



Rhythm Pharmaceuticals Reports Third Quarter 2021 Financial Results

November 2, 2021

-- U.S. and EU regulatory filings submitted for IMCIVREE[®] (setmelanotide) for treatment of Bardet-Biedl and Alström syndromes; launch preparations underway --

-- Delivered a total of 22 presentations at three major medical conferences --

-- New presentations include first-ever data showing improvements in health-related quality of life in rare genetic diseases of obesity --

-- IMCIVREE third quarter net sales reach \$1M --

-- Management to Host Conference Call at 8:00 a.m. ET --

BOSTON, Nov. 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 reported financial results and provided a business update for the third quarter ended September 30, 2021.

"We continue to execute across our expanding integrated clinical and commercial strategy to deliver setmelanotide and its potential clinical benefit to patients with rare genetic diseases of obesity," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "Our team completed regulatory submissions in both the United States and European Union recently, positioning IMCIVREE[®] (setmelanotide) as the first-ever therapy to address the unmet needs of hyperphagia and severe obesity that affect the lives of patients and families living with Bardet-Biedl and Alström syndromes. Our initial U.S. commercial experience with POMC, PCSK1, and LEPR deficiency obesities continues to provide valuable learnings as we expand the number of health care providers testing patients with early-onset, severe obesity and hyperphagia and work with payers to ensure patients who need therapy can access it. With effective patient services in place, patients have achieved positive responses and stayed on therapy. We believe these commercial achievements provide a strong foundation for a successful launch in BBS and Alström syndrome in mid-2022."

Dr. Meeker continued, "In parallel, we continue to advance our robust development strategy for setmelanotide. Including this week's The Obesity Society's ObesityWeek[®], we recently delivered a total of 22 presentations that support setmelanotide's potential ability to improve the lives of patients and the families who care for them. With updated sequencing data from our Uncovering Rare Obesity[®] (URO) testing program complementing presentations on efficacy and improved quality of life data, we have strong confidence in setmelanotide's potential to deliver meaningful benefit and our ability to identify patients. We look forward to continuing to execute across our pipeline and deliver on our promise to transform the care and treatment of rare genetic diseases of obesity."

Third Quarter and Recent Business Highlights:

Regulatory Updates:

Bardet-Biedl Syndrome and Alström Syndrome:

- In October, Rhythm announced the completion of its Type II variation application to the European Medicines Agency (EMA) for IMCIVREE for the treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS or Alström syndrome.
- In September, Rhythm announced the completion of its supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for IMCIVREE for the treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS or Alström syndrome. Rhythm requested priority review for the application, which, if granted, could provide a target FDA review period of six-months from the date the sNDA is accepted.
- Also in September, Rhythm announced an Expanded Access Program (EAP) for setmelanotide for the treatment of eligible patients in the United States with severe obesity and hyperphagia due to BBS. The FDA's expanded access regulations are designed to facilitate access to an investigational therapy to treat patients who are unable to participate in clinical trials and have serious or immediately life-threatening diseases or conditions for which there are no comparable or satisfactory alternative treatment options.

POMC and LEPR Deficiency Obesities:

- In September, Rhythm announced that Great Britain's Medicines & Healthcare Products Regulatory Agency (MHRA) has granted marketing authorisation to IMCIVREE 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.

Clinical Development Updates

- This week at ObesityWeek, Rhythm delivered multiple data presentations including: the first-ever health-related quality of

life (HRQOL) data from patients with BBS treated with setmelanotide; efficacy and safety data from its Phase 3 trial of setmelanotide in BBS and Alström syndrome; new hunger reduction data from the SRC1 and SH2B1 deficiency cohorts in its exploratory Phase 2 Basket Trial; new data on utilization of URO; an analysis of the frequency of melanocortin-4 receptor (MC4R) pathway variants in U.S. patients with severe obesity; and a review of single minded-1 (SIM1) missense variants associated with severe obesity.

