



SpringWorks Therapeutics Announces Full Enrollment of Phase 3 DeFi Trial Evaluating Nirogacestat in Adult Patients with Desmoid Tumors

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STAMFORD, Conn., July 22, 2020 (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 achieved full enrollment in its Phase 3 DeFi trial evaluating nirogacestat, an investigational gamma secretase inhibitor, in adult patients with progressing desmoid tumors. As previously disclosed, SpringWorks expects to report topline results from the DeFi trial in the second or third quarter of 2021.

"Desmoid tumors are debilitating and disfiguring soft-tissue tumors and there is a significant need for an FDA-approved therapy for patients living with this devastating disease. We are delighted to have reached another milestone for the nirogacestat program by completing enrollment of the DeFi trial," said Saqib Islam, Chief Executive Officer of SpringWorks. "This achievement represents an important step toward our goal of bringing this new potential therapy to patients with desmoid tumors. We look forward to completing the trial and reporting data from the study next year."

The DeFi trial is a global, randomized, double-blind, placebo-controlled Phase 3 trial to evaluate the efficacy, safety and tolerability of nirogacestat in adult patients with progressing desmoid tumors. The study was designed to enroll 118 patients across approximately 50 sites in the United States and Europe. Patients have been randomized 1:1 to receive 150 mg of nirogacestat or placebo twice daily. Key eligibility criteria included tumor progression by $\geq 20\%$ as measured by Response Evaluation Criteria in Solid Tumors (RECIST 1.1) within 12 months prior to the first dose of study treatment. The primary endpoint is progression-free survival and secondary endpoints include safety and tolerability measures, as well as objective response rate, changes in tumor volume assessed by MRI, and changes in patient-reported outcomes. More information about the DeFi trial is available at www.clinicaltrials.gov under the identifier [NCT03785964](https://clinicaltrials.gov/ct2/show/study/NCT03785964).

Nirogacestat has received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors (June 2018) and from the European Commission for the treatment of soft tissue sarcoma (September 2019). 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 (November 2018 and August 2019).

About Desmoid Tumors

Desmoid tumors, also referred to as aggressive fibromatosis or desmoid-type fibromatosis, are rare and often debilitating and disfiguring soft tissue tumors characterized by a growth pattern that can invade surrounding healthy tissues, including joints, muscle and viscera. While they can arise in any part of the body, the most common sites are the upper and lower extremities, abdominal wall, thoracic areas, and the head and neck. The severity of a desmoid tumor can vary based on the location of the tumor and the aggressiveness of its growth pattern. Desmoid tumors can cause significant morbidities, including severe pain, internal bleeding, incapacitating loss of range of motion, and, in rare cases, death.¹

Desmoid tumors typically occur in patients between the ages of 15 to 60 years, and are more commonly diagnosed in young adults between 30-40 years of age, with a two-to-three times higher prevalence in females.^{1,2} It is estimated that there are 1,000 to 1,500 new cases diagnosed per year in the United States.^{3,4}

Historically, desmoid tumors were treated with surgical resection, but this approach has become less favored due to a high recurrence rate after surgery.⁵ There are currently no FDA-approved therapies for the treatment of desmoid tumors.

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 soluble BCMA from the cell surface. By inhibiting gamma secretase, membrane-bound BCMA can be preserved, increasing target density while reducing levels of soluble BCMA, which may serve as a decoy receptor 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 pursuing a combination therapy approach to evaluate nirogacestat as a BCMA potentiator across modalities by collaborating with industry leaders. To date, SpringWorks has entered into two clinical collaborations to evaluate nirogacestat in combination with GSK's BCMA antibody-drug conjugate belantamab mafodotin and with Allogene's allogeneic BCMA CAR-T cell therapy ALLO-715.

About SpringWorks Therapeutics

SpringWorks is a clinical-stage biopharmaceutical company applying a precision medicine approach to acquiring, developing and commercializing life-changing medicines for underserved patient populations suffering from devastating rare diseases and cancer. SpringWorks has a differentiated portfolio of small molecule targeted oncology product candidates and is advancing two potentially registrational clinical trials in rare tumor types, as well as several other 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 industry leaders to expand its portfolio. 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, as amended, including, without limitation, statements regarding SpringWorks' clinical trials and its strategy, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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, those related to SpringWorks' financial results, the timing for completion of SpringWorks' clinical trials of its product candidates, 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, supply chain, strategy, goals and anticipated timelines, competition from other biopharmaceutical companies, and other risks identified in the section entitled "Risk Factors" in Item 1A of Part II of SpringWorks' Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings with the Securities and Exchange Commission. SpringWorks cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. SpringWorks disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent SpringWorks' views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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