Rhythm Pharmaceuticals Presents Data from its Long-term Extension Study of Setmelanotide Showing Sustained and Deepened BMI Reduction in Patients with Hypothalamic Obesity at One Year at ObesityWeek® 2023

October 17, 2023

-- Patients with hypothalamic obesity (n=12) achieved mean BMI reduction of 25.5% at one year on setmelanotide treatment --

-- Three of 11 pediatric patients with hypothalamic obesity achieved normal weight at one year based on NIH, WHO weight classifications --

-- Additional long-term study data show clinically relevant weight reductions in patients with Bardet-Biedl syndrome and POMC or LEPR deficiency obesity --

-- Conference call scheduled for October 18, 2023, at 8:00 a.m. ET --

BOSTON, Oct. 17, 2023 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company focused on transforming the lives of patients and their families living with hyperphagia and severe obesity caused by rare melanocortin-4 receptor (MC4R) pathway diseases, today announced several data presentations showing that setmelanotide therapy resulted in sustained and deepened weight loss in patients with severe obesity caused by rare MC4R pathway diseases during The Obesity Society's Annual Meeting at ObesityWeek ®.

Rhythm and its collaborators delivered a total of six presentations at the conference in Dallas from October 14 to 17. Presentation highlights include the following results from Rhythm's open-label, long-term extension studies evaluating setmelanotide in individuals with hypothalamic obesity, Bardet-Biedl syndrome (BBS) or obesity due to POMC or LEPR deficiency, as of a data cutoff date of June 13, 2023:

- 25.5% reduction in mean body mass index (BMI) from baseline in patients with hypothalamic obesity (n=12) at one year;
- 16.0% reduction in mean BMI in adult patients with Bardet-Biedl syndrome (BBS) (n=9) at three years;
- 0.7 reduction in mean BMI Z score in pediatric patients younger than 18 with BBS (n=15) at three years;
- 20.3% reduction in mean BMI in adult patients with obesity due to POMC or LEPR deficiency (n=11) at four years; and
- 1.2 reduction in mean BMI Z score in pediatric patients younger than 18 due to POMC or LEPR deficiency at four years.

"We are excited to highlight the data showing meaningful, long-term benefits of setmelanotide in patients living with hyperphagia and severe obesity caused by rare MC4R pathway diseases at ObesityWeek," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "We believe the one-year BMI reduction of more than 25% in patients with hypothalamic obesity – where individuals trended towards normal body weight – is particularly encouraging as it shows continued improvement over our previously reported 16-week and six-month data. The hypothalamic obesity data affirm our confidence as we advance our pivotal, Phase 3 trial and work to bring setmelanotide to patients and families facing this challenging disease for which there are no approved, effective therapies."

Hypothalamic Obesity Data at One Year
Twelve patients who enrolled in Rhythm's open-label, 16-week Phase 2 trial and who also enrolled in the long-term extension trial and reached one year or more on setmelanotide were included in the one-year data analysis. In addition to the BMI and BMI Z score reductions provided above, highlights from the late-breaking poster, "Weight Reduction in Patients With Hypothalamic Obesity Treated with Setmelanotide for 12 Months" by lead author Christian L. Roth, M.D., Seattle Children's Research Institute, include:

- Mean change of -1.1 in BMI Z score from baseline in pediatric patients (n=11) at one year on therapy;
- Three of 11 pediatric patients achieved normal weight at one year, as defined by the U.S. National Institutes of Health (NIH) and World Health Organization (WHO) (>5th to <85th BMI percentile);
- Eleven of 12 patients (91.7%) improved by one or more weight classes based on BMI or BMI percentile as defined by the NIH and WHO; and
- Body composition changes were favorable, with larger percent decreases in total fat mass compared with lean muscle mass.

There were no serious adverse events (AE), no AEs that led to study discontinuation during the trial, and no new safety concerns were observed.

Bardet-Biedl Syndrome Data at Three Years
Three years of treatment with setmelanotide showed sustained, meaningful benefit in weight-related measures in patients with BBS, as reported in a poster entitled, "3-Year Setmelanotide Weight Outcomes in Patients with Bardet-Biedl Syndrome and Obesity" by lead author Jack Yanovski, M.D., Ph.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health.