- In October at the Obesity Medicine Association's Overcoming Obesity 2021 Conference (OMA), the Company presented new HRQOL data from the Phase 3 trials evaluating setmelanotide in POMC or LEPR deficiency obesities that confirmed setmelanotide treatment led to sustained, clinically meaningful HRQOL improvements in a majority of patients; results from in-depth patient interviews conducted in POMC and LEPR patients enrolled in Rhythm's pivotal Phase 3 trials, which highlighted that reduced hunger and improved satiety resulting from setmelanotide treatment substantially and meaningfully changed patients' lives; and two presentations detailing updated results from Rhythm's URO genetic testing of approximately 8,500 people in the United States with early-onset, severe obesity.
- In September at the 59th Annual European Society for Paediatric Endocrinology (ESPE) Meeting, Rhythm and its collaborators delivered three oral and four poster presentations, including a new subgroup analysis of data from its Phase 3 clinical trial in BBS, which showed that patients treated with setmelanotide achieved statistically significant weight loss and hunger reduction compared to patients treated with placebo during a 14-week, double-blind treatment period, as well as an interim analysis from its exploratory Phase 2 Basket Trial, which showed that setmelanotide achieved clinically meaningful weight loss or BMI-Z reduction in 30% (9 of 30) of study participants with obesity due to variants of the SRC1 gene, and 43% (15 of 35) of study participants with obesity due to variants of the SH2B1 gene, including 16p11.2 chromosomal deletions.

Corporate

- In September 2021, Rhythm announced the promotion of Linda Shapiro Manning, M.D., Ph.D., to Chief Medical Officer. She succeeded Murray Stewart, M.D., who transitioned to the role of Senior Medical Advisor.

Key Upcoming Milestones:

Rhythm expects to achieve the following near-term milestones:

- Initiate DAYBREAK, an exploratory, Phase 2, two-stage, placebo-controlled trial of setmelanotide in patients with variants in one of 31 genes with strong or very strong MC4R pathway relevance in the fourth quarter of 2021.
- Initiate EMANATE, a Phase 3, randomized, double-blind, placebo-controlled trial to evaluate setmelanotide in five independent sub-studies in patients with obesity due to a heterozygous variant of POMC/PCSK1 or LEPR; certain variants of the SRC1 gene, certain variants of the SH2B1 gene, or PCSK1 N221D deletions within the MC4R pathway in the fourth quarter of 2021 or the first quarter of 2022.
- Initiate a Phase 3, randomized, double-blind trial in patients currently on daily setmelanotide therapy ("switch study") 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 in the fourth quarter of 2021.
- Initiate multi-center, one-year, open-label Phase 3 trial in pediatric patients ages 2 to 6 years old with obesity due to biallelic POMC, PCSK1 or LEPR deficiency, or with a clinical diagnosis of BBS with genetic confirmation in the fourth quarter of 2021.
- Initiate a Phase 3, randomized, double-blind trial in patients naïve to setmelanotide therapy ("*de novo* study") to evaluate the weekly formulation of setmelanotide in patients with BBS in the first half of 2022.
- Announce new 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.
- Announce longer-term follow-up data from the ongoing exploratory Phase 2 Basket Study evaluating setmelanotide in patients with heterozygous POMC/PCSK1 obesity, heterozygous LEPR obesity, certain variants of the SRC1 gene and certain variants of the SH2B1 gene in the first half of 2022.

Third Quarter 2021 Financial Results:

