Rhythm Pharmaceuticals Reports First Quarter 2022 Financial Results and Business Update

May 3, 2022

-- Patient identification and physician engagement ongoing in preparation for U.S. commercial launch in June 2022 in BBS and Alström syndrome, pending FDA approval --

-- First commercial patients treated with IMCIVREE® (setmelanotide) in France under paid early access program --

-- First patients enrolled in Phase 3 EMANATE trial and Phase 2 DAYBREAK trial --

-- Multiple abstracts accepted for presentation at ENDO 2022 --

-- Management to host conference call today at 8:30 a.m. ET --

BOSTON, May 03, 2022 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company committed to transforming the care of people living with rare genetic diseases of obesity, today reported financial results and provided a business update for the first quarter ended March 31, 2022.

“We are excited by the progress we are making towards our long-term vision of transforming the care of individuals living with rare genetic diseases of obesity,” said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. “We continue to build out our U.S. and international commercial organizations while advancing patient identification efforts to support a successful U.S. launch for setmelanotide in Bardet-Biedl and Alström syndromes in June, pending U.S. Food and Drug Administration (FDA) approval. We achieved our first European sales in France during the quarter and continue to have constructive market access discussions with authorities in several key European markets.”

Dr. Meeker continued, “Additionally, our robust clinical development program is advancing with patients enrolled in multiple phase 2 and 3 clinical trials. We have optimized our ongoing Phase 3 EMANATE trial to focus exclusively on patient populations with the highest probability of responding to setmelanotide and narrowed our Phase 2 DAYBREAK trial to more efficiently evaluate rare variants associated with ten prioritized genes. In the months ahead, we look forward to reporting interim data from our Phase 2 trial in hypothalamic obesity and our Phase 2 Basket Study in obesity due to a variant in the melanocortin-4 receptor (MC4R).”

First Quarter and Recent Business Highlights:

Update on Bardet-Biedl and Alström Syndromes:

- Rhythm continues to execute on ongoing physician and patient education and engagement efforts, as well as patient identification efforts and additional strategies in support of a potential U.S. commercial launch of setmelanotide for the treatment of obesity and hyperphagia in patients with Bardet-Biedl syndrome (BBS).
- The Company’s supplemental New Drug Application (sNDA) for IMCIVREE ® (setmelanotide) 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 is under review by the FDA, with a Prescription Drug User Fee Act (PDUFA) goal date of June 16, 2022.
- Rhythm’s Type II variation application to the European Medicines Agency (EMA) for setmelanotide for the treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS is also under review. Rhythm anticipates that the EMA’s Committee for Medicinal Products for Human Use (CHMP) will make its recommendation on this application in the third quarter of 2022.
- The Company also announced today that on April 22, 2022, the CHMP recommended the European Commission (EC) approve a modification to the summary product characteristics (SmPC) for IMCIVREE for biallelic POMC, PSCK1 or LEPR deficiency that would allow for treating patients who have moderate and severe renal impairment with an adjustment for more gradual dose escalation and a lower maximum dose. The final EC decision on this amendment is anticipated to come in July 2022, and this same dosing modification request is being considered as part of the scheduled review for BBS.

International Updates:

- Today, Rhythm announced that the first patients have been treated with IMCIVREE in France under a paid early access program. The French Haute Autorité de Santé (HAS) granted paid early access for IMCIVREE for patients with POMC, PCSK1 or LEPR deficiency obesity in January 2022.

