Rhythm Pharmaceuticals Reports Second Quarter 2021 Financial Results

August 3, 2021

-- Received European Commission authorization of IMCIVREE for treatment of obesity and control of hunger associated with POMC, PCSK1 and LEPR deficiencies --

-- Setmelanotide selected for evaluation as a "Highly Specialised Technology" by Great Britain's National Institute for Health and Care Excellence --

-- On track to submit sNDA to FDA and MAA Type II amendment to EMA for setmelanotide in BBS and Alström syndromes in 2H 2021 --

-- Five new Phase 2 and 3 clinical trials planned to initiate in 2H 2021 --

-- Management to host conference call at 8 a.m. ET --

BOSTON, Aug. 03, 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 reported financial results and provided a business update for the second quarter ended June 30, 2021.

"We have made tremendous progress in the second quarter towards our goal of transforming the care of patients with rare genetic diseases of obesity globally," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "We are pleased with our first full quarter of IMCIVREE® (setmelanotide) commercial availability in the United States with positive engagements with patients, prescribers and payors. We recently secured European Commission marketing authorization 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, enabling us to expand patient access to IMCIVREE. From a market access standpoint, we are encouraged that regulatory authorities, such as National Institute for Health and Care Excellence (NICE) in the United Kingdom, recognize these obesities as rare genetic diseases for which there are no available treatment options."

Dr. Meeker continued, "In parallel, we are executing on our clinical development and regulatory strategy to bring setmelanotide to substantially more patients suffering from rare genetic diseases of obesity. We look forward to completing supplementary regulatory submissions in the second half of this year to both the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), seeking marketing authorization for setmelanotide for Bardet-Biedl and Alström syndromes, and we are excited to continue advancing our broad clinical development program in additional patient populations. With agreement from both the FDA and EMA, we are poised to initiate five clinical trials of setmelanotide: the pivotal Phase 3 EMANATE trial with five sub-studies in heterozygous POMC, PCSK1 or LEPR deficiency obesities and SRC1 and SH2B1 deficiency obesities, the Phase 2 DAYBREAK trial in 31 additional genes each with strong or very strong ties to the MC4R pathway, as well as a Phase 3 pediatrics trial for children younger than 6 and two registrational trials for our weekly formulation of setmelanotide. Taken together, we believe these efforts may enable us to help many more people with rare genetic diseases of obesity with a potential treatment for their insatiable hunger or hyperphagia and early-onset, severe obesity."

Second Quarter and Recent Business Highlights:

Pipeline and Business Developments:

POMC and LEPR Deficiency Obesities:

- In July 2021, Rhythm announced that the European Commission (EC) granted marketing authorization to IMCIVREE for the treatment of obesity and the control of hunger associated with 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 Great Britain, Rhythm's marketing authorisation application for IMCIVREE is under review by the Medicines & Healthcare Products Regulatory Agency (MHRA). The Company today announced that IMCIVREE has been selected for evaluation as a "Highly Specialised Technology" (HST) by the National Institute for Health and Care Excellence (NICE). HST is a specific status reserved for rare and severe diseases.

Bardet-Biedl Syndrome and Alström Syndrome:

- Today, Rhythm provided an update on its regulatory strategy for setmelanotide for the treatment of Alström syndrome. Based on feedback from both the FDA and EMA, Rhythm now plans to submit a supplemental New Drug Application (sNDA) to the FDA and Type II variation marketing authorization application (MAA) to the EMA in the second half of 2021, which will cover both BBS and Alström syndrome.
- Also in July 2021, Rhythm announced a collaborative research agreement with the Clinical Registry Investigating Bardet-Biedl Syndrome (CRIBBS) to initiate a population study focused on the natural history of weight gain, hyperphagia and quality of life in patients with BBS.

Additional Clinical Development Updates:

Today, Rhythm announced it has reached agreement with the FDA and EMA on five new Phase 2 and Phase 3 clinical trials, all of which the Company expects to initiate in the second half of 2021:

- **EMANATE**: a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate setmelanotide in the five genes within the melanocortin-4 receptor (MC4R) pathway in which Rhythm previously achieved proof of concept, as announced in January. This trial is comprised of five independent sub-studies evaluating setmelanotide in patients with: heterozygous POMC/PCSK1 obesity; heterozygous LEPR obesity; certain variants of the SRC1; certain variants of SH2B1 genes; or PCSK1 N221D deletions within the MC4R pathway;
- **DAYBREAK**: an exploratory, Phase 2, two-stage, placebo-controlled trial of setmelanotide in patients with variants in one of 31 additional genes with strong or very strong MC4R pathway relevance. Patients with a variant in one of the 31 genes who show an initial response to treatment with setmelanotide will enter stage 2 where they will be randomized to a placebo withdrawal arm or continuation on setmelanotide;
- **Pediatric patients:** a Phase 3, open-label trial evaluating setmelanotide in children between the ages of 2 and 6 years old with obesity due to biallelic POMC, PCSK1 or LEPR deficiency or BBS;
- **Weekly formulation:**
  - Phase 3 study in patients currently on daily setmelanotide therapy ("switch study"), that is a randomized, double-blind trial to evaluate the efficacy of daily and weekly formulations of setmelanotide in patients with obesity due to biallelic POMC, PCSK1 or LEPR deficiency or BBS;
  - Phase 3, randomized, double-blind study in patients naïve to setmelanotide therapy ("*de novo* study"), that includes a cross-over period to evaluate the weekly formulation of setmelanotide in patients with BBS.
- **Hypothalamic obesity:** In July 2021, the Company initiated an exploratory Phase 2 clinical trial evaluating setmelanotide in people living with hypothalamic obesity. Hypothalamic obesity is a rare, acquired form of extreme obesity that occurs following damage to the hypothalamic regions of the brain, which are responsible for controlling physiological functions such as hunger and weight regulation. Rhythm believes a subset of patients with hypothalamic obesity have the potential to see reductions in weight and hunger with setmelanotide if their MC4 receptor is sufficiently intact.

