Rubius Therapeutics Reports Initial Clinical Data from Ongoing Phase 1/2 Trial of RTX-240 in Patients with Advanced Solid Tumors, Demonstrating Single-Agent Activity

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RTX-240 Generated Partial Responses in Metastatic Anal Cancer and Metastatic Uveal Melanoma Patients; No DLTs or Related Grade 3/4 Adverse Events

RTX-240 Promoted Trafficking of NK and T Cells into Tumor Microenvironment

Initial Clinical Data Provide Evidence of Broad Potential of RED PLATFORM® Across Pipeline of Cancer and Autoimmune Programs

Company to Host Conference Call Today at 8:00 a.m. EDT

CAMBRIDGE, Mass., March 15, 2021 (GLOBE NEWSWIRE) -- Rubius Therapeutics, Inc. (Nasdaq:RUBY), a clinical-stage biopharmaceutical company that is genetically engineering red blood cells to create an entirely new class of cellular medicines called Red Cell Therapeutics™, today announced initial clinical, pharmacodynamic and tumor trafficking data from its ongoing Phase 1/2 clinical trial of RTX-240 in patients with advanced solid tumors. The Company also shared tumor trafficking data from one patient with relapsed/refractory acute myeloid leukemia (AML) in the second Phase 1 arm of the study. The Company believes these data provide initial proof-of-concept of the RED PLATFORM® by providing evidence that red blood cells can be engineered to mimic the human immune system and stimulate adaptive and innate immunity to generate clinical responses in cancer patients with refractory disease.

“These initial data are incredibly exciting and demonstrate that RTX-240 has the potential to generate single-agent activity in patients with solid tumors, including a cold tumor such as metastatic uveal melanoma, where other treatments have failed to induce responses in patients,” said Christina Coughlin, M.D., Ph.D., chief medical officer at Rubius Therapeutics. “The encouraging safety results, including a single event of Grade 1 liver toxicity, and preliminary efficacy data for RTX-240 to date give us the potential to realize the power of immune agonists for the treatment of cancer.”

Initial Efficacy Data

Five (5) dose cohorts were completed in the solid tumor trial at the time of the data cutoff on February 28, 2021 (n=16), with 16 patients evaluable for safety (primary outcome measure) and 15 patients evaluable for efficacy (secondary outcome measure) based on RECIST v1.1.

The study is continuing to enroll patients and despite the fact that dose optimization is still ongoing, RTX-240 generated:

- A confirmed partial response (PR) with a 54% reduction in the target lesions at the 1e8 dose administered every 4 weeks in a patient with metastatic anal cancer whose disease had progressed on anti-PD-L1 therapy. Treatment of this patient was ongoing 8 months following the first dose at data cutoff;
- An unconfirmed PR with complete resolution of the target hepatic lesion and resolution of 14/15 hepatic lesions at the 1e10 dose administered every 4 weeks in a patient with metastatic uveal melanoma whose disease had progressed on anti-PD-1 therapy. Treatment of this patient was ongoing 4 months following the first dose at data cutoff; and
- Stable disease (SD) was observed in 6 patients, including 4 individual patients with stable disease for at least 12 weeks:
    - Non-small cell lung cancer (disease stabilization for 12 weeks with treatment ongoing as of the data cutoff);
    - Soft tissue sarcoma (disease stabilization for 4 months);
    - Pancreatic cancer (disease stabilization for 3 months); and
    - Prostate cancer (disease stabilization for 4 months).

“We believe these data provide clinical validation of our RED PLATFORM ® and de-risk our oncology pipeline of Red Cell Therapeutics,” said Pablo J. Cagnoni, M.D., president and chief executive officer. “Given the encouraging initial safety and preliminary efficacy data for RTX-240, we plan to initiate a Phase 2 expansion cohort in the first quarter of 2022, and a new Phase 1 arm of the ongoing RTX-240 clinical trial to evaluate RTX-240 in combination with anti-PD-1 therapy in patients with advanced solid tumors during the second half of 2021.”

Initial Safety Data

The most common treatment-related Grade 1/2 adverse events were fatigue (n=4), chills, nausea, decreased appetite and arthralgias all reported in 3 patients each. There were no treatment-related Grade 3/4 adverse events, no dose-limiting toxicities and a single Grade 1 event of liver toxicity.

Ten (10) immune-related adverse events (irAE) were observed among 5 patients with no reported treatment-related Grade 3/4 irAEs. Grade 2 treatment-related irAEs included pneumonitis (n=1), adrenal insufficiency (n=1) and hypothyroidism (n=1).

Pharmacodynamic Data

In addition to evaluating safety and preliminary efficacy data, the trial is evaluating the pharmacodynamic effects of RTX-240:

- RTX-240 stimulated innate and adaptive immunity as demonstrated by the activation and/or expansion of NK or memory CD8+ T cells in all patients, with 9/16 patients showing activation and expansion in both cell types. There was an overall trend towards a dose response in absolute NK cell numbers (expansion);
- Detailed NK cell analysis showed an increased percentage of $CD16^{+}CD56^{dim}$ (mature NK cells) and $CD56^{bright}$ (immature NK cells) across dose levels
    - These cell subtypes are associated with cytotoxicity and cytokine production respectively; and
- RTX-240 induced expression of key NK cell activation receptors, including NKp30 and the ratio of cells expressing the activation receptor NKG2D versus the inhibitory receptor NKG2A
    - This specific signature of NK cell receptor expression may allow selection of specific tumor types with predicted sensitivity to RTX-240.

