Rhythm Pharmaceuticals Reports Fourth Quarter and Full Year 2020 Financial Results

March 1, 2021

-- Received FDA approval of IMCIVREE™ (setmelanotide), the first-ever therapy for chronic weight management in patients with obesity due to POMC, PCSK1 or LEPR deficiency --

-- Announced positive topline data from Phase 3 pivotal trial evaluating setmelanotide in Bardet-Biedl and Alström syndromes; on-track to complete regulatory submissions to FDA and EMA for BBS in 2H 2021 --

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

-- Advancing broad development program for setmelanotide, with five Phase 2 and 3 clinical studies expected to initiate in 2021 in MC4R pathway-related rare genetic diseases of obesity --

-- Strengthened financial position with net proceeds of $98.5M from sale of Rare Pediatric Disease PRV and $161.6M from public offering, extending cash runway through at least the second half of 2023 –

BOSTON, March 01, 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 fourth quarter and full year ended December 31, 2020.

"We enter 2021 with tremendous momentum on our journey to transform the care of people with rare genetic diseases of obesity," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "In recent months, we secured our first approval of IMCIVREE, validating the melanoticortin-4 receptor (MC4R) pathway as an important therapeutic target and bringing the first-ever therapy to people suffering from obesity due to POMC, PCSK1 or LEPR deficiency. The patients with defects in the MC4R pathway we have studied to date, including those with our approved indications and patients who participated in our Phase 2 Basket Study, have severe obesity and have largely failed other treatment modalities."

Dr. Meeker continued, "We also announced positive topline data from our pivotal, Phase 3 trial in Bardet-Biedl syndrome (BBS), and we achieved proof-of-concept in multiple additional genetic diseases of obesity, paving the way for a potentially registration-enabling trial this year. On the heels of these recent achievements, we are entering our next phase as we begin to commercialize IMCIVREE and work to expand setmelanotide's reach to address the unmet needs of many more people with a range of genetic variants in the MC4R pathway. We look forward to completing regulatory submissions to both the FDA and the EMA seeking marketing authorization for setmelanotide for the treatment of obesity in patient with BBS in the second half of 2021 and, in parallel, initiating new trials in a broad clinical program. Following the sale of our priority review voucher (PRV) and recent public offering, we are well-funded, with sufficient resources to advance the development of setmelanotide while supporting the patient community and driving awareness of genetic testing to identify and properly diagnose people with these rare conditions."

Fourth Quarter and Recent Business Highlights:

Pipeline and Recent Developments:

- In January 2021, Rhythm announced new proof-of-concept interim data from its ongoing Phase 2 Basket Study across individuals with heterozygous (HET) obesity due to a genetic variant in one of the two alleles of the *POMC*, *PCSK1*, or *LEPR* gene, obesity due to SRC1 deficiency (SRC1) or obesity due to SH2B1 deficiency (SH2B1). 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.
- In December 2020, Rhythm announced positive topline results from the pivotal Phase 3 clinical trial evaluating setmelanotide in Bardet-Biedl syndrome (BBS) and Alström syndrome. The study met its primary and all key secondary endpoints, demonstrating statistically significant and clinically meaningful reductions in weight and hunger scores, with patients with BBS comprising all primary endpoint responders. No patients with Alström syndrome met the primary endpoint. Rhythm subsequently announced data from a predefined exploratory endpoint in January, demonstrating that setmelanotide was associated with statistically significant and clinically meaningful reductions in BMI-Z scores for BBS patients younger than 18 years old.
- In November 2020, Rhythm announced that the U.S. Food and Drug Administration (FDA) approved IMCIVREE 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. Visit www.IMCIVREE.com for full Prescribing Information.

- Also in November 2020, Rhythm presented new clinical data on setmelanotide at The Obesity Society's ObesityWeek® 2020. The presentations included interim data from a Phase 2 study evaluating a once-weekly formulation of setmelanotide in healthy obese volunteers, which demonstrated safety and efficacy results comparable to the daily-dosing regimen, and additional data from the long-term extension study in obesity due to POMC deficiency, which showed durable weight loss and reductions in hunger at up to three years on setmelanotide therapy.

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.
- In November 2020, Rhythm announced the appointments of Camille L. Bedrosian, M.D., and Lynn Tetrault, J.D., to its Board of Directors.

Key Upcoming Milestones:

Rhythm expects to achieve the following milestones in 2021:

Commercial and Regulatory Milestones:

- Make IMCIVREE commercially available in the United States for obesity due to POMC, PCSK1 and LEPR deficiencies in the first quarter of 2021.
- Obtain regulatory approval from the European Commission and make IMCIVREE commercially available in Europe in POMC, PCSK1 and LEPR deficiency obesities 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 patient with BBS in the second half of 2021.

Clinical Milestones:

- Initiate a Phase 2 clinical trial of setmelanotide in hypothalamic obesity in the first half of 2021.
- Announce new top-line data from the ongoing exploratory Phase 2 Basket Study evaluating setmelanotide in MC4R-rescuable patients in the first half of 2021.
- Announce full data from the pivotal Phase 3 trial evaluating setmelanotide in Bardet-Biedl and Alström Syndromes in the first half of 2021.
- 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 an expanded 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.

