Rubius Therapeutics Reports First Quarter 2022 Financial Results and Provides Business Update

May 10, 2022

Presented Updated Clinical Data from Monotherapy Phase 1 Arm of RTX-240 Clinical Trial in Advanced Solid Tumors, Showing Clinical Responses with Favorable Tolerability in PD-(L)1 Refractory Disease

Expanded Ongoing Phase 1 Arm of RTX-240 + Pembrolizumab to Focus on Non-Small Cell Lung Cancer (NSCLC) and Renal Cell Carcinoma (RCC)

Dosing Patients in Phase 1 Clinical Trial of RTX-224 in Select Solid Tumors; Initial Results Expected 4Q'22 or 1Q'23

Successfully Scaled Manufacturing to 200L Bioreactors

Company Provides Update on Phase 1 Clinical Trial of RTX-321 in Advanced Human Papilloma Virus (HPV) 16-Positive Cancers

CAMBRIDGE, Mass., May 10, 2022 (GLOBE NEWSWIRE) -- Rubius Therapeutics, Inc. (Nasdaq: RUBY), a clinical-stage biopharmaceutical company that is biologically engineering red blood cells to create an entirely new class of cellular medicines called Red Cell Therapeutics™ for the treatment of cancer and autoimmune diseases, today reported first quarter 2022 financial results and provided a business update.

"With the updated results showing single-agent activity and encouraging tolerability of monotherapy RTX-240 in patients whose disease progressed on PD-(L)1 inhibitors, we believe we have the opportunity to develop RTX-240 as a combination therapy with immune checkpoint inhibitors in earlier lines of therapy, where the greatest need exists for patients with NSCLC and RCC," said Pablo J. Cagnoni, M.D., president and chief executive officer. "We have expanded our Phase 1 arm of RTX-240 in combination with pembrolizumab to focus on less heavily pretreated patients with NSCLC and RCC. We plan to report initial clinical results from the combination arm in advanced solid tumors and initial data from the NSCLC and RCC patients in the second half of 2022."

Dr. Cagnoni continued, "We believe RTX-321 has shown promising pharmacodynamic effects with dramatic expansion of CD4+ T cells, which is one of the key cells involved in the mechanism by which IL-12 stimulates a broad anti-tumor response. Importantly, we continue to see no dose-limiting toxicities and no treatment-related adverse events, giving us confidence that we may be able to safely exploit IL-12's potent antitumor activity with RTX-224, our second broad immune agonism program. RTX-224 expresses higher copy numbers of IL-12 on the cell surface than does RTX-321. Given the additional investment required to dose escalate and the eventual need for a companion diagnostic for patient selection for RTX-321, we are focusing our resources at this time on advancing our broad agonism approach with RTX-240 and RTX-224."

Recent Highlights

Broad Immune Stimulation

RTX-240

RTX-240 is an allogeneic, off-the-shelf cellular therapy product candidate that is engineered to simultaneously present hundreds of thousands of copies of the costimulatory molecule 4-1BB ligand (4-1BBL) and IL-15TP (trans-presentation of IL-15 on IL-15Rα) in their native forms. RTX-240 is designed to broadly stimulate the immune system by activating and expanding both NK and CD8+ memory T cells to generate an anti-tumor response.

Monotherapy RTX-240 in Advanced Solid Tumors

- Reported updated clinical data from the monotherapy Phase 1 arm of RTX-240 in relapsed/refractory or locally advanced solid tumors at the American Association for Cancer Research Annual Meeting in April 2022
- Results included updated safety (n=34) and efficacy (n=27) data from 9 completed dose cohorts at the time of the March 4, 2022, data cutoff
- There were three partial responses (PR) in NSCLC, anal cancer and uveal melanoma patients:
    - an unconfirmed PR (uPR) with 41% decrease of all target lesions and a notable decrease of an external protruding chest wall mass in a patient with NSCLC whose disease had progressed on prior anti-PD-L1 therapy;
    - a confirmed PR with a 54% reduction in the target lesions in a patient with metastatic anal cancer whose disease had progressed on anti-PD-L1 therapy; and
    - a uPR with 100% decrease of the target hepatic lesion and resolution of multiple non-target hepatic lesions in a patient with metastatic uveal melanoma whose disease had progressed on anti-PD-1 therapy
- The uPR in NSCLC and 5 cases of stable disease (SD) were observed across the 3e10 cohorts, including 3 SDs in

patients with metastatic NSCLC and 2 with RCC supporting the Company's decision to expand the Phase 1 arm of RTX-240 plus pembrolizumab to NSCLC and RCC patients
    - One patient each with NSCLC and RCC remained on monotherapy treatment with SD greater than 6 months as of the cutoff date
    - All of these patients had experienced disease progression on prior anti-PD-(L)1 therapy

- RTX-240 was shown to have been generally well tolerated with no treatment-related or investigator-identified immune-related Grade 3/4 adverse events (AE's) and no dose-limiting toxicities.

