Rubius Therapeutics Provides Operational Update and Outlines 2021 Objectives at the 39th Annual J.P. Morgan Healthcare Conference

January 11, 2021

Initial Clinical Data Show RTX-240 Stimulates Innate and Adaptive Immunity
(NK Cells and T Cells) Supporting Proof of Mechanism –
Additional Results to be Presented in Early 2021

IND Cleared and Patient Screening Underway for Phase 1 Clinical Trial of RTX-321 in
Advanced Human Papillomavirus-Positive Cancers

Increased Productivity and Extended Product Shelf Life at Fully Owned Manufacturing Facility

CAMBRIDGE, Mass., Jan. 11, 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 provided an operational update and announced its 2021 objectives. Pablo J. Cagnoni, M.D., chief executive officer, will present these updates and review 2020 achievements on Wednesday, January 13, 2021, at 8:20 a.m. EST at the virtual 39th Annual J.P. Morgan Healthcare Conference.

“Rubius Therapeutics made significant progress in advancing our oncology pipeline and in-house manufacturing capabilities in 2020,” said Pablo J. Cagnoni, M.D., president and chief executive officer. “To date, in the initial data from the Phase 1 clinical trial of RTX-240 in advanced solid tumors, we have observed activation and expansion of both target cell populations, NK and T cells, indicating the ability of RTX-240 to stimulate both innate and adaptive immune responses. We plan to present additional clinical results in early 2021, and we plan to submit for presentation at a scientific conference.”

By showing that RTX-240 is activating and expanding NK and T cells, Rubius Therapeutics believes that the full data set from the Phase 1 clinical trial will unlock the potential of the RED PLATFORM® across the entire pipeline of Red Cell Therapeutics for the treatment of cancer.

Clinical Program Updates

RTX-240 Phase 1/2 Clinical Trial for the Treatment of Advanced Solid Tumors and Relapsed/Refactory Acute Myeloid Leukemia (AML)

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 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.

- To date, Rubius has completed dosing of 5 cohorts (n=14) in the Phase 1/2 RTX-240 solid tumor clinical trial. Trial enrollment continues in additional cohorts.
- Key takeaways from initial data to date show:
    - No treatment-related Grade 3 or Grade 4 adverse events and no dose limiting toxicities observed (n=14)
    - All patients showed activation of NK or T cells or both cell types (n=14)
    - In the majority of patients (n=8), all of the following were observed across dose levels:
        - Activation of NK cells, activation of T cells, expansion of NK cells and expansion of T cells
- As more patients are enrolled and data mature, the Company expects to disclose additional clinical results, including
    - additional safety and tolerability data;
    - biomarkers associated with the activation and expansion of NK and T cells in peripheral blood
    - immune cell trafficking into tumors assessed by optional tumor biopsies from participating patients; and
    - potential responses as measured by objective response rate
- Enrollment continues in the Phase 1 clinical trial of RTX-240 in relapsed/refractory AML

RTX-321 Artificial Antigen-Presenting Cell (aAPC) Development Program for Human Papillomavirus (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 to mimic human T cell-APC interactions.

- The Investigational New Drug (IND) application has been cleared and patients are being screened in the Phase 1 clinical

trial of RTX-321 in advanced HPV 16+ cancers, including cervical cancer, head and neck cancer and anal cancer

Manufacturing Update and Recent Achievements

Recognizing the importance of controlling manufacturing to produce consistent and reproducible product at greater scale, Rubius acquired, renovated and operationalized a manufacturing facility in Smithfield, RI. The site has achieved the following milestones:

- Provided consistent cGMP supply for the two Phase 1 arms in the ongoing RTX-240 clinical trial in advanced solid tumors and relapsed/refractory AML
    - Increased productivity in manufacturing of cGMP supply of RTX-240 in 50L bioreactors
    - Increased liquid in-vial shelf life from 28 to 52 days for RTX-240
    - Continuously met red blood cell identity (CD233+, mean corpuscular hemoglobin, purity, enucleation cell population) and target product profile criteria (protein expression, cell viability) for clinical supply lots
- Completed engineering runs and now producing cGMP supply for the Phase 1 clinical trial of RTX-321 for advanced HPV 16-positive cancers
    - Introduced frozen drug substance for the first time as part of the IND application for RTX-321, resulting in a truly off-the-shelf cellular therapy with a potential shelf life of up to several years
    - Following liquid reformulation, RTX-321 drug product has an in-vial shelf life of 52 days
- Significant potential to expand manufacturing capabilities based on future supply needs and for potential commercial production

Preclinical Data 2020 Summary

The Company presented preclinical oncology data for RTX-240 and RTX-321 at the following conferences:

- Society for Immunotherapy of Cancer (SITC) Annual Meeting;
- Federation of Clinical Immunology Societies (FOCIS) Virtual Annual Meeting;
- American Association for Cancer Research (AACR) Tumor Immunology Conference; and
- American Society of Gene & Cell Therapy 23rd Annual Meeting

Anticipated 2021 Catalysts and Operational Objectives

- Present additional clinical data for the Phase 1 RTX-240 solid tumor trial in early 2021;
- Continue to enroll patients with AML in the second Phase 1 arm of the RTX-240 clinical trial;
- Dose the first patient in the RTX-321 clinical trial in HPV-positive tumors;
- Continue to produce cGMP material for the RTX-240 and RTX-321 clinical trials; and
- Present an integrated clinical program for RTX-240, including plans for expansion cohorts, and oncology pipeline

Listen to the Webcast

A live audio webcast of Dr. Cagnoni's presentation will be available on January 13, 2021 at 8:20 a.m. EST within the Investors & Media section of the Rubius Therapeutics website. An archived replay will be accessible for 30 days following the event.

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 regarding the therapeutic potential of our pipeline of Red Cell Therapeutics, including RTX-240 for the treatment of patients with relapsed/refractory or locally advanced solid tumors and RTX-321 for the treatment of HPV 16-positive cancers, our expectations regarding the timing, enrollment, additional data from and success of the future cohorts and phases of the clinical trial of RTX-240, our expectations regarding the biological effects of RTX-240 on innate and adaptive immunity, including activation and increased numbers of NK cells and T cells in the clinical trial of RTX-240, and our expectations regarding the full data set from the Phase 1 clinical trial and its ability to unlock the potential of the RED PLATFORM across our entire pipeline of Red Cell Therapeutics for the treatment of cancer, timelines related to the Phase 1 clinical trial of RTX-321, our expectations regarding our ability to expand manufacturing capabilities, our expectations regarding the potential shelf life of our frozen drug substance for RTX-321, our expectations regarding our cash runway and 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 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 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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