Fourth Quarter and Full Year 2020 Financial Results:

- **Cash Position:** As of December 31, 2020, cash, cash equivalents and short-term investments were approximately $172.8 million, as compared to $292.5 million as of December 31, 2019. Cash, cash equivalents and short-term investments as of December 31, 2020 do not include net proceeds of $98.5 million received upon sale of Rhythm's Rare Pediatric Disease PRV in February 2021, or net proceeds of approximately $161.6 million from Rhythm's underwritten public offering of common stock, which closed in February 2021.
- **R&D Expenses:** R&D expenses were $22.0 million in the fourth quarter of 2020 and $90.5 million for the year ended December 31, 2020, as compared to $24.8 million in the fourth quarter of 2019 and $109.5 million for the year ended December 31, 2019. The year-over-year decrease was primarily due to completion early in 2020 of our GO-ID genotyping study and the Phase 3 studies of setmelanotide in obesity due to POMC, PCSK1 or LEPR deficiency and a decrease in travel and conference spending due to COVID-19 restrictions. This decrease was partially offset by increases in the expanded Phase 2 Basket Study and the initiation of a new renal insufficiency pharmacokinetics study in 2020. During the year, there also was a $3.0 million payment under the licensing agreement with Ipsen related to regulatory milestones associated with the FDA approval of IMCIVREE.
- **S,G&A Expenses:** S,G&A expenses were $13.1 million for the fourth quarter of 2020 and $46.1 million for the year ended

December 31, 2020, as compared to $9.4 million for the fourth quarter of 2019 and $36.6 million for the year ended December 31, 2019. The year-over-year increase was primarily due to commercialization efforts focused on market access, patient engagement and disease awareness. In addition, there was an increase of approximately $0.9 million in cash related charges incurred with the separation agreements with our former chief executive officer and chief commercial officer, and $4.9 million in non-cash related stock compensation expenses related with those separation agreements as well as the hiring of the Company's current CEO in July.

- **Net Loss:** Net loss was $34.9 million for the fourth quarter of 2020 and $134.0 million for the year ended December 31, 2020, or a net loss per basic and diluted share of $0.79 and $3.04, respectively, as compared to a net loss of $33.0 million for the fourth quarter of 2019 and $140.7 million for the year ended December 31, 2019, or a net loss per basic and diluted share of $0.78 and $3.86, respectively.

Financial Guidance: Based on its current operating plans, Rhythm expects that its existing cash, cash equivalents and short-term investments as of December 31, 2020, together with an aggregate of approximately $260.1 million in net proceeds from the February 2021 sale of its Rare Disease PRV and the February 2021 follow-on public offering, will be sufficient to fund its operating expenses and capital expenditure requirements through 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 Annual Report on Form 10-K for the year ended December 31, 2020 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
(in thousands, except share and per share data)

	Three months ended December 31,		Year ended December 31,	
	2020	**2019**	**2020**	**2019**
Operating expenses:				
Research and development	$ 21,954	$ 24,810	$ 90,450	$ 109,450
Selling, general, and administrative	13,119	9,414	46,125	36,550
Total operating expenses	35,073	34,224	136,575	146,000
Loss from operations	(35,073)	(34,224)	(136,575)	(146,000)
Other income (expense):				
Interest income, net	176	1,268	2,579	5,271
Total other income:	176	1,268	2,579	5,271
Net loss	$ (34,897)	$ (32,956)	$ (133,996)	$ (140,729)
Net loss per common share, basic and diluted	$ (0.79)	$ (0.78)	$ (3.04)	$ (3.86)
Weighted average common shares outstanding, basic and diluted	44,216,694	42,213,180	44,127,220	36,422,450

RHYTHM PHARMACEUTICALS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 100,854	$ 62,294
Short-term investments	71,938	230,165
Prepaid expenses and other current assets	8,876	9,945
Total current assets	181,668	302,404
Property and equipment, net	3,195	3,671
Right-of-use asset	1,807	2,045
Restricted cash	403	403
Total assets	$ 187,073	$ 308,523
Liabilities and stockholders’ equity		
Current liabilities:		
Accounts payable	$ 4,900	$ 10,415

Accrued expenses and other current liabilities	12,559	13,530
Lease liability	535	472
Total current liabilities	17,994	24,417
Long-term liabilities:		
Lease liability	2,551	3,086
Total liabilities	20,545	27,503
Commitments and contingencies		
Stockholders' equity:		
Preferred Stock, $0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2020 and December 31, 2019	—	—
Common stock	44	44
Additional paid-in capital	625,762	606,307
Accumulated other comprehensive income	49	—
Accumulated deficit	(459,327)	(325,331)
Total stockholders' equity	166,528	281,020
Total liabilities and stockholders' equity	$ 187,073	$ 308,523

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