SpringWorks Therapeutics Enters into Sponsored Research Agreement with Fred Hutchinson Cancer Research Center to Further Evaluate Nirogacestat as a BCMA Potentiator in Multiple Myeloma

September 18, 2020

STAMFORD, Conn., Sept. 18, 2020 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a clinical-stage biopharmaceutical company focused on developing life-changing medicines for patients with severe rare diseases and cancer, today announced that it has entered into a sponsored research agreement with Fred Hutchinson Cancer Research Center (Fred Hutch) to further explore the ability of SpringWorks' investigational gamma secretase inhibitor (GSI), nirogacestat, to modulate B-cell maturation antigen (BCMA) and potentiate BCMA-targeting therapies, including radioimmunotherapies, in a variety of preclinical and patient-derived multiple myeloma models developed by researchers at Fred Hutch. Damian Green, M.D., Associate Member of the Clinical Research Division at Fred Hutch and Associate Professor at the University of Washington School of Medicine, will serve as the Principal Investigator for this research.

Gamma secretase inhibition disrupts the cleavage and shedding of BCMA from the surface of myeloma cells. In preclinical models, the team at Fred Hutch was the first to show that gamma secretase inhibition can increase BCMA surface density on malignant plasma cells and concurrently decrease soluble BCMA to enhance the activity of BCMA-targeted therapies.[1,2] Nirogacestat has demonstrated similar results.[3] In addition, emerging and published clinical data from Fred Hutch suggest that a GSI may increase antitumor efficacy of BCMA-targeted autologous CAR T cell therapy in patients with relapsed and refractory multiple myeloma.[1,4]

"We have already begun to see multiple myeloma patients appear to benefit from the ability of a GSI to potentiate BCMA-directed therapies," said Dr. Green. "Given the clinical experience with nirogacestat and the commitment that SpringWorks has made to combining their GSI with BCMA-directed therapies, I look forward to expanding on the important work that the Fred Hutch has already done in this area and collaborating with SpringWorks to explore this therapeutic hypothesis further."

"Fred Hutch scientists have been leaders in developing novel treatment approaches for multiple myeloma and have presented promising preclinical and clinical data combining GSIs with BCMA-directed therapies," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "We believe that nirogacestat has the potential to become a cornerstone of BCMA combination therapies across modalities and are delighted to be working with Dr. Green to build upon the encouraging results demonstrated to date. Our ultimate goal is to develop nirogacestat in such a way as to improve clinical outcomes for patients with multiple myeloma."

About Nirogacestat
Nirogacestat is an investigational, oral, selective, small molecule, gamma secretase inhibitor in Phase 3 clinical development for desmoid tumors, which are rare and often debilitating and disfiguring soft-tissue tumors. Gamma secretase cleaves multiple transmembrane protein complexes, including Notch, which is believed to play a role in activating pathways that contribute to desmoid tumor growth.

In addition, gamma secretase has been shown to directly cleave membrane-bound BCMA, resulting in the release of the BCMA extracellular domain, or ECD, from the cell surface. By inhibiting gamma secretase, membrane-bound BCMA can be preserved, increasing target density while reducing levels of soluble BCMA ECD, which may serve as decoy receptors for BCMA-directed therapies. Nirogacestat's ability to enhance the activity of BCMA-directed therapies has been observed in preclinical models of multiple myeloma. SpringWorks is evaluating nirogacestat as a BCMA potentiator and has three collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, a CAR T cell therapy and a bispecific antibody. In addition, SpringWorks and Fred Hutchinson Cancer Research Center have entered into a sponsored research agreement to further characterize the ability of nirogacestat to modulate BCMA and potentiate BCMA directed therapies using a variety of preclinical and patient-derived multiple myeloma models developed by researchers at Fred Hutch.

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors (June 2018) and from the European Commission for the treatment of soft tissue sarcoma (September 2019). The FDA also granted Fast Track and Breakthrough Therapy Designations for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis (November 2018 and August 2019).

About SpringWorks Therapeutics
SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for underserved patient populations suffering from devastating rare diseases and cancer. SpringWorks has a differentiated portfolio of small molecule targeted oncology product candidates and is advancing two potentially registrational clinical trials in rare tumor types, as well as several other programs addressing highly prevalent, genetically defined cancers. SpringWorks' strategic approach and operational excellence in clinical development have enabled it to rapidly advance its two lead product candidates into late-stage clinical trials while simultaneously entering into multiple shared-value partnerships with industry leaders to expand its portfolio. For more information, visit www.springworkstx.com and follow @SpringWorksTx on Twitter and LinkedIn.

SpringWorks 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 SpringWorks' clinical trials and its 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 related to SpringWorks' financial results, the timing for completion of

SpringWorks' clinical trials of its product candidates, whether and when, if at all, SpringWorks' product candidates will receive approval from the U.S. Food and Drug Administration, or FDA, or other foreign regulatory authorities, uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks' business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines, competition from other biopharmaceutical companies, and other risks identified in the section entitled "Risk Factors" in Item 1A of Part II of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings with the Securities and Exchange Commission. SpringWorks cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. SpringWorks disclaims 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 SpringWorks' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

SpringWorks Media/Investor Contact
Kim Diamond
203-561-1646
kdiamond@springworkstx.com

References

[1] Pont MJ, Hill T, Cole GO, et al. γ-Secretase inhibition increases efficacy of BCMA-specific chimeric antigen receptor T cells in multiple myeloma. *Blood*. 2019;134(19):1585-1597. doi:10.1182/blood.2019000050.

[2] Hill T, Pont MJ, Abbott J, et al. Gamma secretase inhibition increases recognition of multiple myeloma by BCMA-specific chimeric antigen receptor modified T cells, Presented at: Annual Meeting of the Society for Immunotherapy of Cancer (SITC). November 8-12, 2017. National Harbor, MD.

[3] Eastman S, Shelton C, Gupta I, Krueger J, Blackwell C, Bojczuk. Synergistic activity of belantamab mafodotin (anti-BCMA immuno-conjugate) with PF-03084014 (gamma-secretase inhibitor) in Bcma-expressing cancer cell lines. *Blood*. 2019;134(supplement_1):4401. doi.org/10.1182/blood-2019-123705.

[4] Cowen AJ, Pont M, Sather BD, et al. Efficacy and safety of fully human Bcma CAR T cells in combination with a gamma secretase inhibitor to increase Bcma surface expression in patients with relapsed or refractory multiple myeloma. *Blood*. 2019;134(supplement_1):204. doi.org/10.1182/blood-2019-129405.