Rhythm Pharmaceuticals Announces Preliminary Fourth Quarter and Full Year 2024 Net Product Revenues, Pipeline Advancements and Upcoming Milestones

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-- Preliminary unaudited net revenues from global sales of IMCIVREE® (setmelanotide) of approximately $42 million for the fourth quarter of 2024 and approximately $130 million for the full year of 2024 --

-- On track to report topline data from global Phase 3 trial evaluating setmelanotide in acquired hypothalamic obesity in the first half of 2025 --

-- Completed enrollment in supplemental Japanese cohort of Phase 3 trial of setmelanotide in acquired hypothalamic obesity --

-- Completed enrollment in two substudies in Phase 3 EMANATE trial of setmelanotide in genetically-caused MC4R pathway diseases --

-- Plan to initiate new Phase 2 trial exploring setmelanotide in Prader-Willi syndrome --

BOSTON, Jan. 10, 2025 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company focused on transforming the lives of patients living with rare neuroendocrine diseases, today announced preliminary unaudited net revenues from global sales of IMCIVREE® (setmelanotide) for the fourth quarter and full year of 2024, pipeline advancement updates and upcoming milestones.

“Rhythm enters 2025 poised for the next level of growth. Over the past two years, we have established the commercial viability of our rare MC4R pathway diseases franchise by demonstrating steady continued growth in an increasing number of countries, and this year we are looking forward to a series of readouts from our robust clinical development pipeline,” said David Meeker, M.D., Chairman, Chief Executive Officer and President of Rhythm. “Our Phase 3 trial in acquired hypothalamic obesity (HO) remains on track, and we completed enrollment in the supplemental 12-patient Japanese cohort which will form the basis for a Japanese regulatory filing and the significant opportunity to treat hypothalamic obesity there. We are set to begin our congenital HO substudy with the potential to further expand the opportunity related to injury to and or failure of the hypothalamus to develop. These indications represent significant unmet medical needs and potentially transformative opportunities for Rhythm.”

Dr. Meeker continued, “We have completed enrollment of what we believe to be the two most promising substudies in the Phase 3 EMANATE trial. Based on the unmet need and severity of Prader-Willi syndrome (PWS) and learnings from our initial study, we plan to initiate an exploratory Phase 2 study with higher doses of setmelanotide over a longer duration of 6 months. As we previously indicated, 2024 was a year of execution and we expect 2025 will be a year of readouts.”

Preliminary Unaudited Fourth Quarter and Full Year 2024 Net Product Revenues
Based on preliminary unaudited financial information, Rhythm expects net revenues from global sales of IMCIVREE to be approximately $42 million for the fourth quarter of 2024, an increase of 26% percent on a sequential basis from the third quarter of 2024. Net revenues for the full year of 2024 are expected to be approximately $130 million, compared to $77.4 million for the full year of 2023. The sequential quarter over quarter increase was due to growth in reimbursed patients on therapy and inventory growth in the United States. U.S. sales of IMCIVREE contributed approximately 74% of fourth quarter preliminary unaudited net product revenues and approximately 73% of full-year 2024 revenues. The Company plans to report its fourth quarter and full year 2024 financial results in late February 2025.

Pipeline Advancement and Upcoming Milestones

Setmelanotide

Acquired Hypothalamic Obesity (HO)

- The Company is on track to report topline data from the pivotal, 120-patient cohort of its global, Phase 3 trial evaluating setmelanotide in acquired HO in the first half of 2025.
- Rhythm has completed enrollment in its supplemental, 12-patient Japanese cohort of the global Phase 3 trial evaluating setmelanotide in acquired HO. Data from this supplemental cohort will serve as the basis for a regulatory submission in Japan.

Congenital HO

- Rhythm anticipates enrolling the first patients with congenital HO in a 34-week substudy of the ongoing global Phase 3 trial in the first quarter of 2025. This substudy is independent from the pivotal Phase 3 trial in acquired hypothalamic obesity.

Genetically Caused MC4R Pathway Diseases

- Rhythm completed enrollment in the Phase 3 EMANATE trial, which is comprised of four substudies: SH2B1 (n=121); POMC and/or PCSK1 (n=79); SRC1 (n=73); and LEPR (n=23). The four-substudy design of this trial allows for independent data readouts and potential registration for each genetic cohort. The primary endpoint for each substudy is the difference in mean percent change in BMI from baseline to 52 weeks in setmelanotide arm compared to placebo arm. The Company anticipates reporting topline data from the Phase 3 EMANATE trial in the first half of 2026.

Prader-Willi Syndrome (PWS)

- Today, Rhythm announced it plans to initiate a new, 26-week, open-label Phase 2 trial evaluating setmelanotide for treatment of PWS in the first quarter of 2025. Rhythm plans to enroll up to 20 patients with PWS and obesity aged 6 to 65 years old. Patients will be dose escalated to 5 mg/day, as tolerated. The primary endpoints are safety and tolerability. Key secondary endpoints will assess weight, hyperphagia, behavior and pharmacokinetics. This trial will be conducted at a single site in the United States.

