



SpringWorks Therapeutics Enters into Research Collaboration with Leading Cancer Institute to Further Evaluate Nirogacestat as a BCMA Potentiator in Multiple Myeloma

August 30, 2021

-- Research to be Led by Constantine Mitsiades, M.D., Ph.D., at Dana-Farber Cancer Institute --

STAMFORD, Conn., Aug. 30, 2021 (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 collaboration with Dana-Farber Cancer Institute (Dana-Farber). The collaboration is designed to further investigate nirogacestat, SpringWorks' investigational gamma secretase inhibitor (GSI), with anti-B-cell maturation antigen (BCMA) agents in a variety of preclinical multiple myeloma models. Constantine Mitsiades, M.D., Ph.D., Assistant Professor of Medicine at Dana-Farber and Harvard Medical School, will serve as the Principal Investigator for the research, which will utilize preclinical in vivo models from the Mitsiades Lab to simulate the multiple myeloma tumor microenvironment. In addition, the research will also deploy functional genomics approaches to explore determinants of response and mechanisms of resistance to GSI + BCMA combination therapy.

Gamma secretase inhibition prevents the cleavage and shedding of BCMA from the surface of multiple myeloma cells. In preclinical models, nirogacestat has been shown to increase the cell surface density of BCMA and reduce levels of soluble BCMA, thereby enhancing the activity of BCMA-targeted therapies.¹ To date, SpringWorks has entered into clinical collaborations with six industry partners to evaluate nirogacestat in combination with BCMA therapies across modalities.

"SpringWorks has demonstrated its commitment to understanding the science and advancing the clinical exploration of GSI + BCMA combination therapies," said Dr. Mitsiades. "I am pleased to collaborate with them towards the goal of improving clinical outcomes for patients with multiple myeloma while simultaneously enabling the advancement of the underlying science."

"We are delighted to be collaborating with the Mitsiades Lab at Dana-Farber to expand our understanding of nirogacestat's mechanism of action when combined with BCMA therapies," said Badreddin Edris, Ph.D., Chief Operating Officer of SpringWorks. "Dr. Mitsiades and his colleagues have been at the forefront of developing cutting-edge translational models of multiple myeloma and we believe that this collaboration has the potential to yield novel insights that can help us to further refine our approach to improving outcomes for these patients."

Under the terms of the sponsored research agreement, SpringWorks will be responsible for funding the work and will retain an option to exclusively license any new intellectual property emerging from the research collaboration.

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 six collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, two CAR T cell therapies, two bispecific antibodies and a monoclonal antibody. SpringWorks has also formed research collaborations with Fred Hutchinson Cancer Research Center and Dana-Farber Cancer Institute to further characterize the ability of nirogacestat to modulate BCMA and potentiate BCMA therapies using a variety of preclinical multiple myeloma models.

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors and from the European Commission for the treatment of soft tissue sarcoma. 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.

About SpringWorks Therapeutics

SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for patients living with severe rare diseases and cancer. SpringWorks has a differentiated targeted oncology portfolio of small molecule product candidates and is advancing 15 development programs, including two potentially registrational clinical trials in rare tumor types as well as several 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 innovators in industry and academia to expand its portfolio and create more solutions for patients with cancer. For more information, please visit www.springworkstx.com and follow @SpringWorksTx on [Twitter](https://twitter.com/SpringWorksTx) and [LinkedIn](https://www.linkedin.com/company/springworkstx).

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial conditions, including but not limited to current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results, and other future conditions. Words such as, but not

limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. 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, risks relating to: (i) the success and timing of our product development activities, including the initiation and completion of SpringWorks' clinical trials, (ii) the fact that interim data from a clinical study may not be predictive of the final results of such study or the results of other ongoing or future studies, (iii) the success and timing of our collaboration partners' ongoing and planned clinical trials, (iv) our ability to obtain and maintain regulatory approval of any of our product candidates, (v) our plans to research, discover and develop additional product candidates, (vi) our ability to enter into collaborations for the development of new product candidates, (vii) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (viii) our ability to meet any specific milestones set forth herein, and (ix) uncertainties and assumptions regarding the impact of the COVID-19 pandemic on SpringWorks' business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines.

Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

For further information regarding the risks, uncertainties and other factors that may cause differences between SpringWorks' expectations and actual results, you should review the "Risk Factors" in Item 1A of Part I of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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References

¹Eastman S, Shelton C, Gupta I, Krueger J, Blackwell C, Bojczuk P. 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:10.1182/blood-2019-123705.