Rhythm Pharmaceuticals Reports First Quarter 2021 Financial Results

May 3, 2021

-- First U.S. commercial sales of IMCIVREE™ (setmelanotide) completed late in first quarter –

-- Late-breaking data presentations at ENDO 2021 demonstrated continued weight loss with setmelanotide at up to nine months in HET obesity, as well as weight loss data in adults and BMI-Z reductions in adolescents with Bardet-Biedl syndrome --

-- Delivered proof-of-concept data from Phase 2 Basket Study in HET POMC, PCSK1 or LEPR deficiencies, and obesity due to SRC1 and SH2B1 deficiencies --

-- Closed $172.5 million public offering and sold Priority Review Voucher for $100 million, providing additional funding to advance continued development of setmelanotide --

BOSTON, May 03, 2021 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company committed to transforming the treatment paradigm for people living with rare genetic diseases of obesity, today reported financial results and provided a business update for the first quarter ended March 31, 2021.

"This is an exciting time of growth and momentum for Rhythm, as we made several significant steps on our journey to transform the care of patients with rare genetic diseases of obesity and to expand the reach of setmelanotide," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "In the first quarter of 2021, we delivered proof-of-concept data in HET obesity and obesity due to SRC1 or SH2B1 deficiencies, three indications with a combined total addressable population estimated between 100,000 and 200,000 patients in the United States. In addition, we presented compelling Phase 3 data that showed weight loss in adults and BMI-Z reductions in adolescents with Bardet-Biedl syndrome (BBS). We are pleased to have completed our first U.S. commercial sales of IMCIVREE™ (setmelanotide) in the first quarter."

Dr. Meeker continued, "Looking forward, we anticipate an initial European approval of IMCIVREE in obesity due to POMC, PCSK1 and LEPR deficiency in the second half of 2021, and we are putting in place the global infrastructure to support commercial availability. We also remain on track to complete U.S. and EU regulatory submissions for BBS in the second half of 2021. In addition, we expect to initiate a pivotal Phase 3 MC4R pathway trial to evaluate setmelanotide in HETs, SRC1 or SH2B1 deficiencies, a new exploratory Phase 2 Basket trial to evaluate setmelanotide's ability to treat patients with genetic variants in one of 31 additional genes, a registrational trial for our weekly formulation of setmelanotide, an exploratory trial in hypothalamic obesity, and a pediatrics trial for patients between 2 and 6 years old."

First Quarter and Recent Business Highlights:

Pipeline and Business Developments:

- Late in March 2021, Rhythm completed the first commercial sales of IMCIVREE following U.S. Food and Drug Administration (FDA) approval in November 2020. IMCIVREE was approved for chronic weight management in adult and pediatric patients six years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency confirmed by genetic testing.
- In March 2021, Rhythm had three late-breaking data presentations from Phase 2 and Phase 3 studies of setmelanotide during the 103rd Annual Meeting and Expo of the Endocrine Society (ENDO 2021). Sadaf Farooqi, M.D., Ph.D., University of Cambridge, UK, presented proof-of-concept data from the Company's Phase 2 study evaluating setmelanotide in individuals living with heterozygous (HET) obesity due to genetic variants in one of two alleles of the *POMC, PCSK1* or *LEPR* gene. The oral presentation included new weight loss data that showed patients with HET obesity who were classified as setmelanotide-responsive at three months continued to lose weight as they remained on treatment, with a mean weight loss of 12.3 percent at nine months on therapy.
- Additional poster presentations at ENDO 2021 included previously disclosed topline Phase 3 data in BBS and Alström syndromes and new analyses of adverse events in Phase 2 and Phase 3 studies in POMC, PCSK1, or LEPR deficiency showing consistent safety results for setmelanotide.
- Rhythm also presented an encore poster of the topline Phase 3 BBS data at the 2021 Pediatric Endocrine Society Virtual Annual Meeting on April 30.
- In January 2021, Rhythm announced new proof-of-concept interim data from its ongoing Phase 2 Basket Study across individuals with HET obesity, obesity due to SRC1 deficiency or obesity due to SH2B1 deficiency. Across all three populations, setmelanotide led to meaningful weight loss in approximately 30 percent to greater than 50 percent of treated patients. Rhythm believes that these data, coupled with updated sequencing results, suggest that there are approximately 100,000-200,000 potentially setmelanotide-responsive patients with HET, SRC1 or SH2B1 obesity in the United States.
- Also in January 2021, Rhythm announced that it has leveraged its proprietary gene curation and selection strategy to identify an additional 31 genes with strong or very strong MC4R pathway relevance, paving the way for the Company to