- **Cash Position:** As of September 30, 2021, cash, cash equivalents and short-term investments were approximately \$328.4 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 (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, partially offset by cash used to fund operating activities in 2021.
- **Revenue:** Product net revenues relating to sales of IMCIVREE in the United States were \$1.0 million for the third quarter of 2021. Rhythm did not generate any product revenues in the third quarter of 2020 as IMCIVREE was approved for commercial use by the FDA in November 2020.
- **R&D Expenses:** R&D expenses were \$27.5 million in the third quarter of 2021, as compared to \$23.0 million in the third quarter of 2020. The year-over-year increase was primarily related to a \$4.4 million increase related to new and planned

clinical trials, including the Phase 2 DAYBREAK and Phase 3 EMANATE trials, Phase 3 pediatrics trial, Phase 2 hypothalamic obesity study, and increased enrollment in the open-label, long-term extension study, as well as an increase of \$2.7 million in salaries and benefits due to hiring additional employees to support the growth of Rhythm's research and development programs. These increases were partially offset by a decrease of \$1.4 million in reduced purchases of clinical supply materials and \$0.7 million in costs associated with accessing sequencing data from third-party biobanks to further Rhythm's genetic research efforts.

- **S,G&A Expenses:** S,G&A expenses were \$17.5 million for the third quarter of 2021, as compared to \$11.3 million for the third quarter of 2020. The year-over-year increase was primarily related to an increase of \$3.0 million due to compensation and benefits related costs associated with additions to the executive leadership team, increased headcount to support expanding business operations as well as to establish commercial operations in the United States and internationally; an increase of \$1.9 million due to increased professional fees and consulting services to support the build out of commercial operations in the United States and internationally as well as corporate legal and consulting support for international expansion; and an increase of \$0.9 million related to marketing activities for IMCIVREE.
- **Net Loss:** Net loss was \$35.1 million for the third quarter of 2021, or a net loss per basic and diluted share of \$0.70, as compared to a net loss of \$33.8 million for the third quarter of 2020, or a net loss per basic and diluted share of \$0.77.

Year to Date 2021 Financial Results:

- **Revenue:** Product revenues relating to sales of IMCIVREE in the United States were \$1.3 million for the nine months ended September 30, 2021. Rhythm did not generate any product revenues in the nine months ended September 30, 2020 as IMCIVREE was approved for commercial use by the FDA in November 2020.
- **R&D Expenses:** R&D expenses were \$72.6 million for the nine months ended September 30, 2021, as compared to \$68.5 million for the nine months ended September 30, 2020. The increase of \$4.1 million was primarily due to an increase of \$5.9 million in compensation and benefits due to hiring additional employees to support the growth of Rhythm's research and development programs, as well as an increase of \$2.4 million in costs related to new clinical trials, including the Phase 2 DAYBREAK and Phase 3 EMANATE trials, the Phase 3 pediatrics trial, QTc study, Phase 2 hypothalamic obesity study, and increased enrollment in the open-label, long-term extension study; and an increase of \$1.1 million related to costs associated with pursuing the evaluation of setmelanotide in additional indications. These increases were partially offset by a decrease in costs associated with Rhythm's Go-ID study, which has been completed, as well as decrease of \$3.0 million in milestone expense associated with the license agreement with Ipsen on filing the NDA with the FDA and filing the Marketing Authorisation Application with the EMA; \$1.1 million in professional services fees related to regulatory filings; \$0.8 million related to reduced purchases of clinical supply material for setmelanotide; and \$0.7 million in costs associated with accessing sequencing data from third party biobanks.
- **S,G&A Expenses:** S,G&A expenses were \$47.5 million for the nine months ended September 30, 2021, as compared to \$33.0 million for the nine months ended September 30, 2020. The increase of \$14.5 million was primarily related to an increase of \$7.1 million due to increased compensation and benefits-related costs associated with additions to the executive leadership team, increased headcount to support expanding business operations as well as to establish commercial operations in the United States and internationally; an increase of \$4.0 million due to increased professional fees and consulting services to help support the build out of Rhythm's commercial operations in the United States and internationally, as well as corporate legal and consulting support for Rhythm's international expansion; an increase of \$1.6 million associated with expenses incurred on the sale of Rhythm's PRV; an increase of \$1.1 million due to increased costs associated with office support and insurance costs for Rhythm's expanding workforce; and an increase of \$0.7 million associated with expenses incurred related to marketing activities for IMCIVREE.
- **Other income, net:** Other income increased by \$97.9 million in the nine months ended September 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 \$8.0 million for the nine months ended September 30, 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 Loss:** Net loss was \$26.7 million for the nine months ended September 30, 2021, or a net loss per basic and diluted share of \$0.54, as compared to a net loss of \$99.1 million for the nine months ended September 30, 2020, or a net loss per basic and diluted share of \$2.25.