Tumor Infiltration Data

Immune cell trafficking into the tumor microenvironment (TME) was assessed by tumor biopsies from participating patients with solid tumors (optional; n=4) and AML (standard of care; n=1).

- Trafficking of T and NK cells into the TME was observed in 3/5 patients (1.6 to 10-fold increases), including one patient each with metastatic mesothelioma, metastatic soft tissue sarcoma and refractory AML. Tumor infiltration was not observed in patients with ovarian cancer (n=1) and heavily pretreated melanoma (n=1);
- There was increased expression of PD-L1 observed in 3/4 patients with solid tumors, suggesting an improved immune-permissive TME; and
- In one patient with AML, trafficking of T and NK cells into the bone marrow was associated with increases in the cellularity of the marrow.

Upcoming Anticipated Milestones

In order to realize the full potential of RTX-240, the Company's other oncology programs and the RED PLATFORM, in the next 12 months, Rubius plans to execute several critical milestones:

- Present additional clinical results from the RTX-240 solid tumor Phase 1 clinical trial;
- Select the recommended RTX-240 Phase 2 dose, schedule and specific solid tumor types that will be pursued in the Phase 2 expansion cohort;
- Report initial clinical results for the second Phase 1 arm of the RTX-240 clinical trial in relapsed/refractory AML;
- Initiate the Phase 1 clinical trial of RTX-240 in combination with anti-PD-1 therapy in advanced solid tumors in 2H'21;
- Report initial Phase 1 clinical results for RTX-321 for the treatment of HPV 16-positive cancers by 1Q'22; and
- Submit an Investigational New Drug Application for RTX-224 by year-end.

Conference Call

The Company will host a conference call and webcast at 8:00 a.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 1-800-289-0045 (domestic) or 1-615-622-8086 (international) five minutes prior to the start of the call and providing the passcode 1294064. An archived webcast will be accessible for 90 days after the event.

About RTX-240

RTX-240 is an allogeneic, off-the-shelf cellular therapy product candidate that is designed 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 expected 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

This is a Phase 1/2 open label, multicenter, multidose, first-in-human dose-escalation and expansion study designed to determine the safety and tolerability, pharmacokinetics, maximum tolerated dose and a recommended Phase 2 dose and dosing regimen of RTX-240 in adult patients with relapsed/refractory or locally advanced solid tumors or with relapsed/refractory acute myeloid leukemia. The trial will also assess the pharmacodynamics of RTX-240 measured by changes in T and NK cell number and function relative to baseline and anti-tumor activity. The study will include a monotherapy dose escalation phase followed by an expansion phase in specified tumor types during the Phase 2 portion of the trial. The extent to which the COVID-19 pandemic may impact Rubius' ability to enroll patients in the trial will depend on future developments.

About RTX-321

RTX-321 is an allogeneic, off-the-shelf artifical antigen-presenting cell therapy product candidate that is designed to express 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 to mimic human T cell-APC interactions. In preclinical studies, RTX-321 was shown to have a dual mechanism of action by functioning as an antigen-presenting cell to boost HPV 16 antigen-specific T cell responses and promoting broad immune system stimulation of both innate and adaptive immunity.

About RTX-224

RTX-224 is an allogeneic 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 broader T cell- agonist, while also retaining the ability to activate and expand NK cells. It is expected to produce a broad and potent anti-tumor T cell response, an innate immune response and show 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.

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 genetically 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 Top Places to Work in Massachusetts by the Boston Globe, and its manufacturing site was recently named 2020 Top 5 Best Places to Work in Rhode Island among medium-sized companies 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 therapeutic potential of our pipeline of Red Cell Therapeutics, including RTX-240, our expectations regarding the timing, enrollment, data from and success of the future cohorts and phases of the clinical trial of RTX-240, including the Phase 1/2 clinical trial of RTX-240, our plans to initiate a RTX-240 Phase 2 expansion cohort, an RTX-240 Phase 1 clinical trial in combination with an anti-PD-1 therapy in advanced solid tumors and file an Investigational New Drug application for RTX-224 over the next twelve months, our expectations regarding the biological effects of RTX-240 on innate and adaptive immunity and the related therapeutic benefits, our expectations regarding the initial preliminary data from RTX-240 and the related therapeutic benefits and validation of our RED PLATFORM 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 and other risks identified in our SEC filings, including our Annual Report on Form 10-K for the year ended December 31, 2020, and subsequent filings with the SEC and risks and uncertainties related to the severity and duration of the impact of COVID-19 on our clinical trials, 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. We explicitly disclaim any obligation to update any forward-looking statements.

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