 42 patients with BBS who were treated with setmelanotide in Rhythm's Phase 2 or Phase 3 trial continued into the LTE. As of the data cutoff, 30 and 19 of these patients had received at least 18 and 24 months of setmelanotide therapy, respectively. The data were presented in a poster, "Long-term Efficacy of Setmelanotide in Patients with Bardet-Biedl Syndrome," by Jesús Argente, M.D., Ph.D., Universidad Autónoma de Madrid in Spain. Highlights include:

- Mean (SD) percent change in BMI across all patients was −9.5% (10.5%; n=30) and −14.3% (11.6%; n=19) at 18 and 24 months, respectively;
- Patients 18 years old or older achieved a percent change in weight of −8.6% (10.3%; n=15) and −14.9% (10.4%; n=6) at 18 and 24 months of treatment, respectively;
- Six of 15 patients (40%) and five of six patients (83.3%) achieved ≥10% weight reduction at 18 and 24 months of treatment, respectively;
- Patients younger than 18 years old achieved a mean (SD) change in BMI Z score of −0.83 (0.50; n=13) and −0.72 (0.54; n=12) at 18 and 24 months of treatment, respectively;
- All patients younger than 18 years of age had a BMI Z score reduction of ≥0.2 points. Twelve of 13 patients (92.3%) and 9 of 12 patients (75%) younger than 18 years of age achieved BMI Z score reductions of ≥0.3 points at 18 and 24 months of treatment, respectively; and
- As of the data cutoff, a total of 38 patients were receiving ongoing treatment in the LTE trial; four patients discontinued treatment, one due to an adverse event that was not related to treatment.

POMC or LEPR deficiency obesity (biallelic)
A total of 24 patients with POMC or LEPR deficiency obesity who were treated with setmelanotide in Rhythm's Phase 2 or Phase 3 trial continued into the LTE. As of the data cutoff, 21 and 15 of these patients had received at least 24 or 36 months of setmelanotide therapy, respectively. These data were presented in a poster entitled, "Long-term Efficacy of Setmelanotide in Patients With POMC or LEPR Deficiency Obesity," by Karine Clément, M.D., Ph.D., Professor of Nutrition at Pitié-Salpêtrière Hospital, Sorbonne Université and Head of the INSERM Nutriomics Laboratory in Paris. Highlights include:

- Across all patients, mean (SD) percent change in BMI was −16.7% (16.0%; n=21) and −17.5% (20.5%; n=15) after 24 and 36 months of treatment, respectively.
- Patients 18 years old or older achieved a mean (SD) percent change in body weight of −16.7% (16.2%; n=10) and −13.5%

(15.9%; n=8) after 24 and 36 months of treatment, respectively.
- Seven of 10 patients (70%) and five of eight patients (62.5%) achieved ≥10% weight reduction after 24 and 36 months of treatment, respectively.
- Patients younger than 18 years old achieved a mean (SD) change in BMI Z score of −0.94 (0.95; n=10) and −0.73 (1.41; n=4) after 24 and 36 months, respectively.
- Eight of 10 patients (80%) and two of four patients (50%) younger than 18 years old achieved BMI Z score reductions of ≥0.3 points at 24 and 36 months of treatment, respectively.
- As of the data cutoff, a total of 24 patients were receiving ongoing treatment in the LTE trial; three patients discontinued treatment, none due to adverse events.

Consistent with prior clinical observations, setmelanotide was generally well tolerated in the LTE trial across both indications and no new safety signals were observed.

The data presented from each LTE trial cohort were all as of a cutoff date of Oct. 29, 2021.

All Rhythm's presentations from ENDO will be available on the Publications and Presentations section of its website: https://www.rhythmtx.com/publications/.

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 is currently assigned a Prescription Drug User Fee Act (PDUFA) goal date of June 16, 2022, for the treatment of obesity and control of hunger in adult and pediatric patients six years of age and older with Bardet-Biedl Syndrome (BBS) or Alström syndrome. A Type II variation application to the European Medicines Agency seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS also is under review. 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. 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 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 the anticipated timing for initiation of clinical trials and release of clinical trial data and our expectations surrounding potential regulatory submissions, approvals and timing thereof, our business strategy and plans 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 quarter ended March 31, 2022 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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