



SpringWorks Therapeutics Announces Clinical Trial Collaboration and Supply Agreement with Regeneron to Evaluate Nirogacestat in Combination with REGN5458 in Patients with Relapsed or Refractory Multiple Myeloma

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-- Collaboration Represents SpringWorks' Eighth Clinical Collaboration and Highlights Continued Execution on Strategy to Advance Nirogacestat in Combination with BCMA Therapies --

STAMFORD, Conn., April 19, 2022 (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 and supply agreement with Regeneron Pharmaceuticals, Inc. to evaluate nirogacestat, SpringWorks' investigational gamma secretase inhibitor, in combination with Regeneron's investigational bispecific antibody targeting B-cell maturation antigen (BCMA) and CD3, REGN5458, 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 are delighted to enter into our eighth BCMA clinical collaboration as we continue to advance nirogacestat as a potentially best-in-class cornerstone of BCMA-directed therapies," said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. "Our goal is to improve clinical outcomes for patients with multiple myeloma and we look forward to working with Regeneron to evaluate nirogacestat in combination with REGN5458."

Under the terms of the agreement, Regeneron is responsible for the clinical development and will assume all costs associated with the study, other than expenses related to the manufacturing and supply of nirogacestat and certain expenses related to intellectual property rights.

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 eight collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities, including with an antibody-drug conjugate, two CAR T cell therapies, four 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 18 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](https://twitter.com/SpringWorksTx) and [LinkedIn](https://www.linkedin.com/company/springworkstx).

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 the timing for initiation, enrollment, progress and completion of SpringWorks' clinical trials or third-party clinical trials of its product candidates, the timing for expected data readouts from partners and partners' clinical trials, the expected benefits of collaborations, the fact that interim results from a clinical study may not be predictive of the final

results of such study or the results of other ongoing or future studies, 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 involving its product candidates, supply chain, strategy, goals and anticipated timelines, competition from other biopharmaceutical companies, and other risks identified in SpringWorks' SEC filings.

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' Annual Report on Form 10-K for the year ended December 31, 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.