Rubius Therapeutics Reports Updated Clinical Data at AACR from the Ongoing Monotherapy Phase 1 Arm of the Phase 1/2 Clinical Trial of RTX-240 in Advanced Solid Tumors Demonstrating Single-Agent Activity and Favorable Tolerability

April 8, 2022

Best Responses Include Partial Responses in Certain Patients with Non-Small Cell Lung Cancer, Metastatic Anal Cancer and Metastatic Uveal Melanoma with No Treatment-Related Grade 3/4 Adverse Events or Dose-Limiting Toxicities as of the Cutoff Date

Expanding Ongoing Phase 1 Arm of RTX-240 + Pembrolizumab to Focus on Non-Small Cell Lung Cancer and Renal Cell Carcinoma

Management to Host Conference Call Today at 1:15 p.m. EDT to Discuss Clinical Data and Clinical Development Next Steps for RTX-240

CAMBRIDGE, Mass., April 08, 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 announced updated clinical data from the ongoing monotherapy Phase 1 arm of the Phase 1/2 clinical trial of RTX-240 in patients with advanced solid tumors at the American Association for Cancer Research Annual Meeting. The Company is hosting a webcast to discuss these data as well as data from the monotherapy Phase 1 arm of RTX-240 in patients with acute myeloid leukemia (AML) today at 1:15 p.m. EDT.

“Recent advances in immuno-oncology have transformed the treatment of cancer and improved outcomes for certain patients. Yet, of the estimated 40 percent of patients eligible for immunotherapy, the majority do not have durable responses. In addition, combinations of immune checkpoint inhibitors have higher toxicity, underscoring the need for safer and more effective immunotherapy combination treatments,” said Alexander I. Spira, M.D., Ph.D., FACP, director of the Virginia Cancer Specialists Research Institute and the Phase 1 Trial Program, and a clinical investigator in all of Rubius’ oncology clinical trials. “In this Phase 1 trial of heavily pretreated patients with advanced solid tumors, RTX-240 demonstrated single-agent activity with encouraging tolerability results, including in patients whose disease had progressed on prior PD-1/PD-L1-based treatment regimens. Based on these data, I believe RTX-240 has the potential to be an ideal candidate to be developed as a combination therapy with immune checkpoint inhibitors, especially in earlier lines of therapy.”

“We believe the encouraging results of monotherapy RTX-240 reported provide clinical support of the RED PLATFORM® and the development of our entire oncology pipeline of Red Cell Therapeutics given the programmable nature of our platform,” said Pablo J. Cagnoni, M.D., president and chief executive officer. “With multiple data milestones expected over the next 12 months, Rubius Therapeutics’ pipeline of oncology Red Cell Therapeutics has the opportunity to show potential benefit in additional types of cancer.”

Updated Data from the Phase 1 Trial of RTX-240 in Patients with Advanced Solid Tumors

Nine dose cohorts (n=34) were completed in the monotherapy solid tumor arm of the trial at the time of the data cutoff on March 4, 2022, with 34 patients evaluable for safety (primary outcome measure) and 27 patients evaluable for efficacy (secondary outcome measure). Enrollment continues in the 5e10 Q3W dose cohort.

As of the cutoff date, disease control was observed in 10 patients (1 partial response, 2 unconfirmed partial responses and 7 with stable disease), 9 of whom had experienced disease progression on prior anti-PD-1/anti-PD-L1 therapy.

There were three best responses of partial response (PR) in non-small cell lung cancer (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 non-small cell lung cancer (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
- An 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.

Stable disease was observed in 5 patients, including 3 with metastatic NSCLC and 2 with renal cell carcinoma (RCC) across the 3e10 cohorts, 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.

As of the cutoff date, RTX-240 has been shown to have been generally well tolerated with no treatment-related or investigator-identified immune-related Grade 3/4 adverse events (AEs) 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 will be further explored in the combination expansion cohort of NSCLC and RCC patients.

“Immune agonists and cytokines have been the focus of oncology research given their known importance for immune activation. However, current approaches have been unable to overcome toxicity challenges, resulting in a narrow therapeutic index, particularly in combination with checkpoint inhibitors. With today’s updated clinical data showing that RTX-240 generated clinical responses with favorable tolerability results in patients whose tumors had progressed on therapy with anti-PD-1/PD-L1 antibodies, we believe these data support the potential of immune agonists for the treatment of cancer,” said Larry Turka, M.D., chief scientific officer and head of translational medicine at Rubius Therapeutics. “Given the clinical results observed, we are expanding the ongoing Phase 1 arm of RTX-240 in combination with pembrolizumab to patients with NSCLC and RCC who have had fewer prior treatment regimens. This cohort is expected to inform our strategy of advancing RTX-240 in combination with pembrolizumab in a Phase 2 clinical trial.”