- Based on the totality of clinical, tolerability and pharmacodynamic data, a recommended monotherapy Phase 2 dose of 5e10 cells administered every 3 weeks was selected
    - This dose is being further explored in the combination expansion cohort of NSCLC and RCC patients
    - Enrollment continues in the monotherapy arm of the trial at the recommended Phase 2 dose of 5e10 cells administered every 3 weeks

RTX-240 + Pembrolizumab in Advanced Solid Tumors

- Advanced enrollment in the Phase 1 combination arm of RTX-240 plus pembrolizumab in patients with advanced solid tumors
    - Expanded ongoing Phase 1 arm to enroll up to 20 patients each with NSCLC and RCC who are less heavily pretreated in preparation for a future Phase 2 clinical trial of RTX-240 in combination with pembrolizumab in an earlier line of therapy

RTX-224

RTX-224 is an allogeneic, off-the-shelf cellular therapy product candidate that is engineered to express hundreds of thousands of copies of 4-1BBL and IL-12 on the cell surface. In contrast to RTX-240, RTX-224 is designed as a broad immune agonist of both adaptive and innate responses, activating CD8+ and CD4+ T cells, promoting antigen presentation and activating and expanding NK cells. It is expected to produce a broad and potent anti-tumor T cell response, an innate immune response and have anti-tumor activity in those tumor types with known sensitivity to T cell killing, including tumor types with high mutational burden, PD-L1 expression and prior activity of checkpoint inhibitors.

- Continuing dose escalation in the Phase 1/2 clinical trial of RTX-224 in selected relapsed/refractory or locally advanced solid tumors that include non-small cell lung cancer, cutaneous melanoma, head and neck squamous cell carcinoma, urothelial (bladder) carcinoma and triple-negative breast cancer
- Initial clinical results are expected by year-end or during the first quarter of 2023

Antigen-Specific Immune Stimulation

RTX-321 Artificial Antigen-Presenting Cell (aAPC) Development Program for HPV 16-Positive Cancers

RTX-321 is an allogeneic, off-the-shelf aAPC therapy product candidate that is engineered to induce a tumor-specific immune response by expanding antigen-specific T cells. RTX-321 expresses hundreds of thousands of copies of an HPV peptide antigen bound to major histocompatibility complex class I proteins, the costimulatory molecule 4-1BBL and the cytokine IL-12 on the cell surface and is designed to mimic human T cell-APC interactions.

Three dose cohorts were completed (n=9) with one patient with anal squamous cell carcinoma with SD ongoing at 16 weeks at the highest dose cohort to date of 1e10 administered every three weeks. Prior to enrollment, the patient experienced disease progression on anti-PD-1 therapy. RTX-321 was generally well tolerated with no DLTs or Grade 3/4 treatment-related AE's. Consistent with the combined mechanism of action of IL-12 and 4-1BBL, increases in activated CD4+ T cells, activated CD8+ T cells and activated NK cells were observed at the higher dose levels.

Manufacturing

- Scaled manufacturing to 200L bioreactors in support of a potential future pivotal trial for RTX-240 and potential commercialization
    - This scaleup represents 4 times more cells than what was produced using the 50L bioreactor

Anticipated 2022 Catalysts and Operational Objectives

To evaluate the full potential of RTX-240, Rubius' other oncology programs and the RED PLATFORM, Rubius plans to execute several critical milestones within the next 12 months and has sufficient cash runway into the second half of 2023:

- Report initial Phase 1 clinical results for RTX-240 in combination with pembrolizumab in advanced solid tumors and data from the initial enrolled NSCLC and RCC patients in the second half of 2022;
- Select a clinical candidate for the first autoimmune program in type 1 diabetes during the second half of 2022; and
- Report initial Phase 1 clinical results for RTX-224 for the treatment of advanced solid tumors by year-end or during the first

quarter of 2023.

