SpringWorks Therapeutics Announces Nirogacestat Achieved Primary and All Key Secondary Endpoints in Phase 3 DeFi Trial in Adult Patients with Progressing Desmoid Tumors

May 24, 2022

-- Results Showed Statistically Significant Improvement in Progression-Free Survival (PFS) Compared to Placebo (Hazard Ratio (HR) = 0.29; P < 0.001) --

-- Statistical Significance Was Also Achieved on All Key Secondary Endpoints, Including Objective Response Rate (ORR) and Patient-Reported Outcomes (PROs) --

-- Nirogacestat Was Generally Well Tolerated with a Manageable Safety Profile --

-- Additional Data Expected to be Presented at Medical Conference in the Second Half of 2022 --

-- NDA Submission to the U.S. FDA Planned for Second Half of 2022 --

-- Company to Host Conference Call at 8:30 a.m. Eastern Time --

STAMFORD, Conn., May 24, 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 positive topline results from the DeFi trial, a double-blind, placebo-controlled Phase 3 trial evaluating the efficacy, safety and tolerability of nirogacestat, an investigational oral gamma secretase inhibitor, in adult patients with progressing desmoid tumors.

The DeFi trial met its primary endpoint of improving progression-free survival (PFS), demonstrating a statistically significant improvement for nirogacestat over placebo, with a 71% reduction in the risk of disease progression (hazard ratio (HR) = 0.29 (95% CI: 0.15, 0.55); p < 0.001). In addition, the trial met all key secondary endpoints, with nirogacestat demonstrating statistically significant improvements as compared to placebo in objective response rate (ORR) and patient-reported outcomes (PROs). Nirogacestat was generally well tolerated with a manageable safety profile. The majority of women of childbearing potential had adverse events consistent with ovarian dysfunction. Other adverse events were generally consistent with previously reported data.

Additional data are expected to be presented at an upcoming medical conference in the second half of 2022 and SpringWorks plans to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) in the second half of 2022.

“Desmoid tumors are aggressive soft-tissue tumors that can lead to severe negative outcomes for patients, including long-lasting pain, disfigurement, and amputation. In rare cases, when vital organs are impacted, desmoid tumors can also be life-threatening,” said Saqib Islam, Chief Executive Officer of SpringWorks. “Today’s announcement represents a significant milestone towards our goal of bringing the first approved therapy to the desmoid tumor community. We look forward to sharing the DeFi trial data with the FDA and to presenting detailed study results at a medical meeting later this year.”

Nirogacestat has received Orphan Drug Designation from the 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 the DeFi Trial

DeFi (NCT03785964) is an ongoing, 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 study randomized 142 patients 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 the first dose of study treatment. The primary endpoint is progression-free survival, as assessed by blinded independent central review. Secondary and exploratory endpoints include 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).

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 organs are impacted, they can be life-threatening.[2,5]

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

Historically, desmoid tumors were treated with surgical resection, but this approach has become less favored due to a high recurrence rate after surgery.[1,4,9] 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 B cell maturation antigen (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 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, 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.

Conference Call Details

SpringWorks will host a conference call and webcast today, Tuesday, May 24, 2022, at 8:30 a.m. Eastern Time to discuss the DeFi trial data. Participants can listen to the call by dialing +1 (844) 946-0285 (domestic) or +1 (602) 585-9676 (international) and providing the conference ID 2268304. A live webcast presentation can be accessed through the Investors & Media section of the Company's website at https://ir.springworkstx.com. A replay of the webcast will be available on the SpringWorks website for a limited time following the event.

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 and LinkedIn.

SpringWorks Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, 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, our plans to report additional data from the Phase 3 DeFi clinical trial at an upcoming medical conference, the potential for the results of the Phase 3 DeFi clinical trial to support an NDA submission, the timing of our planned NDA submission for nirogacestat, and our plans for seeking regulatory approval for and making nirogacestat available to desmoid tumor patients, if approved, as well as relating to 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 topline or interim data from the Phase 3 DeFi trial or other clinical studies may not be predictive of the final or more detailed 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) the timing of our planned regulatory submissions and interactions, including the NDA for nirogacestat planned for the second half of 2022 and the timing and outcome of decisions made by the U.S. Food and Drug Administration (FDA) and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; (v) whether FDA or other regulatory authorities will require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including nirogacestat and mirdametinib, (vi) our ability to obtain and maintain regulatory approval of any of our product candidates, (vii) our plans to research, discover and develop additional product candidates, (viii) our ability to enter into collaborations for the development of new product candidates, (ix) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, (x) our ability to meet any specific milestones set forth herein, and (xi) 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 March 31, 2022, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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References

[1] Kasper B, Baumgarten C, Garcia J, et al; Desmoid Working Group. An update on the management of sporadic desmoid-type fibromatosis: a European Consensus Initiative between Sarcoma PAtients EuroNet (SPAEN) and European Organization for Research and Treatment of Cancer (EORTC)/Soft Tissue and Bone Sarcoma Group (STBSG). Ann Oncol. 2017;28(10):2399-2408.

[2] Penel N, Chibon F, Salas S. Adult desmoid tumors: biology, management and ongoing trials. Curr Opin Oncol. 2017;29(4):268-274.

[3] Xie Y, Xie K, Gou Q, He J, Zhong L, Wang Y. Recurrent desmoid tumor of the mediastinum: a case report. Oncol Lett. 2014;8(5):2276-2278.

[4] Skubitz KM. Biology and treatment of aggressive fibromatosis or desmoid tumor. Mayo Clin Proc. 2017;92(6):947-964.

[5] Joglekar SB, Rose PS, Sim F, Okuno S, Petersen I. Current perspectives on desmoid tumors: the Mayo Clinic approach. Cancers (Basel). 2011;3(3):3143-3155.

[6] Penel N, Coindre JM, Bonvalot S, et al. Management of desmoid tumours: a nationwide survey of labelled reference centre networks in France. Eur J Cancer. 2016;58:90-96.

[7] van Broekhoven DLM, Grünhagen DJ, den Bakker MA, van Dalen T, Verhoef C. Time trends in the incidence and treatment of extra-abdominal and abdominal aggressive fibromatosis: a population-based study. Ann Surg Oncol. 2015;22(9):2817-2823.

[8] Orphanet Report Series: Rare Diseases collection. Prevalence and incidence of rare diseases: bibliographic data. Number 1, January 2022. Accessed April 28, 2022. https://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf.

[9] The Desmoid Tumor Working Group. The management of desmoid tumors: a joint global evidence-based consensus guideline approach for adult and pediatric patients. Accessed April 10, 2022. https://dtrf.org/wp-content/uploads/2020/02/Desmoid_Paper_2018_A4_RL_Web300-1.pdf.