- PWS is a rare genetic disorder that results in a number of physical, mental and behavioral problems. A key feature of PWS is a constant sense of hunger that usually begins at about 2 years of age. PWS is estimated to affect approximately 400,000 people worldwide and approximately 20,000 people in the United States. Currently, there are no approved therapies for the treatment of PWS that effectively reduce extreme hyperphagia or address low energy expenditure.

Bivamelagon (LB54640)

- Rhythm is on track to complete enrollment in the Phase 2 trial evaluating bivamelagon, an oral MC4R agonist, in acquired HO in the first quarter of 2025.

RM-718

- Following acceptance of a protocol amendment, Rhythm expects to begin dosing patients with acquired HO in Part C of the Phase 1 trial evaluating RM-718, a weekly MC4R agonist, in the first quarter of 2025. The Company plans to enroll up to 30 patients with acquired hypothalamic obesity for 16 weeks in Part C of this Phase 1 trial.

Financial Disclosure Advisory
This release contains certain estimated preliminary financial results for the fourth quarter and fiscal year ended December 31, 2024. These estimates are based on the information available to the Company at this time. The Company's financial closing procedures for the fourth quarter and full year 2024 are not yet complete and, as a result, actual results may vary from the estimated preliminary results presented here due to the completion of the Company's financial closing and audit procedures. The estimated preliminary financial results have not been audited or reviewed by the Company's independent registered public accounting firm. These estimates should not be viewed as a substitute for the Company's full interim or annual financial statements. Accordingly, you should not place undue reliance on this preliminary data.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with rare neuroendocrine diseases. Rhythm's lead asset, IMCIVREE ® (setmelanotide), an MC4R agonist designed to treat hyperphagia and severe obesity, is approved by the U.S. Food and Drug Administration (FDA) to reduce excess body weight and maintain weight reduction long term in adult and pediatric patients 2 years of age and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or genetically confirmed pro-opiomelanocortin (POMC), including proprotein convertase subtilisin/kexin type 1 (PCSK1), deficiency or leptin receptor (LEPR) deficiency. Both the European Commission (EC) and the UK's Medicines & Healthcare Products Regulatory Agency (MHRA) have authorized setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 2 years of age and above. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare diseases, as well as investigational MC4R agonists LB54640 and RM-718, and a preclinical suite of small molecules for the treatment of congenital hyperinsulinism. Rhythm's headquarters is in Boston, MA.

Setmelanotide Indication
In the United States, setmelanotide is indicated to reduce excess body weight and maintain weight reduction long term in adult and pediatric patients aged 2 years and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (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).

In the European Union and the United Kingdom, setmelanotide is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 2 years of age and above. In the European Union and the United Kingdom, setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

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 BBS or POMC, PCSK1, or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity

Contraindication

Prior serious hypersensitivity to setmelanotide or any of the excipients in IMCIVREE. Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported.

WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Spontaneous penile erections in males and sexual adverse reactions in females have occurred. Inform patients that these events may occur and instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Depression and Suicidal Ideation: Depression, suicidal ideation and depressed mood have occurred. Monitor patients for new onset or worsening depression or suicidal thoughts or behaviors. Consider discontinuing IMCIVREE if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported. If suspected, advise patients to promptly seek medical attention and discontinue IMCIVREE.

Skin Hyperpigmentation, Darkening of Pre-existing Nevi, and Development of New Melanocytic Nevi: Generalized or focal increases in skin pigmentation, darkening of pre-existing nevi, development of new melanocytic nevi and increase in size of existing melanocytic nevi have occurred. Perform a full body skin examination prior to initiation and periodically during treatment to monitor pre-existing and new pigmented 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. Serious and fatal adverse reactions including “gasping syndrome” can occur in neonates and low birth weight infants treated with benzyl alcohol preserved drugs.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥20%) included skin hyperpigmentation, injection site reactions, nausea, headache, diarrhea, abdominal pain, vomiting, depression, and spontaneous penile erection.

USE IN SPECIFIC POPULATIONS

Treatment with IMCIVREE is not recommended when breastfeeding. Discontinue IMCIVREE when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

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 section 4.8 of the Summary of Product Characteristics for information on reporting suspected adverse reactions in Europe.

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, potential regulatory submissions, approvals and timing thereof of setmelanotide and other product candidates, including bivamelagon (LB54640) and RM-718; the announcement of data from our clinical trials, including our global Phase 3 trial evaluating setmelanotide in patients with acquired hypothalamic obesity; the ongoing enrollment of patients in our clinical trials; the potential benefits of any of the Company’s products or product candidates for any specific disease indication or at any dosage;

expectations surrounding potential clinical trial results, regulatory submissions and approvals our business strategy and plans, including regarding the ongoing commercialization of setmelanotide, expectations surrounding net revenues and sales and reimbursement of IMCIVREE, our anticipated financial performance for any period of time, including preliminary unaudited net product revenues, for the fourth quarter and full year ending December 31, 2024, our participation in upcoming events and presentations; and the timing of any of the foregoing. 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 net revenues and anticipated financial results for the fiscal year ended December 31, 2024, 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, our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel, and general economic conditions, and the other important factors discussed under the caption “Risk Factors” in Rhythm’s Quarterly Report on Form 10-Q for the three months ended September 30, 2024 and 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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