SpringWorks Therapeutics Announces Dosing of First Patient in Phase 1b/2 Trial Evaluating Nirogacestat in Combination with Elranatamab (PF-06863135) in Patients with Relapsed or Refractory Multiple Myeloma

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STAMFORD, Conn., Dec. 06, 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 the first patient has been dosed in a Phase 1b/2 trial evaluating nirogacestat, SpringWorks' investigational gamma secretase inhibitor (GSI), in combination with elranatamab (PF-06863135) Pfizer's investigational B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody, in patients with relapsed or refractory multiple myeloma.

Gamma secretase inhibition prevents the cleavage and shedding of BCMA from the surface of 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, including CD3 bispecific antibodies.[1,2]

"We are very pleased to be dosing patients in this study, which is one of six collaborations evaluating the combination of nirogacestat with a BCMA-targeted therapy as part of our broader effort to explore our gamma secretase inhibitor's role as a potential cornerstone of BCMA combination therapy," said Saqib Islam, Chief Executive Officer of SpringWorks. "Our goal is to improve treatment options for patients with multiple myeloma and we look forward to generating data with our collaborators to determine if adding nirogacestat can potentiate the activity of BCMA-directed therapies for these patients."

The Phase 1b/2 trial, which is one sub-study of Pfizer's umbrella MagnetisMM-4 trial (NCT05090566), is an open-label study evaluating the safety, tolerability and preliminary efficacy of elranatamab in combination with nirogacestat in patients with relapsed or refractory multiple myeloma. The trial is being advanced pursuant to a clinical trial collaboration agreement between SpringWorks and Pfizer. Under the terms of the agreement, Pfizer is sponsoring and conducting the Phase 1b/2 study and is assuming all costs other than expenses related to the manufacturing of nirogacestat and certain expenses related to intellectual property rights. The companies have formed a joint development committee to manage the clinical study.

About Elranatamab

Elranatamab is an investigational B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody being investigated in relapsed or refractory multiple myeloma. Binding affinity to BCMA and CD3 has been optimized, to potentially elicit more potent T-cell-mediated anti-myeloma activity. Elranatamab is being investigated as a subcutaneous administration, which is intended to allow higher doses than intravenous administration without increasing adverse events.

Elranatamab has been granted Orphan Drug Designations by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of multiple myeloma. The U.S. FDA and EMA have also granted elranatamab Fast Track Designation for the treatment of patients with multiple myeloma who are refractory to at least one proteasome inhibitor, one immunomodulatory drug, and one anti-CD38 antibody and the PRIME scheme for the treatment of multiple myeloma, respectively.

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. 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 16 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, visit http://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 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 September 30, 2021, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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References

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[2] Eastman 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.