# SpringWorks Therapeutics Announces FDA Acceptance and Priority Review of New Drug Application for Nirogacestat for the Treatment of Adults with Desmoid Tumors

February 27, 2023

**– PDUFA Action Date Set for August 27, 2023 –**

STAMFORD, Conn., Feb. 27, 2023 (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, announced today that the U.S. Food and Drug Administration (FDA) has accepted the Company's New Drug Application (NDA) for nirogacestat, an investigational gamma secretase inhibitor, for the treatment of adults with desmoid tumors. The NDA was granted Priority Review and has been given a Prescription Drug User Fee Act (PDUFA) action date of August 27, 2023. The FDA's Priority Review designation is given to investigational medicines that treat a serious condition and offer significant improvements in safety or effectiveness. In addition, the FDA has stated that it is not currently planning to hold an advisory committee meeting to discuss the application.

"People with desmoid tumors can experience severe pain and other debilitating morbidities, and we are excited by the opportunity to potentially transform the standard of care for these patients," said Saqib Islam, Chief Executive Officer of SpringWorks. "The acceptance of our NDA for nirogacestat with Priority Review represents a significant milestone in our ambition to provide the first approved therapy for patients with desmoid tumors. We look forward to working closely with the FDA during the review process and remain focused on ensuring that we are well-positioned to expeditiously serve the desmoid tumor patient and the physician communities following approval."

The NDA is being reviewed under the FDA's Real-Time Oncology Review (RTOR) program and is based on the previously announced positive results from the Phase 3 DeFi trial, a global, randomized, double-blind, placebo-controlled trial evaluating nirogacestat in adult patients with desmoid tumors. The FDA granted Fast Track and Breakthrough Therapy designations to nirogacestat for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis. Nirogacestat has also received Orphan Drug designation from the FDA for the treatment of desmoid tumors.

**About the DeFi Trial**
DeFi (NCT03785964) is a global, randomized (1:1), double-blind, placebo-controlled Phase 3 trial evaluating the efficacy, safety and tolerability of nirogacestat in adult patients with progressing desmoid tumors. The double-blind phase of the study randomized 142 patients (nirogacestat, n=70; placebo n=72) to receive 150 mg of nirogacestat or placebo twice daily. Key eligibility criteria included tumor progression by ≥20% as measured by Response Evaluation Criteria in Solid Tumors (RECIST 1.1) within 12 months prior to screening. The primary endpoint was progression-free survival, as assessed by blinded independent central review, or death by any cause. Secondary and exploratory endpoints included safety and tolerability measures, objective response rate (ORR), duration of response, changes in tumor volume assessed by magnetic resonance imaging (MRI), and changes in patient-reported outcomes (PROs). DeFi includes an open-label extension phase, which is ongoing.

**About Desmoid Tumors**
Desmoid tumors are rare, aggressive, locally invasive, and potentially morbid tumors of the soft tissues.[1,2] While they do not metastasize, desmoid tumors are associated with a high rate of recurrence.[2,3,4] Sometimes referred to as aggressive fibromatosis, or desmoid fibromatosis, these soft tissue tumors can be serious, debilitating, and, in rare cases when vital structures are impacted, they can be life-threatening.[2,5]

Desmoid tumors are most commonly diagnosed in patients between the ages of 20 and 44 years, with a two-to-three times higher prevalence in females.[4,6,7,8] It is estimated that there are 1,000-1,650 new cases diagnosed per year in the United States.[7,8,9]

Historically, desmoid tumors were treated with surgical resection, but this approach has become less favored due to a high recurrence rate after surgery.[1,4,10] There are currently no FDA-approved therapies for the treatment of desmoid tumors.

**About Nirogacestat**
Nirogacestat is an oral, selective, small molecule gamma secretase inhibitor in Phase 3 clinical development for desmoid tumors and in Phase 2 clinical development for ovarian granulosa cell tumors. Nirogacestat is an investigational drug for which safety and efficacy have not been established.

Gamma secretase cleaves multiple transmembrane protein complexes, including Notch, which is believed to play a role in activating pathways that contribute to growth of desmoid and ovarian granulosa cell tumors. Gamma secretase has also been shown to directly cleave membrane-bound B cell maturation antigen (BCMA), resulting in the release of the BCMA extracellular domain (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 several collaborations with industry-leading BCMA developers to evaluate nirogacestat in combinations across modalities. 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 with severe rare diseases and cancer. SpringWorks has a differentiated targeted oncology pipeline spanning solid tumors and hematological cancers, including two late-stage 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 unlock the full potential for 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, as amended, including, but not limited to, statements concerning the potential for nirogacestat to become an important new treatment for patients with desmoid tumors, expectations regarding the timing and results of the FDA's review of the NDA for nirogacestat, including the FDA's PDUFA target action date for the NDA, and the adequacy of the data contained in the NDA to serve as the basis for an approval of nirogacestat for the treatment of adults with desmoid tumors. 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) whether the preclinical and clinical results of the nirogacestat studies will meet the regulatory requirements for an approval by the FDA of nirogacestat for the treatment of adults with desmoid tumors, (ii) interactions with the FDA, including reviews and inspections, the timing related thereto and the outcome thereof, (iii) the potential therapeutic benefits, safety profile and effectiveness of nirogacestat, (iv) whether the NDA for nirogacestat will be approved, (v) if approved, whether nirogacestat will be commercially successful, and (vi) 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 II of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.*

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