Rubius Therapeutics Recaps 2021 Achievements and Outlines 2022 Objectives Across the RED PLATFORM at the 40th Annual J.P. Morgan Healthcare Conference

January 10, 2022

Continuing Dose Escalation in Single-Agent Phase 1 RTX-240 Clinical Trial in Advanced Solid Tumors with No Dose-Limiting Toxicities Observed to Date and an NK Cell Dose Response with Clinical Results Expected in Q1'22

Initial Clinical Results Expected from the Phase 1 Clinical Trial of RTX-321 in HPV 16-Positive Cancers During and the RTX-240 Phase 1 Combination Clinical Trial with Pembrolizumab in 2H'22

First Patient Expected to be Dosed in Phase 1/2 Clinical Trial of RTX-224 in Patients with Selected Advanced Solid Tumors in Q1'22

Demonstrated Tolerance Induction with Bystander Suppression in Type 1 Diabetes Preclinical Program with Findings Translatable to Multiple T Cell-Mediated Autoimmune Diseases

CAMBRIDGE, Mass., Jan. 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 provided an overview of the Company's achievements in 2021 and outlined its objectives for 2022. Pablo J. Cagnoni, M.D., president and chief executive officer, will present these updates on Wednesday, January 12, 2022, at 8:15 a.m. EST at the virtual 40th Annual J.P. Morgan Healthcare Conference.

"In 2021, Rubius Therapeutics demonstrated strong execution in advancing our clinical oncology pipeline and showing preclinical proof of concept of our tolerance induction approach in autoimmunity that could extend well beyond type 1 diabetes to other T cell-mediated diseases," said Pablo J. Cagnoni, M.D., president and chief executive officer, of Rubius Therapeutics. "With the initial clinical results from the Phase 1 clinical trial of RTX-240 in patients with advanced solid tumors reported in March 2021, we provided clinical validation of the RED PLATFORM® and increased our likelihood of success across our entire oncology pipeline of Red Cell Therapeutics. With multiple data milestones on the horizon in 2022, we are on the cusp of potentially further validating the RED PLATFORM and benefiting an even greater number of patients."

Anticipated 2022 Catalysts and Operational Objectives

- Present additional clinical results from the Phase 1 arm of the RTX-240 Phase 1/2 clinical trial in advanced solid tumors and the Phase 1 arm in relapsed/refractory acute myeloid leukemia (AML) during the first quarter of 2022
- Initiate RTX-240 Phase 2 expansion cohorts in select solid tumor types during the first quarter of 2022
- Report initial clinical results from the Phase 1 clinical trial of RTX-321 in patients with advanced HPV 16-positive cancers during the second half of 2022
- Present initial clinical data from the Phase 1 arm of the RTX-240 clinical trial in combination with pembrolizumab in patients with advanced solid tumors during the second half of 2022
- Scale to 200L bioreactors by mid-2022 to support potential pivotal trial and eventual commercialization

2021 Achievements and Operational Updates

RED PLATFORM

- Enabling rapid and repeatable parallel generation of therapeutic candidates with the programmable RED PLATFORM
  - 1,000 different therapeutic proteins biologically engineered since platform inception, underscoring the highly versatile and programmable nature of the platform
  - The platform creates multiple modalities for the treatment of cancer and autoimmune disease and the ability to express hundreds of thousands of copies of therapeutic proteins on or within the cell to access numerous immune pathways
- Achieved clinical validation of the RED PLATFORM with initial clinical results from the single-agent RTX-240 Phase 1 clinical trial in advanced solid tumors, reported in March 2021
  - RCTs are well tolerated, induce the desired biological effect and generate clinical benefit in certain patients with advanced solid tumors
- Advancing next generation artificial antigen-presenting cells (aAPCs) with loadable MHC Class I, enabling the presentation of multiple antigens on a single RCT and broadening the potential patient population with a library of HLA types

Oncology

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 a potent anti-tumor response.

- Established clinical proof of concept of RTX-240 in advanced solid tumors, based on initial results reported in March 2021, potentially increasing the likelihood of clinical success across the oncology pipeline
- Escalated the dose of single-agent RTX-240 in the Phase 1 solid tumor clinical trial to three doses of 5e10 cells followed by 1e10 cells until disease progression or unacceptable toxicity, based on no dose-limiting toxicities observed to date, a clear dose response in the increase of NK cells and other pharmacodynamic effects
    - Additional clinical results are expected from this trial and the Phase 1 arm in relapsed/refractory AML during the first quarter of 2022
    - The Company plans to initiate RTX-240 Phase 2 expansion cohorts in select solid tumor types during the first quarter of 2022
- Continuing dose escalation in the RTX-240 Phase 1 combination study with pembrolizumab in patients with advanced solid tumors with initial clinical data expected during the second half of 2022

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 interleukin-12 (IL-12) on the cell surface. While the lead oncology product candidate, RTX-240, is designed to broadly stimulate the immune system by activating and expanding NK and CD8+ memory T cells, RTX-224 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 known responsiveness to checkpoint inhibitors.

