Rubius Therapeutics Announces Extensive Preclinical Data for Three Red Cell Therapeutic Oncology Programs at the 2019 American Association for Cancer Research Annual Meeting

April 2, 2019

CAMBRIDGE, Mass., April 02, 2019 (GLOBE NEWSWIRE) -- Rubius Therapeutics, Inc. (Nasdaq:RUBY), a clinical-stage biopharmaceutical company that is generating red blood cells and bioengineering them into an entirely new class of cellular medicines, today announced that the company presented preclinical data from its emerging oncology pipeline of Red Cell Therapeutics™ at the 2019 American Association for Cancer Research (AACR) Annual Meeting in Atlanta.

RCT™ oncology product candidates are engineered to express combinations of co-stimulatory molecules and cytokines on the cell surface in their natural conformation that directly engage T and NK cells to activate the adaptive and innate immune systems through direct cell-cell interaction, replicating how the immune system naturally functions, to attack and kill tumors. Additionally, and in contrast to adoptive or autologous cell therapy approaches that require engineering a patient's own T cells, Rubius Therapeutics has created artificial antigen presenting cells (aAPCs) that are designed to induce a tumor-specific immune response and dramatically expand tumor-specific T cells in vivo. These T cells are then expected to traffic to tumors and deliver an anti-tumor effect.

"Today, Rubius Therapeutics presented compelling preclinical data from our growing oncology pipeline, supporting our potentially groundbreaking approach in immuno-oncology," said Pablo J. Cagnoni, M.D., chief executive officer of Rubius Therapeutics. "The Red Cell Therapeutics (RCTs) RTX-240 (4-1BBL and IL-15TP) and RTX-224 (4-1BBL and IL-12) each potently stimulated different components of the immune system and demonstrate a potentially wide therapeutic window, impressive antitumor activity and no observed toxicity when compared to agonists antibodies or recombinant cytokines. Additionally, RTX-224 in combination with anti-PD-1 antibody demonstrated substantial tumor shrinkage in a difficult-to-treat MC38 colon cancer model. We also presented data showing that our RCT artificial antigen presenting cells, or RTX-aAPCs, activate and significantly expand antigen-specific T cells to reduce tumor burden with no observed toxicity. These unique, allogeneic cell therapy product candidates could transform the immuno-oncology treatment landscape."

Data Summaries

RTX-240 (4-1BBL and IL-15TP) Red Cell Therapeutic Product Candidate

RTX-240, an Allogeneic Red Cell Therapeutic Expressing 4-1BBL and IL-15TP, Exhibits Potent In Vitro and In Vivo Activity and a Favorable Preclinical Safety Profile

- RTX-240 is an allogeneic cellular therapy product candidate engineered to replicate the human immune system by stimulating the adaptive and innate immune systems to generate an immune response.
- RTX-240 simultaneously presents hundreds of thousands of copies of 4-1BB ligand (4-1BBL) and IL15TP, a fusion of IL-15 and IL-15 receptor alpha, in their native forms to activate and expand T and NK cells for the potential treatment of solid tumors.
- In the results presented today, RTX-240 demonstrated a potentially wide therapeutic window with potent immune stimulation, antitumor activity and no observed toxicity.
- 4-1BBL and IL-15TP demonstrated synergistic and complementary effects in promoting innate and adaptive immunity:
  - RTX-240's cellular presentation of the native conformation of 4-1BBL led to more potent activation - 10-fold higher activation - of the 4-1BB pathway compared to a 4-1BB agonist antibody in vitro.
  - A murine surrogate for RTX-240, called mRBC-240, promoted significant expansion and activation of key cells driving innate and adaptive immune responses in vivo, including activation and proliferation of CD8 T cells and NK cells.
  - mRBC-240 demonstrated potent antitumor activity by significantly reducing the number of lung metastases and increasing the number of NK cells in the lung, including terminally differentiated NK cells, compared to control mice in a B16F10 mouse model.
- mRBC-240 resulted in no observed liver toxicity in vivo, likely due its restriction to the vasculature.
- Rubius plans to file an Investigational New Drug application for RTX-240 by early 2020.

RTX-224 (4-1BBL and IL-12) Red Cell Therapeutic Product Candidate

RTX-224, an Allogeneic Red Cell Therapeutic Expressing 4-1BBL and IL-12, Exhibits Potent In Vitro and In Vivo Activity and a Favorable Preclinical Safety Profile

- RTX-224 is an allogeneic cellular therapy product candidate engineered to replicate the human immune system by stimulating the adaptive and innate immune systems to generate an immune response.

