SpringWorks Therapeutics Announces FDA Approval of OGSIVEO™ (nirogacestat) as the First and Only Treatment for Adults with Desmoid Tumors

November 27, 2023

– Approval based on positive data from Phase 3 DeFi trial, in which OGSIVEO significantly improved progression-free survival and objective response rate, with rapid and sustained improvements in pain, physical functioning and overall quality of life –

– SpringWorks to host conference call tomorrow at 8:00 a.m. ET –

A Media Snippet accompanying this announcement is available by clicking on this link.

STAMFORD, Conn., Nov. 27, 2023 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a commercial-stage biopharmaceutical company focused on severe rare diseases and cancer, announced today that the U.S. Food and Drug Administration (FDA) has approved OGSIVEO™ (nirogacestat), an oral gamma secretase inhibitor, for the treatment of adult patients with progressing desmoid tumors who require systemic treatment.[1] The FDA previously granted breakthrough therapy, fast track and orphan drug designations to nirogacestat for the treatment of desmoid tumors.

“Our team is honored to deliver the first FDA-approved therapy for patients with desmoid tumors. This community has been waiting for an effective treatment that not only shrinks their tumors but also significantly improves pain, which is the most debilitating symptom reported by people living with desmoid tumors,” said Saqib Islam, Chief Executive Officer of SpringWorks. "We are pleased with the broad label, which includes all progressing adult patients and specifically references improvement in pain, and believe OGSIVEO has the potential to become the new standard of care for people living with these devastating tumors. This is a watershed moment for the desmoid tumor community and we would like to extend our gratitude to the patients, families, investigators, and advocacy groups involved in the journey to making OGSIVEO available in the U.S.”

Desmoid tumors are locally aggressive and invasive soft-tissue tumors that can lead to substantial morbidity.[2,3] In addition, when vital structures are impacted, desmoid tumors can be life-threatening.[3] Although they do not metastasize, desmoid tumors are often refractory to existing off-label systemic therapies and associated with recurrence rates of up to 77% following surgical resection.[4-6] Desmoid tumor experts and treatment guidelines now recommend systemic therapies as first-line intervention instead of surgery for most tumor locations requiring treatment.[6]

“Desmoid tumors can have a significant impact on people’s lives and are difficult to manage due to their invasive nature and high rates of recurrence. OGSIVEO is a highly innovative therapy with efficacy data demonstrating both meaningful antitumor activity and a significant improvement in desmoid tumor symptoms,” said Mrinal M. Gounder, M.D., sarcoma medical oncologist at Memorial Sloan Kettering Cancer Center (MSK) in New York City and an investigator in the Phase 3 DeFi trial. “As a treating physician, it was encouraging to see in the DeFi trial that OGSIVEO achieved statistically significant and clinically meaningful improvements across the primary and all key secondary endpoints, while also having a manageable safety profile. This approval represents an important therapeutic advance for patients.”

The FDA approval of OGSIVEO is based on the results from the Phase 3 DeFi trial, which were published in the March 9, 2023 edition of the *New England Journal of Medicine*.[7] OGSIVEO met the primary endpoint of improving progression-free survival (PFS), demonstrating a statistically significant improvement 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). Median PFS was not reached in the OGSIVEO arm and was 15.1 months in the placebo arm. Confirmed objective response rate (ORR) based on RECIST v1.1 was 41% with OGSIVEO versus 8% with placebo (p<0.001); the complete response rate was 7% in the OGSIVEO arm and 0% in the placebo arm. The median time to first response was 5.6 months with OGSIVEO and 11.1 months with placebo.[7] PFS and ORR improvements were in favor of OGSIVEO regardless of baseline characteristics including sex, tumor location, tumor focality, treatment status, previous treatments, mutational status, and history of familial adenomatous polyposis.[7,8] OGSIVEO also demonstrated early and sustained improvements in patient-reported outcomes (PROs), including pain (p<0.001), desmoid tumor-specific symptoms (p<0.001), physical/role functioning (p<0.001), and overall health-related quality of life (p≤0.01).[7]

OGSIVEO exhibited a manageable safety and tolerability profile. The most common adverse events (≥15%) reported in patients receiving OGSIVEO were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea. Please see Important Safety Information below, including Warnings & Precautions relating to diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, and embryo-fetal toxicity.[1]

“Today is an extraordinary day for the desmoid tumor community. This approval is the culmination of a collaborative effort between the patient community, academia and the biopharmaceutical industry, who worked together with tenacity and persistence to advance promising science,” said Jeanne Whiting, Executive Director Emeritus and Co-Founder of the Desmoid Tumor Research Foundation. “Our hope is that patients and their families will benefit from greater awareness of desmoid tumors, faster diagnoses, and better outcomes now that there is an approved and effective treatment.”