Clinical Development Updates:

- In April 2022, Rhythm announced that the first patient was enrolled in its Phase 3 EMANATE trial. With recently announced modifications to the trial design, EMANATE now includes four independent sub-studies evaluating setmelanotide in patients with obesity due to a heterozygous variant of the POMC or PCSK1 gene, the LEPR gene, the SRC1 gene or the SH2B1 gene. These modifications were intended to optimize the design of EMANATE, with the goal of focusing on rare patient populations that the Company believes have the highest likelihood of success.
- In April 2022 at the Pediatric Endocrine Society Annual Meeting (PES), Rhythm and its collaborators presented new data from the Company's Phase 3 clinical trial in BBS, which showed that setmelanotide improved body weight measures, as well as total cholesterol, high-density lipoprotein cholesterol, low-density cholesterol and triglycerides in treated patients. Also at PES, Rhythm presented data demonstrating clinically beneficial reductions in BMI Z score and BMI in pediatric and adolescent patients with BBS; characterizing the negative impacts of hyperphagia and the resulting food-seeking behaviors on the lives of patients with BBS and their caregivers; and highlighting the safety and tolerability of setmelanotide across the 561 patients treated across the setmelanotide clinical development program.
- Also in April 2022, Rhythm announced modifications to optimize the design of its ongoing Phase 2 DAYBREAK trial to focus initially on rare variants associated with 10 prioritized MC4R-relevant genes, which the Company and key opinion leaders believe have the highest probability of success.

Key Upcoming Milestones:

- Rhythm today announced that six abstracts have been accepted for presentation at the Endocrine Society Annual Meeting & Expo (ENDO), being held June 11-14, 2022 in Atlanta, GA. Dr. Jesús Argente, Universidad Autónoma de Madrid in Spain, will deliver an oral presentation of 12-month data from long-term extension trials of setmelanotide in patients with obesity due to heterozygous variants in POMC, PCSK1, and LEPR. In addition, five abstracts will be delivered as poster presentations, including:
    - Long-term Efficacy of Setmelanotide in Patients With Obesity Due to POMC, PCSK1, and LEPR Biallelic Deficiency;
    - Setmelanotide in Patients with Heterozygous POMC, LEPR, SRC1, or SH2B1 Obesity: Design of EMANATE – A Placebo-Controlled Phase 3 Trial;
    - Long-term Efficacy of Setmelanotide in Patients with Bardet-Biedl Syndrome;
    - Body Mass Index and Weight Reductions in Patients with SRC1 Genetic Variant Obesity After 1 Year of Setmelanotide; and
    - Body Mass Index and Weight Reduction in Patients with SH2B1 Genetic Variant Obesity After 1 Year of Setmelanotide.

- Also in mid-2022, Rhythm anticipates announcing:
    - Preliminary data from the ongoing Phase 2 study in patients with hypothalamic obesity.
    - New data from the ongoing exploratory Phase 2 Basket Study evaluating setmelanotide in patients with obesity due to a variant in the MC4 receptor.

First Quarter 2022 Financial Results:

- **Cash Position:** As of March 31, 2022, cash, cash equivalents and short-term investments were approximately $241.0 million, as compared to $294.9 million as of December 31, 2021.
- **Revenue**: Product net revenues relating to sales of IMCIVREE were $1.5 million for the first quarter of 2022, as compared to $35.0 thousand for the first quarter of 2021. IMCIVREE became commercially available in late March 2021.
- **R&D Expenses:** R&D expenses were $32.5 million in the first quarter of 2022, as compared to $19.9 million in the first quarter of 2021. The year-over-year increase was due to an increase of $9.4 million in clinical trial costs associated with new and planned clinical trials, including the Phase 2 DAYBREAK and Phase 3 EMANATE trials, Phase 3 pediatrics trial, QTc study, Phase 2 hypothalamic obesity study and increased enrollment in the long-term extension study; an increase of $3.8 million due to increased purchases of clinical supply material; an increase of $1.0 million in development milestones earned by Camurus related to the weekly formulation of setmelanotide and an increase of $0.4 million related to increased number of genetic testing performed. These increases were partially offset by the conclusion of prior studies, as well as a decrease of $2.0 million in costs associated with medical affair consulting.
- **S,G&A Expenses:** S,G&A expenses were $21.4 million for the first quarter of 2022, as compared to $14.5 million for the first quarter of 2021. The year-over-year increase was primarily due to an increase of $3.3 million due to increased compensation and benefits-related costs associated with additional headcount to support expanding business operations, as well as to establish commercial operations in the United States and internationally; an increase of $2.3 million related to marketing activities for IMCIVREE; an increase of $1.0 million due to increased costs associated with office support and insurance costs for Rhythm's expanding workforce; and an increase of $0.2 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.
- **Net (Loss)/Income:** Net loss was $52.8 million for the first quarter of 2022, or a net loss per basic and diluted share of

($1.05), as compared to a net income of $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.