POMC and LEPR Deficiency Data at Four Years
Long-term treatment with setmelanotide demonstrated sustained weight-related efficacy in pediatric and adult patients with obesity due to POMC or LEPR deficiency, as reported in the oral presentation, "Four-Year Setmelanotide Weight Outcomes of Patients with POMC and LEPR Deficiency

Obesity" by lead author Wendy K. Chung, M.D., Ph.D., Division of Molecular Genetics, Department of Pediatrics, Columbia University, New York, NY.

Rhythm announced additional presentations including:

- In an oral presentation, "Impact of Setmelanotide on Metabolic Syndrome Risk in Patients with POMC and LEPR Deficiency" by lead author Martin Wabitsch, M.D., Ph.D., Department of Pediatrics and Adolescent Medicine, University of Ulm in Germany, data showed intervention with setmelanotide may reduce the risk of future metabolic syndrome, cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) in patients with obesity due to POMC or LEPR deficiency obesity.
- In a poster titled, "Cardiac, Renal, and Endocrine/Diabetes Mellitus Outcomes in Children with Bardet-Biedl Syndrome" by lead author Jeremy Pomeroy, Ph.D., M.S., of the Marshfield Clinic Research Institute, researchers showed that the severity of obesity was associated with increased prevalence of cardiac, endocrine/diabetes, and renal outcomes early in life based on an analysis of 318 pediatric patients with BBS enrolled in the Clinical Registry Investigating BBS (CRIBBS). Researchers concluded that timely diagnosis and early implementation of hyperphagia and weight management strategies in pediatric patients with BBS may reduce the risk and burden associated with these comorbidities.
- In a poster titled, "Impact of Setmelanotide on Metabolic Syndrome Risk in Patients with Bardet-Biedl Syndrome" by lead author Andrea Haqq, M.D., M.H.S., Division of Pediatric Endocrinology at the University of Alberta, data showed that treatment response with one year of setmelanotide was associated with reductions in MetS-Z-BMI score in pediatric patients with BBS, which are associated with reduced risk of metabolic syndrome, CVD and T2DM.

In addition, the Company will host an investor conference call and webcast to discuss these data presentations on Wednesday, October 18, 2023, at 8:00 a.m. ET. This conference call will be accessible under "Events & Presentations" in the Investor Relations section of the Company's website at www.rhythmtx.com. A replay will be available on the Rhythm website for 30 days following the presentation.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with hyperphagia and severe obesity caused by rare melanocortin-4 receptor (MC4R) diseases. Rhythm's lead asset, IMCIVREE (setmelanotide) is approved by the U.S. Food and Drug Administration (FDA) and authorized by the European Commission (EC) and the UK's Medicines & Healthcare Products Regulatory Agency (MHRA) for use in accordance with product labeling. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare MC4R pathway diseases, as well as a preclinical suite of investigational candidates for the treatment of congenital hyperinsulinism. Rhythm's headquarters is in Boston, MA.

Setmelanotide Indication
In the United States, setmelanotide is indicated for chronic weight management in adult and[i] pediatric patients 6 years of age and older with monogenic or syndromic obesity due to POMC, PCSK1 or LEPR deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1 or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS) and BBS.

In the European Union, setmelanotide is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS) or genetically confirmed loss-of-function biallelic proopiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.

In Canada, setmelanotide is indicated for the treatment of obesity due to Bardet-Biedl syndrome (BBS) or genetically-confirmed biallelic pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance in adults and children 6 years of age and above.

Limitations of Use
Setmelanotide is not indicated for the treatment of patients with the following conditions as setmelanotide 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, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity.

In Europe, Setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

WARNINGS AND PRECAUTIONS

Skin Monitoring: Setmelanotide may lead to generalized increased skin pigmentation and darkening of pre-existing naevi because of its pharmacologic effect. Full body skin examinations should be conducted annually to monitor pre-existing and new skin pigmentary lesions before and during treatment with setmelanotide.

Heart Rate and Blood Pressure Monitoring: Heart rate and blood pressure should be monitored as part of standard clinical practice at each medical visit (at least every 6 months) for patients treated with setmelanotide.

