SpringWorks Therapeutics Announces Presentation of Additional Data from Phase 3 DeFi Trial of Nirogacestat in Adults with Desmoid Tumors at the 2023 CTOS Annual Meeting

November 1, 2023

- Nirogacestat Treatment Demonstrated Rapid and Sustained Improvements in Functional Status Compared to Placebo Across Multiple Assessment Tools -

STAMFORD, Conn., Nov. 01, 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, today announced the presentation of additional data from the Phase 3 DeFi trial at the 2023 Connective Tissue Oncology Society (CTOS) Annual Meeting, being held November 1-4, 2023. These data demonstrate the impact of nirogacestat, an investigational gamma secretase inhibitor, on physical and role functioning in adults with desmoid tumors. Data from the DeFi trial demonstrated statistically significant and clinically meaningful improvements across all primary and key secondary endpoints and were previously presented at leading medical congresses and published in the March 9, 2023 edition of the *New England Journal of Medicine*.[1-3]

"Desmoid tumors are locally aggressive and invasive soft tissue tumors that can cause severe pain and functional impairment. These impairments can be physical, such as difficulty walking or carrying out daily tasks, or role-related, such as difficulty caring for children or working, and they severely impact the day-to-day lives of patients," said Jim Cassidy, M.D., Ph.D., Chief Medical Officer of SpringWorks. "We are pleased that the robust data from our Phase 3 DeFi trial demonstrated that nirogacestat provided clinically meaningful improvements in key patient-reported outcomes, including pain as well as both physical and role functioning. We look forward to the opportunity to bring this important new medicine to the desmoid tumor community following anticipated U.S. regulatory approval."

Poster Presentation at the 2023 CTOS Meeting

Impact of Nirogacestat on Functional Status in Patients with Desmoid Tumors: Results from the Phase 3 DeFi Study

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Poster #: P 188
Poster Session Date and Time: Thursday, November 2, 5:30-6:30 p.m. CEST

As previously reported in the DeFi trial (NCT03785964), nirogacestat met its primary endpoint of significantly improving progression-free survival compared to placebo in adult patients with progressing desmoid tumors (hazard ratio: 0.29 [95% CI, 0.15–0.55]; P<0.001). Nirogacestat also achieved a significant and clinically meaningful improvement in physical and role functioning status, a key secondary endpoint, compared with placebo at Cycle 10 (p<0.001). The most frequently reported treatment-emergent adverse events that occurred in participants receiving nirogacestat were diarrhea (84%), ovarian dysfunction (75% of women of childbearing potential), nausea (54%), fatigue (51%), hypophosphatemia (42%), and maculopapular rash (32%).

During the DeFi study, the impact of nirogacestat on functional status was evaluated. Changes from baseline in physical and role functioning were compared between nirogacestat and placebo at Cycle 10, the prespecified time point for key secondary endpoints. Statistically significant and clinically meaningful improvements in physical and role functioning were observed with nirogacestat compared with placebo at Cycle 10 across all three assessment tools used: the GOunder/Desmoid Tumor Research Foundation DEsmoid Impact Scale (GODDESS DTIS) Physical Functioning (PF) subscale, the European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) PF and Role Functioning (RF) subscales, and the Patient-Reported Outcomes Measurement Information System Physical Function Short Form 10a (PROMIS PF10a) tool. Improvements in functional status were rapid, becoming evident as early as Cycle 2 (the first post-treatment time point evaluated) and these improvements were maintained through Cycle 24 across multiple tools measuring physical and role functioning.

The following results are being presented at CTOS:

- Nirogacestat significantly improved mean physical functioning score from baseline per the GODDESS DTIS PF domain compared with placebo at the pre-specified time point. The GODDESS DTIS PF domain captures varying degrees of vigorous and moderate daily activity, including moving and reaching.
- Nirogacestat significantly improved mean physical functioning score from baseline per the EORTC QLQ-C30 PF subscale compared with placebo at the pre-specified time point. The EORTC QLQ-C30 PF subscale captures the concepts of strenuous activities, taking a long walk, taking a short walk, need to stay in a bed or chair, and help with eating, dressing, washing, and using the toilet.
- Nirogacestat significantly improved mean role functioning score from baseline per the EORTC QLQ-C30 RF subscale compared with placebo at the pre-specified time point. The EORTC QLQ-C30 RF subscale captures the concepts of work or other daily activities and hobbies or leisure activities.
- At Cycle 10, patients receiving nirogacestat were five times more likely to have a clinically meaningful improvement in physical functioning (GODDESS DTIS Physical Functioning and EORTC QLQ-C30 Physical Functioning), and twice as likely to have a clinically meaningful improvement in role functioning (EORTC QLQ-C30 Role Functioning) than those receiving placebo. By Cycle 4, the mean PROMIS PF10a score in the nirogacestat arm reached the average physical

function observed in the general U.S. population whereas the score of the placebo arm did not.

"Treatment goals for patients with desmoid tumors often focus on tumor growth endpoints, such as progression-free survival, but reducing pain and improving functioning are also very important since these have a significant impact on patients' quality of life," said Bernd Kasper, M.D., Ph.D., University of Heidelberg, Mannheim Cancer Center, Mannheim, Germany and Principal Investigator of the DeFi trial. "It is very encouraging that patients experienced meaningful improvements in their functional status while on nirogacestat and that these improvements were sustained over the course of the study."

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 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). DeFi includes an open-label extension phase, which is ongoing.

About Desmoid Tumors

Desmoid tumors are rare, aggressive, locally invasive, potentially morbid tumors of the soft tissues.[4,5] While they do not metastasize, desmoid tumors are associated with a high rate of recurrence.[4-6] 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.[5,8]

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.[7-10] It is estimated that there are 1,000-1,650 new cases diagnosed per year in the United States.[10-12]

Historically, desmoid tumors were treated with surgical resection, but this approach has become less favored due to a high recurrence rate after surgery.[4,7,13] 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. SpringWorks is also evaluating nirogacestat as a potential treatment for patients with ovarian granulosa cell tumors and for patients with multiple myeloma as part of several B-cell maturation agent (BCMA) combination therapy regimens in collaboration with leaders in industry and academia. Nirogacestat is an investigational drug for which safety and efficacy have not been established.

The U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for nirogacestat for the treatment of adults with desmoid tumors, which is being reviewed under the FDA's Real-Time Oncology Review program. The NDA has been given a Prescription Drug User Fee Act (PDUFA) action date of November 27, 2023. The FDA also 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. In addition, 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.

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 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 X (formerly Twitter), LinkedIn, and YouTube.

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, 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, the potential for nirogacestat to become an important new treatment for adult 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, 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 a clinical study 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 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, (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 maintain adequate patent

protection and successfully enforce patent claims against third parties, (ix) our ability to enter into collaborations for the development of new product candidates, (x) our ability to establish manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our product candidates and scale production, and (xi) our ability to meet any specific milestones set forth herein.

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 June 30, 2023, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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