initiate an expanded exploratory Phase 2 Basket study in these new genes.

Corporate:

- In February 2021, Rhythm completed a public offering of 5,750,000 shares of its common stock at a public offering price of $30.00 per share, which included the full exercise by the underwriters of their option to purchase up to an additional 750,000 shares, for aggregate gross proceeds of approximately $172.5 million, before underwriting discounts, commissions, and offering expenses.
- In January 2021, Rhythm announced the sale of its Rare Pediatric Disease Priority Review Voucher (PRV) for $100 million. The PRV was granted to Rhythm by the FDA with the approval of IMCIVREE for chronic weight management in adult and pediatric patients six years of age and older with obesity due to POMC, PCSK1 or LEPR deficiency.

Key Upcoming Milestones:

Rhythm expects to achieve the following milestones in 2021:

Regulatory Milestones:

- Complete regulatory review by the European Commission and, pending approval, make IMCIVREE commercially available in Europe in obesity due to POMC, PCSK1 and LEPR deficiency in the second half of 2021.
- Complete regulatory submissions to both the FDA and the EMA seeking marketing authorization for setmelanotide for the treatment of obesity in patients with BBS in the second half of 2021; the Company expects to determine next steps for Alström syndrome upon completing a full analysis of the final data from the Phase 3 trial.

Clinical Milestones:

- Initiate a Phase 2, multi-center, open-label, proof-of-concept study designed to explore the potential of setmelanotide in people living with hypothalamic obesity, which is most often caused by trauma to the hypothalamus during surgical resection of a tumor, in the first half of 2021. The Company believes a subset of patients with hypothalamic obesity may have the potential for weight loss with setmelanotide if their MC4 receptor is sufficiently intact.
- Announce new topline data from the ongoing exploratory Phase 2 Basket Study evaluating setmelanotide in MC4R-rescuable patients in the second half of 2021.
- Announce full data from the pivotal Phase 3 trial evaluating setmelanotide in BBS and Alström syndrome at a medical meeting in the second half of 2021, following topline data presentations in March and April.
- Initiate a Phase 2 clinical trial of setmelanotide in pediatric patients aged two to six years old in the second half of 2021.
- Pending FDA feedback, initiate a pivotal Phase 3 MC4R pathway trial of setmelanotide in patients with HET obesity, as well as SRC1 and SH2B1 deficiency obesities, in the second half of 2021.
- Initiate a new exploratory Phase 2 Basket Study of setmelanotide in patients with variants in one of 31 additional genes with strong or very strong MC4R pathway relevance in the second half of 2021.
- Initiate a Phase 3 potentially registration-enabling trial for the weekly formulation of setmelanotide in the second half of 2021.

First Quarter 2021 Financial Results:

- **Cash Position:** As of March 31, 2021, cash, cash equivalents and short-term investments were approximately $404.8 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 PRV 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, offset by cash used to fund operating activities in the first quarter of 2021.
- **Revenue:** Product revenues relating to sales of IMCIVREE, which became commercially available late in March, were $35.0 thousand for the first quarter of 2021. Rhythm did not generate any product revenues in the first quarter of 2020.
- **R&D Expenses:** R&D expenses were $19.9 million in the first quarter of 2021, as compared to $22.5 million in the first quarter of 2020. The year-over-year decrease was primarily related to purchases of setmelanotide API and drug product in the first quarter of 2020 for clinical trials and preparation for commercialization. The Company completed the GO-ID genotyping study, the Phase 3 studies of setmelanotide in obesity due to POMC, PCSK1 or LEPR deficiency and the weekly formulation study in early to mid 2020. These clinical trial decreases were partially offset by increases in costs associated with the expanded Phase 2 Basket Study and initiation of a new renal insufficiency pharmacokinetics study in late 2020.
- **S,G&A Expenses:** S,G&A expenses were $14.5 million for the first quarter of 2021, as compared to $12.8 million for the first quarter of 2020. The year-over-year increase was primarily due to $1.6 million in expenses incurred with the sale of Rhythm's PRV.
- **Other income, net:** Other income increased by $99.0 million due primarily to the sale of Rhythm's PRV in February 2021.
- **Provision for income taxes:** The Company recorded a tax provision of $22.0 million for the period ended March 31,

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 $43.8 million for the first quarter of 2021, or a net income per basic and diluted share of $0.92 and $0.90, respectively, as compared to a net loss of $34.2 million for the first quarter of 2020, or a net loss per basic and diluted share of ($0.78).

Financial Guidance: Based on its current operating plans, Rhythm expects that its existing cash, cash equivalents and short-term investments as of March 31, 2021, will be sufficient to fund its operating expenses and capital expenditure requirements into at least the second half of 2023.

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), has been approved by the 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. IMCIVREE is the first-ever FDA approved 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. For healthcare professionals, visit www.UNcommonObesity.com for more information. For patients and caregivers, visit www.LEADforRareObesity.com for more information. The company is based in Boston, MA.

IMCIVREE™ (setmelanotide) Indication
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).

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, management changes, 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 March 31, 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.

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Statements of Operations

(in thousands, except share and per share data)

(Unaudited)

	Three months ended March 31,	
	2021	**2020**
Product revenue, net	$ 35	$ —
Costs and expenses:		
Cost of sales	4	—
Research and development	19,911	22,504
Selling, general, and administrative	14,518	12,796
Total costs and expenses	34,433	35,300
Loss from operations	(34,398)	(35,300)
Other income (expense):		
Other income	100,000	—
Interest income, net	154	1,136
Total other income, net	100,154	1,136
Income (loss) before taxes	65,756	(34,164)
Provision for income taxes	22,006	—
Net income (loss)	$ 43,750	$ (34,164)
Net income (loss) per share		
Basic	$ 0.92	$ (0.78)
Diluted	$ 0.90	$ (0.78)
Weighted-average common shares outstanding		
Basic	47,638,565	44,049,843
Diluted	48,501,697	44,049,843

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets

(in thousands, except share and per share data)

(Unaudited)

	March 31, 2021	**December 31, 2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 87,271	$ 100,854
Short-term investments	317,479	71,938
Prepaid expenses and other current assets	7,384	8,876

Total current assets	412,134	181,668
Property and equipment, net	3,006	3,195
Right-of-use asset	1,741	1,807
Intangible assets, net	5,000	—
Restricted cash	328	403
Total assets	$ 422,209	$ 187,073
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 9,147	$ 4,900
Accrued expenses and other current liabilities	7,150	12,559
Lease liability	553	535
Total current liabilities	16,850	17,994
Long-term liabilities:		
Deferred tax liability	22,006	—
Lease liability	2,406	2,551
Total liabilities	41,262	20,545
Commitments and contingencies		
Stockholders' equity:		
Preferred Stock, $0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding at March 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value: 120,000,000 shares authorized; 50,201,758 and 44,235,903 shares issued and outstanding March 31, 2021 and December 31, 2020, respectively	50	44
Additional paid-in capital	796,532	625,762
Accumulated other comprehensive (loss) income	(58)	49
Accumulated deficit	(415,577)	(459,327)
Total stockholders' equity	380,947	166,528
Total liabilities and stockholders' equity	$ 422,209	$ 187,073

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