Final Phase 1 Clinical Results in Relapsed/Refractory AML

Rubius also announced final clinical results from the Phase 1 arm of monotherapy RTX-240 in relapsed/refractory AML. As of the cutoff date of March 4, 2022, seventeen patients were enrolled across 4 dose levels. No DLTs were observed and there were 3 treatment-related Grade 3/4 adverse events. There were no investigator-reported immune-related AEs. Five patients had SD greater than 3 months, and 1 patient had a significant blast count reduction (53% to 6%).

“In this study, RTX-240 has shown activation and expansion of NK and T cells with favorable safety results, which continues to support the proposed mechanism of action of RTX-240. Based on these data, we believe RTX-240 could improve outcomes for AML patients when used as maintenance therapy for patients in remission following high-dose chemotherapy and stem cell transplantation,” continued Dr. Turka. “Based on these data, we believe we have established the necessary foundation to evaluate RTX-240 in the maintenance setting for the treatment of AML. However, to focus our resources on advancing RTX-240 in combination with pembrolizumab in NSCLC and RCC, we do not plan to pursue a separate clinical trial in AML in the near-term.”

Upcoming Anticipated Milestones

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-321 for the treatment of HPV 16-positive cancers during the second half of 2022;
- Report initial Phase 1 clinical results for RTX-240 in combination with pembrolizumab in advanced solid tumors and data from the additional 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 during the first quarter of 2023.

AACR Poster Presentation

Abstract Title: Phase 1 Trial of RTX-240, Allogeneic Red Blood Cells Engineered to Express 4-1BBL and Trans-Presented IL-15, in Patients with Advanced Solid Tumors
Session Title: Phase I Clinical Trials 2
Session Date and Time: Tuesday, April 12, 2022, 9:00 a.m. – 12:30 p.m. ET
Location: New Orleans Convention Center, Exhibit Halls D-H, Poster Section 33
Poster Board Number: 12
Abstract Number: CT187

Conference Call

The Company will host a conference call and webcast at 1:15 p.m. EDT to discuss this update. The audio webcast will be available on the Events and Presentations page within the Investors and Media section of the Rubius Therapeutics website. The update may also be accessed by dialing (800) 289-0045 (domestic) or (615) 622-8086 (international) five minutes prior to the start of the call. The conference ID is 7865329. An archived webcast will be accessible for 90 days after the event.

About RTX-240

RTX-240, Rubius Therapeutics’ lead oncology program, 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 memory T cells to generate a potent anti-tumor response.

About the RTX-240 Clinical Trial

The Phase 1/2 clinical trial of RTX-240 is an open label, multicenter, multidose, first-in-human dose-escalation and expansion study designed to evaluate the safety and tolerability, pharmacokinetics, maximum tolerated dose, a recommended Phase 2 dose and dosing regimen of RTX-240. The trial is also assessing the pharmacodynamics of RTX- 240 measured by changes in T and NK cell number and function relative to baseline and anti-tumor activity. The trial has three separate Phase 1 arms: a monotherapy dose escalation arm in adults with relapsed/refractory or locally advanced solid tumors, a monotherapy dose escalation arm in adults with relapsed/refractory acute myeloid leukemia, and a combination therapy dose escalation arm with pembrolizumab in adults with relapsed/refractory or locally advanced solid tumors.

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 2021 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 our expectations with respect to the potential of our pipeline of Red Cell Therapeutics, our plans to announce results from our RTX-240 trial in patients with solid tumors and AML and to share expected next steps for the Phase 2 clinical development, our expectations regarding our timelines for reporting additional clinical data, our expectations for and beliefs about the initial results from the RTX-240 trial and its validation of the RED PLATFORM and its impact on the potential of our entire oncology platform, and the extent to which the COVID-19 pandemic may impact Rubius' ability to enroll patients in the trial will depend on future developments and our expectations regarding our strategy, business plans and focus. 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, 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.

Contacts:
Investors
Lori Murray, Chief Corporate Affairs Officer
lori.murray@rubiustx.com

Media
Marissa Hanify, Director, Corporate Communications
marissa.hanify@rubiustx.com

Source: Rubius Therapeutics