Financial Guidance: Based on its current operating plans, Rhythm expects that its existing cash, cash equivalents and short-term investments as of September 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 third 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 2167009. 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. Rhythm'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 in July and September 2021, respectively, by the European Commission (EC) and Great Britain's Medicines & Healthcare Products Regulatory Agency (MHRA) 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- and MHRA-authorized therapy for patients with these rare genetic diseases of obesity. The Company submitted a supplemental New Drug Application (sNDA) to the FDA in September 2021 and submitted a Type II variation application to the European Medicines Agency in October 2021 seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS or Alström syndrome in both the United States and European Union.

Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare genetic diseases of obesity and 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. Rhythm's headquarters is 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 $\geq 23\%$) 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 U.S. [Full Prescribing Information](#), [EU SmPC](#) and [MHRA SmPC](#) 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 September 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.

Rhythm Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)
(Unaudited)

	Three months ended September 30,		Nine months ended September 30,	
	2021	2020	2021	2020
Product revenue, net	\$ 1,028	\$ —	\$ 1,337	\$ —
Costs and expenses:				
Cost of sales	222	—	363	—
Research and development	27,539	22,995	72,554	68,496
Selling, general, and administrative	17,507	11,289	47,490	33,006
Total costs and expenses	45,268	34,284	120,407	101,502
Loss from operations	(44,240)	(34,284)	(119,070)	(101,502)
Other income:				
Other income	—	—	100,000	—
Interest income, net	138	466	313	2,403
Total other income, net	138	466	100,313	2,403
Loss before taxes	(44,102)	(33,818)	(18,757)	(99,099)
(benefit from) provision for income taxes	(8,995)	—	7,989	—
Net loss	\$ (35,107)	\$ (33,818)	\$ (26,746)	\$ (99,099)
Net loss per share, basic and diluted	\$ (0.70)	\$ (0.77)	\$ (0.54)	\$ (2.25)
Weighted-average common shares outstanding, basic and diluted	50,246,303	44,142,334	49,374,336	44,097,178
Other comprehensive loss:				
Net loss	\$ (35,107)	\$ (33,818)	\$ (26,746)	\$ (99,099)
Unrealized (loss) gain on marketable securities	—	(392)	(107)	238
Comprehensive loss	\$ (35,107)	\$ (34,210)	\$ (26,853)	\$ (98,861)

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

	Sept. 30, 2021	Dec. 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	\$ 92,372	\$ 100,854
Short-term investments	235,982	71,938
Prepaid expenses and other current assets	7,282	8,876
Total current assets	335,636	181,668
Property and equipment, net	2,956	3,195
Right-of-use asset	1,598	1,807
Intangible assets, net	4,772	—
Restricted cash	328	403
Other long-term assets	10,533	—

Total assets	\$	355,823	\$	187,073
Liabilities and stockholders' equity				
Current liabilities:				
Accounts payable	\$	4,614	\$	4,900
Accrued expenses and other current liabilities		18,265		12,559
Lease liability		588		535
Total current liabilities		23,467		17,994
Long-term liabilities:				
Deferred tax liability		7,989		—
Lease liability		2,104		2,551
Total liabilities		33,560		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 September 30, 2021 and December 31, 2020		—		—
Common stock, \$0.001 par value: 120,000,000 shares authorized; 50,268,312 and 44,235,903 shares issued and outstanding September 30, 2021 and December 31, 2020, respectively		50		44
Additional paid-in capital		808,265		625,762
Accumulated other comprehensive income		21		49
Accumulated deficit		(486,073)		(459,327)
Total stockholders' equity		322,263		166,528
Total liabilities and stockholders' equity	\$	355,823	\$	187,073

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