Corporate

- In July 2021, Rhythm announced an exclusive distribution agreement with Medison Pharma, a leading commercial partner for highly innovative therapies in international markets, for Medison to commercialize IMCIVREE in Israel.
- In July 2021, the Company announced the appointments of two new senior leaders: Pamela Cramer as Chief Human Resources Officer and Linda Shapiro, M.D., Ph.D., as Senior Vice President, Clinical.

Key Upcoming Milestones:

Rhythm expects to achieve the following milestones in 2021:

Regulatory Milestones:

- Complete regulatory submissions to both the FDA and the EMA seeking marketing authorization for setmelanotide for the treatment of obesity in patients with BBS and Alström syndrome in the second half of 2021.

Additional Clinical Milestones:

- Present full data from the pivotal Phase 3 trial evaluating setmelanotide in BBS and Alström syndrome at the 59th Annual European Society for Paediatric Endocrinology (ESPE) Meeting in September 2021, following topline data presentations in March and April;
- Rhythm now anticipates announcing new topline data from the ongoing exploratory Phase 2 Basket Study evaluating setmelanotide in patients with obesity due to a variant in the MC4 receptor, as well as its study in patients with hypothalamic obesity, in the first quarter of 2022.

Second Quarter 2021 Financial Results:

- **Cash Position**: As of June 30, 2021, cash, cash equivalents and short-term investments were approximately $368.2 million, as compared to $172.8 million as of December 31, 2020. This increase includes net proceeds of $98.4 million received upon closing the sale of Rhythm's Rare Pediatric Disease Priority Review Voucher in February 2021, and net proceeds of approximately $161.7 million from Rhythm's underwritten public offering of common stock, which closed in February 2021, partially offset by cash used to fund operating activities in the first half of 2021.
- **Revenue:** Product net revenues relating to sales of IMCIVREE were $0.3 million for the second quarter of 2021. Rhythm did not generate any product revenues in the second quarter of 2020 as IMCIVREE was approved for commercial use by

the FDA in November 2020.

- **R&D Expenses:** R&D expenses were $25.1 million in the second quarter of 2021, as compared to $23.0 million in the second quarter of 2020. The year-over-year increase was primarily related to an increase of $2.3 million for purchases of setmelanotide API and drug product and increase of $1.8 million for hiring full-time employees to support increased clinical development activities; these increases were partially offset by a decrease of $1.9 million due to the absence of development milestone payments in the current quarter.
- **S,G&A Expenses:** S,G&A expenses were $15.5 million for the second quarter of 2021, as compared to $8.9 million for the second quarter of 2020. The year-over-year increase was primarily related to an increase of $4.2 million in salaries and benefits associated with additions to Rhythm's executive leadership team, increased headcount to support Rhythm's expanding business operations as well as establish its commercial operations in the United States and internationally, an increase of $1.7 million for consulting fees to support U.S. and international commercial operations and corporate legal and consulting support for Rhythm's international expansion, and an increase of $0.5 million for increased office support and insurance costs.
- **Net Loss:** Net loss was $35.4 million for the second quarter of 2021, or a net loss per basic and diluted share of $0.70, as compared to a net loss of $31.1 million for the second quarter of 2020, or a net loss per basic and diluted share of $0.71.

Year to Date 2021 Financial Results:

- **Revenue:** Product revenues relating to sales of IMCIVREE were $0.3 million for the six months ended June 30, 2021. Rhythm did not generate any product revenues in the six months ended June 30, 2020 as IMCIVREE was approved for commercial use by the FDA in November 2020.
- **R&D Expenses**: R&D expenses were $45.0 million for the six months ended June 30, 2021, as compared to $45.5 million for the six months ended June 30, 2020. The decrease was primarily due to a $2.0 million decrease related to completing the GO-ID genotyping study, the Phase 3 POMC and LEPR trials and the Phase 2 weekly formulation in early to mid-2020, as well as a $2.2 million decrease in patent and regulatory filing costs. These decreases were partially offset by increased costs related to Rhythm's ongoing extension study, BBS and renal studies. In addition, there was an increase of $3.2 million for hiring full-time employees to support increased clinical development activities and $0.7 million for purchases of setmelanotide API and drug product.
- **S,G&A Expenses**: S,G&A expenses were $30.0 million for the six months ended June 30, 2021, as compared to $21.7 million for the six months ended June 30, 2020. The increase was primarily due to an increase of $4.0 million in salaries and benefits associated with additions to Rhythm's executive leadership team, increased headcount to support Rhythm's expanding business operations as well as to establish its commercial operations in the United States and internationally, an increase of $2.1 million for consulting fees to support U.S. and international commercial operations and corporate legal and consulting support for Rhythm's international expansion, an increase of $0.6 million for increased office support and insurance, and an increase of $1.6 million associated with the expenses incurred on the sale of Rhythm's PRV to Alexion.
- **Other income, net:** Other income increased by $99.0 million in the six months ended June 30, 2021 due primarily to the sale of Rhythm's PRV in February 2021.
- **Provision for income taxes:** The Company recorded a tax provision of $17.0 million for the six months ended June30, 2021, primarily related to the sale of Rhythm's PRV, offset by a tax benefit from ordinary losses. The Company expects to have sufficient tax losses in the current year to offset the income from the sale and thus no current year liability is expected.
- **Net Income/(Loss)**: Net income was $8.4 million for the six months ended June 30, 2021, or a net income per basic and diluted share of $0.17, as compared to a net loss of $65.3 million for the six months ended June 30, 2020, or a net loss per basic and diluted share of $1.48.

Financial Guidance: Based on its current operating plans, Rhythm expects that its existing cash, cash equivalents and short-term investments as of June 30, 2021, will be sufficient to fund its operating expenses and capital expenditure requirements into at least the second half of 2023.

Conference Call Information

Rhythm Pharmaceuticals will host a live conference call and webcast at 8:00 a.m. ET today to discuss this update, as well as review its second quarter 2021 financial results and recent business activities. The conference call may be accessed by dialing (844) 498-0570 (domestic) or (409) 983-9726 (international), and referring to conference ID 6776764. A webcast of the call will be available under "Events and Presentations" in the Investor Relations section of the Rhythm Pharmaceuticals website at http://ir.rhythmtx.com/. The archived webcast will be available on Rhythm Pharmaceuticals' website approximately two hours after the conference call and will be available for 30 days following the call.

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-approved and EC-authorized therapy for 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, 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, including regarding commercialization of setmelanotide, our participation in upcoming events and presentations, and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations. 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 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.

Condensed Consolidated Statements of Operations and Comprehensive Income (Loss)
(in thousands, except share and per share data)
(Unaudited)

	Three months ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Product revenue, net	$ 274	$ —	$ 309	$ —
Costs and expenses:				
Cost of sales	137	—	141	—
Research and development	25,104	22,997	45,015	45,501
Selling, general, and administrative	15,465	8,921	29,983	21,717
Total costs and expenses	40,706	31,918	75,139	67,218
Loss from operations	(40,432)	(31,918)	(74,830)	(67,218)
Other income (expense):				
Other income	—	—	100,000	—
Interest income, net	21	801	175	1,937
Total other income, net	21	801	100,175	1,937
Income (loss) before taxes	(40,411)	(31,117)	25,345	(65,281)
Provision for income taxes	(5,022)	—	16,984	—
Net income (loss)	$ (35,389)	$ (31,117)	$ 8,361	$ (65,281)
Net income (loss) per share				
Basic	$ (0.70)	$ (0.71)	$ 0.17	$ (1.48)
Diluted	$ (0.70)	$ (0.71)	$ 0.17	$ (1.48)
Weighted-average common shares outstanding				
Basic	50,209,484	44,098,860	48,931,127	44,074,352
Diluted	50,209,484	44,098,860	49,644,704	44,074,352
Other comprehensive income (loss):				
Net income (loss)	$ (35,389)	$ (31,117)	$ 8,361	$ (65,281)
Unrealized (loss) gain on marketable securities	79	567	(28)	630
Comprehensive income (loss)	$ (35,310)	$ (30,550)	$ 8,333	$ (64,651)

Rhythm Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)
(Unaudited)

	June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 69,339	$ 100,854
Short-term investments	298,815	71,938
Prepaid expenses and other current assets	10,300	8,876
Total current assets	378,454	181,668
Property and equipment, net	3,051	3,195
Right-of-use asset	1,671	1,807
Intangible assets, net	4,886	—
Restricted cash	328	403
Total assets	$ 388,390	$ 187,073
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,009	$ 4,900
Accrued expenses and other current liabilities	11,880	12,559
Lease liability	570	535
Total current liabilities	17,459	17,994
Long-term liabilities:		
Deferred tax liability	16,984	—
Lease liability	2,258	2,551
Total liabilities	36,701	20,545

Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred Stock, $0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding at June 30, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value: 120,000,000 shares authorized; 50,226,739 and 44,235,903 shares issued and outstanding June 30, 2021 and December 31, 2020, respectively	50	44
Additional paid-in capital	802,584	625,762
Accumulated other comprehensive income	21	49
Accumulated deficit	(450,966)	(459,327)
Total stockholders' equity	351,689	166,528
Total liabilities and stockholders' equity	$ 388,390	$ 187,073

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Source: Rhythm Pharmaceuticals, Inc.