- RTX-224 simultaneously presents hundreds of thousands of copies of 4-1BBL in its native form and IL-12 on the cell surface to activate T and NK cells for the potential treatment of solid tumors.
- In the results presented today, RTX-224 demonstrated a potentially wide therapeutic window with highly potent antitumor activity and no observed toxicity in murine models.
- RTX-224 promoted significant expansion and activation of key cells driving innate and adaptive immune responses in vivo, including NK cell proliferation, NK cell cytotoxic activity, stimulation of IFNγ production and proliferation of CD4- and CD8-positive T cells.
- A murine surrogate for RTX-224, called mRBC-224, demonstrated significant tumor growth inhibition in both a lung metastasis and subcutaneous B16F10 mouse model, and, when combined with anti-PD-1 antibody, demonstrated significant tumor shrinkage in the MC38 colon cancer mouse model.
- In contrast to systemic treatment with recombinant IL-12, mRBC-224 also resulted in no observed organ toxicity in vivo, likely due to its restriction to the vasculature.
- RTX-224 is the second most advanced oncology product candidate within the Rubius Therapeutics pipeline.

Red Cell Therapeutic Artificial Antigen-Presenting Cell (aAPC)

Engineered Red Cell Therapeutics (RCT) as Artificial Antigen Presenting Cells Promote In Vivo Expansion and Antitumor Activity of Antigen-Specific T Cells

- RCT artificial antigen presenting cells (RTX-aAPCs) are engineered to induce a tumor-specific response by expanding tumor-specific T cells against a target antigen.
- Rubius Therapeutics' first aAPC product candidate is for the potential treatment of HPV-positive cancers.
- RTX-aAPC (HPV+) is engineered to express on the cell surface an HPV peptide antigen on the major histocompatibility complex (MHC) I, a costimulatory signal, and a cytokine to recapitulate the human immunobiology of T cell-APC interactions.
- In the results presented today, RTX-aAPCs activate and significantly expand antigen-specific T cells in vitro and in vivo, reduce tumor burden and have no observed toxicity in murine models.
  - RTX-aAPC (HPV+) selectively activated antigen-specific T cells directed against a dominant epitope in HPV-positive cancers.
- Additionally, to demonstrate preclinical proof-of-concept, a murine surrogate aAPC, called mRBC-aAPC (OVA), was engineered to express an OVA peptide antigen on MHC I and the costimulatory molecule 4-1BBL.
- mRBC-aAPC (OVA) dramatically increased expansion of OVA-specific T cells 60-fold higher in the spleen and 30-fold higher in the lymph nodes compared to controls in vivo.
- mRBC-aAPC (OVA) also promoted substantial tumor regressions in an OVA-positive murine model leading to extended survival.
- mRBC-aAPC (OVA) treatment resulted in no body weight changes and no observed liver toxicity.
- These data suggest that antigen-specific T cells are expanded in the vasculature and spleen and subsequently traffic to the tumor.
- Rubius Therapeutics' RTX-aAPC platform is a modular and versatile immunotherapy platform that is designed to target antigen-specific T cells across multiple tumor types using common antigens or neoantigens.

About Rubius Therapeutics Oncology Approach

RCT product candidates can be engineered to express combinations of co-stimulatory molecules and cytokines on the cell surface in their natural conformation to directly engage T and NK cells to activate the adaptive and innate immune systems. The goal is to stimulate these immune cells to proliferate, activate, migrate and, ultimately, to attack and kill tumors. Rubius Therapeutics' lead oncology candidates each are designed to stimulate the immune system in different ways and provide several benefits over existing immuno-oncology approaches: 1) the expression of natural ligands in the appropriate conformation and in synergistic combinations is expected to provide a more potent activation of the immune system; 2) RCTs are confined to the vasculature versus administered systemically, which is expected to result in an improved safety profile; and 3) as a result, RCTs are expected to have a broader therapeutic window.

Additionally, and in contrast to adoptive or autologous cell therapy approaches that require engineering a patient's own T cells, Rubius Therapeutics has created artificial antigen presenting cells (aAPCs) that are designed to induce a tumor-specific immune response and dramatically expand tumor-specific T cells in vivo. These T cells are then expected to traffic to tumors and deliver a potent anti-tumor effect.

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 rare diseases, cancer and autoimmune diseases by leveraging three distinct therapeutic modalities — cellular shielding, potent cell-cell interaction and tolerance induction. For more information, visit **www.rubiustx.com** or follow us on **Twitter** and **LinkedIn**.

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 RCTs, the expected timing and progress of our RCT product candidates, the timeline for us to file an IND for RTX-240, and our strategy, business plans and focus. The words “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “goal,” “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 RCT 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, 2018, and subsequent filings with the SEC. 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.

Contacts:
Lori Melançon
Vice President, Corporate Communications and Investor Relations
+1 (617) 949-5296
lori.melancon@rubiustx.com

Media Contact:
Dan Budwick
1AB
+1 (973) 271-6085
dan@1abmedia.com

Source: Rubius Therapeutics