Rhythm Pharmaceuticals Announces CMO Transition

September 2, 2021

-- Linda Shapiro Manning, M.D., Ph.D., promoted to Chief Medical Officer, effective Sept. 10 --
-- CMO Murray Stewart, M.D., to transition to Senior Medical Advisor --

BOSTON, Sept. 02, 2021 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a biopharmaceutical company aimed at developing and commercializing therapies for the treatment of rare genetic diseases of obesity, today announced Linda Shapiro Manning, M.D., Ph.D., Senior Vice President, Clinical, will be promoted to Chief Medical Officer (CMO) effective September 10, 2021. She will succeed Murray Stewart, M.D., who will transition from his current role to Senior Medical Advisor effective as of the same date.

"We are thrilled to promote Linda to CMO as we initiate our next wave of clinical trials, including our pivotal EMANATE Phase 3 trial and DAYBREAK Phase 2 trial. Linda already has made meaningful contributions across our clinical development, medical and regulatory efforts since coming on board as a senior vice president in July," said David Meeker, Chair, President and Chief Executive Officer of Rhythm. "With her strong track record both as a practicing physician specializing in obesity and deep experience in multiple leadership roles in the biopharmaceutical industry, Linda is the right leader for Rhythm as we expand our understanding of setmelanotide in the treatment of rare genetic diseases of obesity."

Dr. Shapiro joined Rhythm as Senior Vice President, Clinical, in July, bringing more than 20 years of experience in obesity medicine. She spent the previous decade in the biopharmaceutical industry, with clinical development and medical affairs roles at Applied Therapeutics, Boehringer Ingelheim, Merck and Novo Nordisk. In these roles, she led clinical development for assets in type 2 diabetes and cardiometabolic conditions and, at Novo Nordisk, she served as head of medical science and international medical director for the company's GLP-1 and obesity global development programs. Prior to joining industry, Dr. Shapiro practiced medicine in Colorado, obtaining certification and specializing in obesity medicine. She holds a Ph.D. and completed a post-doctoral research fellowship in kinesiology and applied physiology from the University of Colorado, an M.D. from Tulane University School of Medicine, and a bachelor's degree in exercise science from the University of Southern California.

Dr. Shapiro said, "I am excited about what Rhythm is ready to accomplish. Murray has built capable and competent teams across clinical, medical and regulatory as well as positive relationships with external collaborators, and I look forward to leading these teams forward and further supporting the collaborations as we advance our mission of transforming the care of patients with rare diseases of obesity. Setmelanotide has already established itself as a first-in-class precision medicine for people living with obesity due to POMC, PCSK1 or LEPR deficiency, and I believe it has the potential to provide similarly meaningful benefit to people with obesity caused by variants in many other genes in the MC4R pathway."

Dr. Meeker concluded, "Murray has been instrumental in establishing Rhythm as the leader in the development of new medicines and transforming the care for patients with rare genetic diseases of obesity and developing a community of health care providers, patients, caregivers and patient advocates. He led efforts to secure our first U.S. and European approvals, gain regulatory alignment for multiple phase 2 and 3 trials of setmelanotide and prepare Bardet-Biedl and Alström syndrome regulatory submissions. As Murray transitions from the CMO role, we are in a strong position to continue advancing setmelanotide and will be able to continue to leverage Murray's knowledge and experience as an active senior medical advisor supporting our BBS regulatory submissions and clinical development efforts. We look forward to continuing to benefit from Murray's involvement."

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 and EC-approved therapy for patients with 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, and expectations regarding the CMO transition. 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 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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