- Expect to begin dosing patients in the Phase 1/2 clinical trial of RTX-224 in selected relapsed/refractory or locally advanced solid tumors during the first quarter of 2022
    - Select cancers include non-small cell lung cancer, cutaneous melanoma, head and neck squamous cell carcinoma, urothelial (bladder) carcinoma and triple-negative breast cancer
- Presented preclinical data at the Society for Immunotherapy of Cancer's (SITC) 36th Annual Meeting in November 2021, demonstrating that the mouse surrogate of RTX-224, mRBC-224, generated potent anti-tumor activity in B16F10 melanoma models, intravenously and subcutaneously, that was associated with pharmacodynamic changes in the tumors, including activated CD8 + T cells, NK cells and macrophages

Antigen-Specific Immune Stimulation

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

RTX-321 is an allogeneic, off-the-shelf artificial 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.

- Continuing enrollment in the Phase 1 clinical trial of RTX-321 in patients with advanced HPV 16-positive cancers
    - Based on no dose limiting toxicities to date, the Company plans to dose escalate beyond the current cohort of 1e10 cells
- Plan to report initial clinical results during the second half of 2022

Autoimmune Diseases and Type 1 Diabetes

Red Cell Therapeutics for the treatment of autoimmune disease are biologically engineered to express proteins and peptides inside the cell and are designed to be phagocytized, or ingested, by dendritic cells or macrophages to induce tolerance, retraining the immune system to no longer recognize these self-antigens as foreign.

- Demonstrated tolerance induction and bystander suppression in stringent type 1 diabetes preclinical models
    - Established efficacy in the BDC2.5 adoptive transfer model with data supporting that repeated dosing extended duration of disease protection, reversed established inflammation, which is important for the treatment of existing autoimmunity, and induced two types of regulatory T cells, resulting in protection against re-challenge
    - Showed efficacy in non-obese diabetes (NOD) preclinical model
        - Results at 25 weeks exhibit bystander suppression by delivering only two antigens, indicating the mouse surrogate of RTX-T1D prevented or delayed disease caused by many autoantigens
- These findings are potentially translatable beyond type 1 diabetes to multiple autoimmune diseases, including other Rubius' high priority target indications, including multiple sclerosis and celiac disease.

Fully Owned Manufacturing

- Increased cells produced per batch by four times in 50L bioreactors from 2020 to 2021, enabling uninterrupted clinical supply for three Phase 1 arms of the RTX-240 clinical trial and Phase 1 RTX-321 trial
- Additional accomplishments include:
    - High success rate: greater than 90% lot success rate for RTX-240 and RTX-321 clinical supply in 2021
    - Hundreds of doses administered across three arms of RTX-240 Phase 1 and RTX-321 Phase 1 trials
    - High transduction efficiency: greater than 90% of cells are transduced with therapeutic proteins
    - Highly consistent protein expression (dual or triple)
- Introduced frozen drug substance for RTX-321 and RTX-224, enabling inventory storage of greater than two years
- Developing frozen drug product to further simplify supply chain with the goal of making our therapies available around the world
- Bringing all product testing in-house to strengthen supply chain and reduce time-to-product release
- Continuing to invest in the platform to improve productivity and efficiency
- Scaling to 200L bioreactors by mid-2022 to support potential pivotal trial and eventual commercialization

Listen to the Webcast

A live audio webcast of Dr. Cagnoni's presentation will be available on January 12, 2022, at 8:15 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 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 beliefs about Rubius' execution across preclinical and clinical development, Rubius' plans and expected timing to present clinical results for RTX-240 and RTX-321, beliefs that findings from preclinical models will be translatable to multiple T cell-mediated autoimmune diseases, plans to advance and expectations for aAPCs, plans and timing to scale manufacturing, beliefs about the scope and versatility of the programmable RED PLATFORM and the generation of therapeutic candidates, expectations regarding the timing for initiating the RTX-224 trial, expectations regarding the therapeutic potential and safety profile of our pipeline of Red Cell Therapeutics, our interpretations of data, including as to the efficacy of our product candidates with respect to autoimmune diseases and Type 1 diabetes, as well as beliefs about our manufacturing accomplishments and goals and expectations for further manufacturing activities. 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, 2020 and our subsequent filings with the SEC, including our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, 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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