



SpringWorks Therapeutics Announces Clinical Collaboration with AbbVie to Evaluate Nirogacestat in Combination with ABBV-383 in Patients with Relapsed or Refractory Multiple Myeloma

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– Seventh Clinical Collaboration Represents Continued Execution on Strategy to Advance Nirogacestat in Combination with BCMA Therapies –

STAMFORD, Conn., Dec. 10, 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 company has entered into a clinical trial collaboration agreement with AbbVie, Inc. to evaluate nirogacestat, SpringWorks' investigational gamma secretase inhibitor, in combination with ABBV-383, AbbVie's investigational CD3 bispecific antibody directed against B-cell maturation agent (BCMA), in patients with relapsed or refractory multiple myeloma.

Gamma secretase inhibition helps prevent the cleavage and shedding of BCMA from the surface of myeloma cells. In preclinical models, nirogacestat has been shown to increase levels of membrane-bound BCMA and reduce levels of soluble BCMA, thereby helping to enhance the activity of BCMA-targeted therapies, including CD3 bispecific antibodies.^{1,2}

"We continue to progress our strategy to evaluate nirogacestat in combination with BCMA therapies for patients with multiple myeloma and are delighted to enter into our seventh BCMA clinical collaboration. We look forward to working with AbbVie to study nirogacestat in combination with ABBV-383," said Saqib Islam, Chief Executive Officer of SpringWorks. "Together with our industry-leading collaborators, our goal remains to meaningfully improve clinical outcomes for patients with multiple myeloma."

Under the terms of the agreement, AbbVie will sponsor and conduct the Phase 1b study to evaluate the safety, tolerability, and preliminary efficacy of the combination in patients with relapsed or refractory multiple myeloma, and will assume all costs associated with the study, other than expenses related to the manufacturing of nirogacestat and certain expenses related to intellectual property rights. AbbVie and SpringWorks will also form a joint steering committee to manage the clinical study, which is expected to commence in the first half of 2022.

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.^{1,2} SpringWorks is evaluating nirogacestat as a BCMA potentiator and has seven collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, two CAR T cell therapies, three 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-directed 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 17 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 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

¹Karwacz K, Hooper A, Chang C, et al. Abstract 4557: BCMA-CD3 bispecific antibody PF-06863135: Preclinical rationale for therapeutic combinations. *Cancer Research*. 2020. doi:10.1158/1538-7445.am2020-4557.

²Eastman S, Shelton C, Gupta I, Krueger J, Blackwell C, Bojczuk P. Synergistic Activity of Belantamab Mafodotin (anti-BCMA immune-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.