Prolonged Penile Erection: Spontaneous penile erections have been reported in clinical trials with setmelanotide. Patients who have a penile erection lasting longer than 4 hours should be instructed to seek emergency medical attention for potential treatment of priapism.

Depression: In clinical trials, depression has been reported in patients treated with setmelanotide. Patients with depression should be monitored at each medical visit during treatment with setmelanotide. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors.

Pediatric Population: The prescribing physician should periodically assess response to setmelanotide therapy. In growing children, the impact of weight loss on growth and maturation should be evaluated. The prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

Excipients: This medicinal product contains 10 mg benzyl alcohol in each ml. Benzyl alcohol may cause allergic reactions. Patients who are pregnant or breastfeeding should be advised of the potential risk from the excipient benzyl alcohol, which might accumulate over time and cause metabolic acidosis. This medicinal product should be used with caution in patients with hepatic or renal impairment, because of the potential risk from the excipient benzyl alcohol which might accumulate over time and cause metabolic acidosis.

Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free.”

ADVERSE REACTIONS
The most frequent adverse reactions are hyperpigmentation (51%), injection site reaction (39%), nausea (33%), and headache (26%).

USE IN SPECIFIC POPULATIONS

Pregnancy
There are no data from the use of setmelanotide in pregnant women. Animal studies do not indicate direct harmful effects with respect to reproductive toxicity. However, administration of setmelanotide to pregnant rabbits resulted in decreased maternal food consumption leading to embryo-fetal effects. As a precautionary measure, setmelanotide should not be started during pregnancy or while attempting to get pregnant as weight loss during pregnancy may result in fetal harm. If a patient who is taking setmelanotide has reached a stable weight and becomes pregnant, consideration should be given to maintaining setmelanotide treatment as there was no proof of teratogenicity in the nonclinical data. If a patient who is taking setmelanotide and still losing weight gets pregnant, setmelanotide should either be discontinued, or the dose reduced while monitoring for the recommended weight gain during pregnancy. The treating physician should carefully monitor weight during pregnancy in a patient taking setmelanotide.

Breast-feeding
It is unknown whether setmelanotide is excreted in human milk. A nonclinical study showed that setmelanotide is excreted in the milk of nursing rats. No quantifiable setmelanotide concentrations were detected in plasma from nursing pups. A risk to the newborn/infant cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from setmelanotide therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the mother.

Fertility
No human data on the effect of setmelanotide on fertility are available. Animal studies did not indicate harmful effects with respect to fertility.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337. See Summary of Product Characteristics’ APPENDIX V for a list of European national reporting systems to communicate adverse reactions.

Please see the full Prescribing Information for additional Important Safety Information.

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 and our other preclinical investigational candidates, including with respect to our Phase 3 clinical trial evaluating setmelanotide in hypothalamic obesity, the open-label, long-term extension studies evaluating setmelanotide in individuals with hypothalamic obesity, BBS or obesity due to POMC or LEPR deficiencies, the potential benefits of setmelanotide for patients, including those with BBS and hypothalamic obesity, and our participation in upcoming events and presentations. Statements using words 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, risks relating to our liquidity and expenses, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, the ability to achieve necessary regulatory approvals, risks associated with data analysis and reporting, failure to identify and develop additional product candidates, unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, risks associated with the laws and regulations governing our international operations and the costs of any related compliance programs, our ability to obtain or maintain orphan drug designations for setmelanotide or to obtain or maintain exclusivity in any use, the impact of competition, risks relating to product liability lawsuits, inability to maintain our collaborations, or the failure of these collaborations, our reliance on third parties, risks relating to intellectual property, our ability to hire and retain necessary personnel, the impact of the COVID-19 pandemic and general economic conditions on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and the other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended June 30, 2023 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.

Corporate Contact:
David Connolly
Executive Director, Investor Relations and Corporate Communications
Rhythm Pharmaceuticals, Inc.
857-264-4280
dconnolly@rhythmtx.com

Media Contact:
Adam Daley
Berry & Company Public Relations
212-253-8881
adaley@berrypr.com

Source: Rhythm Pharmaceuticals, Inc.