First Quarter 2022 Financial Results

Net loss for the first quarter of 2022 was $52.4 million or $0.58 per common share, compared to $42.3 million or $0.51 per common share in the first quarter of 2021.

In the first quarter of 2022, Rubius invested $38.3 million in research and development (R&D) related to its novel RED PLATFORM® and towards expanding and advancing its product pipeline, compared to $27.7 million in the first quarter of 2021. This year-over-year increase was principally due to a $5.3 million increase in costs related to our lead cancer programs, RTX-240, RTX-321 and RTX-224, primarily from clinical research organization (CRO) and internal manufacturing costs incurred in connection with all three programs. Additionally, platform development, early-stage research and other unallocated expenses increased by $5.6 million due principally to increases of $2.4 million in personnel-related costs and $0.9 million in stock-based compensation related to the increase in headcount to support our expanded operations. Contract research and development and laboratory supplies also increased to support drug discovery and platform development activities.

G&A expenses were $12.6 million during the first quarter of 2022, compared to $13.2 million for the first quarter of 2021. The lower costs were primarily driven by a reduction in stock-based compensation related to stock option awards that fully vested during the third quarter of 2021.

Cash Position

As of March 31, 2022, cash, cash equivalents and investments were $176.5 million, compared to $225.8 million as of December 31, 2021, providing Rubius with a cash runway into the second half of 2023. During the quarter, the Company used $47.1 million of cash to fund operations and $2.4 million to fund capital expenditures, consisting mostly of renovation costs incurred at our manufacturing facility.

Rubius Therapeutics, Inc.
Condensed Consolidated Statement of Operations
(in thousands, except share and per share data)
(unaudited)

	For the three months ended March 31,	
	2022	**2021**
Revenue	$	$
Operating expenses:		
Research and development	38,299	27,677
General and administrative	12,563	13,240
Total operating expenses	50,862	40,917
Loss from operations	(50,862)	(40,917)
Other income (expense), net	(1,550)	(1,413)
Net loss	$ (52,412)	$ (42,330)
Net loss per share, basic and diluted	$ (0.58)	$ (0.51)
Weighted average common shares outstanding, basic and diluted:	90,149,049	82,314,577

Rubius Therapeutics, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands)
(unaudited)

	March 31, 2022	**December 31, 2021**
Cash, cash equivalents and investments	$ 176,517	$ 225,848
Total assets	267,123	318,021
Total liabilities	132,474	139,239
Total stockholders' equity	134,649	178,782

About Rubius Therapeutics
Rubius Therapeutics is a clinical-stage biopharmaceutical company developing a new class of medicines called Red Cell Therapeutics™. The Company's proprietary RED PLATFORM® was designed to biologically engineer and culture Red Cell Therapeutics™ that are selective, potent and off-the-shelf allogeneic cellular therapies for the potential treatment of several diseases across multiple therapeutic areas. Rubius' initial focus is to advance RCT™ product candidates for the treatment of cancer and autoimmune diseases by leveraging two distinct therapeutic modalities — potent cell-cell interaction and tolerance induction. Rubius Therapeutics was recently named among the 2021 Top Places to Work in Massachusetts by the Boston Globe, and its manufacturing site was recently named 2022 Best Places to Work in Rhode Island by Providence Business News. For more information, visit www.rubiustx.com, follow us on Twitter or LinkedIn or like us on Facebook.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding beliefs about Rubius' execution across preclinical and clinical development, Rubius' plans and expected timing to present clinical results for RTX-224, RTX-240 and RTX-321, beliefs about the opportunities for and advantages of our drug candidates, our interpretations of data, including as to the efficacy of our product candidates, expectations regarding the therapeutic potential and

safety profile of our pipeline candidates, beliefs about patients' needs, expectations for our cash position, as well as beliefs about our manufacturing plans and accomplishments. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, those risks and uncertainties related to the development of our Red Cell Therapeutic product candidates and their therapeutic potential, our ability to execute on our plans and expectations, our analyses of clinical and preclinical data and other risks identified in our filings with the U.S. Securities and Exchange Commission (SEC), including our Annual Report on Form 10-K for the year ended December 31, 2021 and subsequent filings with the SEC, including our Quarterly Report on Form 10-Q for the quarter-ended March 31, 2022, which will be filed on or about the date hereof, and risks and uncertainties related to the severity and duration of the impact of COVID-19 on our business and operations. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. We disclaim any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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