Financial Guidance: Based on its current operating plans, Rhythm expects that its existing cash, cash equivalents and short-term investments as of March 31, 2022 will be sufficient to fund its operating expenses and capital expenditure requirements into at least the fourth quarter of 2023.

Conference Call Information
Rhythm Pharmaceuticals will host a live conference call and webcast at 8:30 a.m. ET today to discuss this update, as well as review its first quarter 2022 financial results and recent business activities. The conference call may be accessed by dialing (866) 374-5140 (domestic) or (404) 400 0571 (international) and referring to conference ID 79122322. 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, which was accepted for filing in November 2021 and is currently assigned a Prescription Drug User Fee Act (PDUFA) goal date of June 16, 2022, for the treatment of obesity and control of hunger in adult and pediatric patients six years of age and older with Bardet-Biedl Syndrome (BBS) or Alström syndrome. A Type II variation application to the European Medicines Agency 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 also is under review. 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 45,000 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 and Great Britain, 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, 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, sales of our lead product candidate IMCIVREE, 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, 2022 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.

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

	Three months ended March 31,	
	2022	**2021**
Product revenue, net	$ 1,498	$ 35
Costs and expenses:		
Cost of sales	230	4
Research and development	32,510	19,911
Selling, general, and administrative	21,449	14,518
Total costs and expenses	54,189	34,433
Loss from operations	(52,691)	(34,398)
Other income:		
Other income	—	100,000
Interest income, net	(73)	154
Total other income, net	(73)	100,154
(Loss) income before taxes	(52,764)	65,756
Provision for income taxes	—	22,006
Net (loss) income	$ (52,764)	$ 43,750
Net (loss) income per share		

Basic	$	(1.05)	$	0.92
Diluted	$	(1.05)	$	0.90
Weighted-average common shares outstanding				
Basic		50,326,627		47,638,565
Diluted		50,326,627		48,501,697
Other comprehensive (loss) income:				
Net (loss) income	$	(52,764)	$	43,750
Unrealized (loss) on marketable securities		(628)		(107)
Comprehensive (loss) income	$	(53,392)	$	43,643

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

		March 31, 2022		December 31, 2021
Assets				
Current assets:				
Cash and cash equivalents	$	78,537	$	59,248
Short-term investments		162,427		235,607
Accounts receivable		862		1,025
Prepaid expenses and other current assets		11,623		12,507
Total current assets		253,449		308,387
Property and equipment, net		2,722		2,813
Right-of-use asset		1,442		1,522
Intangible assets, net		8,527		4,658
Restricted cash		328		328
Other long-term assets		18,356		11,815
Total assets	$	284,824	$	329,523
Liabilities and stockholders' equity				
Current liabilities:				
Accounts payable	$	12,010	$	5,737
Accrued expenses and other current liabilities		25,199		30,084
Contract liability		9,440		7,000
Lease liability		625		606
Total current liabilities		47,274		43,427
Long-term liabilities:				
Lease liability		1,781		1,945
Total liabilities		49,055		45,372
Stockholders' equity:				
Common stock, $0.001 par value: 120,000,000 shares authorized; 50,393,731 and 50,283,574 shares issued and outstanding at March 31, 2022 and December 31, 2021, respectively		50		50
Additional paid-in capital		818,051		813,041
Accumulated other comprehensive loss		(629)		(1)
Accumulated deficit		(581,703)		(528,939)
Total stockholders' equity		235,769		284,151
Total liabilities and stockholders' equity	$	284,824	$	329,523

Source: Rhythm Pharmaceuticals, Inc.