SpringWorks Therapeutics Receives Positive CHMP Opinion for Nirogacestat for the Treatment of Adults with Desmoid Tumors

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– If approved, nirogacestat will be the first and only therapy with marketing authorization in the EU for the treatment of desmoid tumors –

– Decision from European Commission expected in the third quarter of 2025 –

STAMFORD, Conn., June 20, 2025 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a commercial-stage biopharmaceutical company focused on severe rare diseases and cancer, announced today that the European Medicine Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the approval of nirogacestat, an oral gamma secretase inhibitor, as monotherapy for the treatment of adults with progressing desmoid tumors who require systemic treatment. The European Commission (EC) will review the CHMP opinion and is expected to make a final decision regarding the approval in the third quarter of 2025.

"The positive opinion from the CHMP reflects the meaningful benefits nirogacestat can offer patients in Europe where currently there are no approved treatment options," said Saqib Islam, Chief Executive Officer of SpringWorks. "We look forward to the European Commission's decision as we strive to bring nirogacestat to desmoid tumor patients globally."

Nirogacestat previously received Orphan Drug designation from the European Commission for the treatment of soft tissue sarcoma. The CHMP opinion was based on the Marketing Authorization Application (MAA) for nirogacestat, which centered on results from the Phase 3 DeFi trial that were published in *The New England Journal of Medicine*.[1] In DeFi, nirogacestat met the primary endpoint of improving progression-free survival (PFS), demonstrating a 71% lower risk of disease progression compared to placebo. Nirogacestat demonstrated a significant improvement in objective response rate as well as early and sustained improvements in patient-reported outcomes (PROs), including pain, physical functioning and overall quality of life.

Nirogacestat exhibited a manageable safety and tolerability profile. The most common adverse reactions reported in patients receiving nirogacestat were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea.

"Desmoid tumors can have a profound impact on patients as well as their loved ones, and the positive CHMP opinion underscores the potential benefit of nirogacestat for these patients," Bernd Kasper, M.D., Ph.D., Professor, University of Heidelberg, Mannheim Cancer Center, Mannheim, Germany, and principal investigator of the DeFi trial. "It is very encouraging that a significant number of people taking nirogacestat experienced reductions in their tumor size and also rapid and sustained relief of their desmoid tumor symptoms, including pain."

Nirogacestat is approved in the U.S. for the treatment of adults with progressing desmoid tumors who require systemic treatment.

About the DeFi Trial
DeFi (NCT03785964) was a global, randomized (1:1), multicenter, double-blind, placebo-controlled pivotal Phase 3 trial that evaluated 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 (PFS), 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 also included an open-label extension phase.

About Desmoid Tumors
Desmoid tumors are rare, aggressive, locally invasive tumors of the soft tissues that can be serious, debilitating, and, in rare cases when vital structures are impacted, life-threatening.[2,3]

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.[4,5] It is estimated that there are 1,300-2,300 new desmoid tumor cases diagnosed per year in the European Union.[6,7]

Although desmoid tumors do not metastasize, they can be associated with recurrence rates of up to 77% after surgical resection.[5,8] Desmoid tumor experts and treatment guidelines now recommend systemic therapies as first-line intervention for most tumor locations requiring treatment.[9,10]

About Nirogacestat

Nirogacestat is an oral, selective, small molecule gamma secretase inhibitor approved in the United States for the treatment of adult patients with progressing desmoid tumors who require systemic treatment. Nirogacestat is not approved for the treatment of any other indication in the United States, or for any indication in any other jurisdiction by any other health authority.

About SpringWorks Therapeutics

SpringWorks is a commercial-stage biopharmaceutical company dedicated to improving the lives of patients with severe rare diseases and cancer. We developed and are commercializing the first and only FDA-approved medicine for adults with desmoid tumors and the first and only FDA-approved medicine for both adults and children with neurofibromatosis type 1 associated plexiform neurofibromas (NF1-PN). We are also advancing a diverse

portfolio of novel targeted therapy product candidates for patients with both solid tumors and hematological cancers.

For more information, visit www.springworkstx.com and follow @SpringWorksTx on X, LinkedIn, Facebook, Instagram 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 and commercialization plans, our preclinical and clinical results, our expectations regarding the timing and results of the EMA's review of our MAA for nirogacestat and our plans to begin its initial launch in the European Union in 2025, our plans to continue to study nirogacestat in BCMA combination therapy regimens 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 fact that topline or interim data from 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, (ii) the success and timing of our collaboration partners' ongoing and planned clinical trials, (iii) the timing of our planned regulatory submissions and interactions, including the timing and outcome of decisions made by the FDA, EMA, and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies, (iv) whether EMA or other regulatory authorities will require additional information or further studies, or may fail or refuse to approve or may delay approval of our product candidates, including nirogacestat, (v) our ability to obtain regulatory approval of any of our product candidates or maintain regulatory approvals granted for our products, (vi) our plans to research, discover and develop additional product candidates, (vii) our ability to enter into collaborations for the development of new product candidates and our ability to realize the benefits expected from such collaborations, (viii) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties, (ix) the adequacy of our cash position to fund our operations through any time period indicated herein, (x) our ability to establish manufacturing capabilities, 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 March 31, 2025 as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' subsequent filings.

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9. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma V.2.2023. ©National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed August 2023. To

view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
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