SpringWorks is dedicated to helping patients with desmoid tumors access OGSIVEO and to providing support throughout their treatment journey. As part of this commitment, the Company is introducing SpringWorks CareConnections™, a comprehensive patient support program that offers personalized services to eligible OGSIVEO patients, including insurance coverage information and access support, financial assistance and personalized educational and emotional support. Physicians and patients can contact 1-844-CARES-55 (1-844-227-3755) or visit www.springworkstxcares.com for more information.

OGSIVEO will be available to order through a specialty pharmacy and specialty distributor network in the United States within five to ten business days. SpringWorks expects to file a Marketing Authorisation Application for OGSIVEO in desmoid tumors with the European Medicines Agency in the first half of 2024.

Conference Call and Webcast Information

SpringWorks will host a conference call and webcast to discuss the FDA approval of OGSIVEO on Tuesday, November 28, 2023, at 8:00 a.m. ET. To join the live webcast and view the corresponding slides, please click here. To access the live call by phone, please pre-register for the call here. Once registration is complete, participants will be provided with a dial-in number and conference code to access the call. A replay of the webcast will be available for a limited time following the event on the Investors and Media section of the Company's website at https://ir.springworkstx.com.

About OGSIVEO ™(nirogacestat)

OGSIVEO™ (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.

OGSIVEO 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.

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.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Diarrhea:** Diarrhea occurred in 84% of patients treated with OGSIVEO. Grade 3 events occurred in 16% of patients. Monitor patients and manage using antidiarrheal medications. Modify dose as recommended.
- **Ovarian Toxicity:** Female reproductive function and fertility may be impaired in patients treated with OGSIVEO. Impact on fertility may depend on factors like duration of therapy and state of gonadal function at time of treatment. Long-term effects on fertility have not been established. Advise patients on the potential risks for ovarian toxicity before initiating treatment. Monitor patients for changes in menstrual cycle regularity or the development of symptoms of estrogen deficiency, including hot flashes, night sweats, and vaginal dryness.
- **Hepatotoxicity:** ALT or AST elevations occurred in 30% and 33% of patients, respectively. Grade 3 ALT or AST elevations (>5 × ULN) occurred in 6% and 2.9% of patients. Monitor liver function tests regularly and modify dose as recommended.
- **Non-Melanoma Skin Cancers:** New cutaneous squamous cell carcinoma and basal cell carcinoma occurred in 2.9% and 1.4% of patients, respectively. Perform dermatologic evaluations prior to initiation of OGSIVEO and routinely during treatment.
- **Electrolyte Abnormalities:** Decreased phosphate (65%) and potassium (22%) occurred in OGSIVEO-treated patients. Phosphate <2 mg/dL occurred in 20% of patients. Grade 3 decreased potassium occurred in 1.4% of patients. Monitor phosphate and potassium levels regularly and supplement as necessary. Modify dose as recommended.
- **Embryo-Fetal Toxicity:** Oral administration of nirogacestat to pregnant rats during the period of organogenesis resulted in embryo-fetal toxicity at maternal exposures below human exposure at the recommended dose of 150 mg twice daily. Advise pregnant women of the potential risk to a fetus. Advise females and males of reproductive potential to use effective contraception during treatment with OGSIVEO and for 1 week after the last dose.

ADVERSE REACTIONS

- The most common (≥15%) adverse reactions were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea.
- Serious adverse reactions occurring in ≥2% of patients were ovarian toxicity (4%).
- The most common laboratory abnormalities (≥15%) were decreased phosphate, increased urine glucose, increased urine protein, increased AST, increased ALT, and decreased potassium.

DRUG INTERACTIONS

- **CYP3A Inhibitors and Inducers:** Avoid concomitant use with strong or moderate CYP3A inhibitors (including grapefruit products, Seville oranges, and starfruit) and strong or moderate CYP3A inducers.
- **Gastric Acid Reducing Agents:** Avoid concomitant use with proton pump inhibitors and H2 blockers. If concomitant use cannot be avoided, OGSIVEO can be staggered with antacids (e.g., administer OGSIVEO 2 hours before or 2 hours after antacid use).
- Consult the full Prescribing Information prior to and during treatment for important drug interactions.

To report suspected adverse reactions, contact SpringWorks Therapeutics at 1-888-400-SWTX (1-888-400-7989) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for OGSIVEO for more information.

About Desmoid Tumors

Desmoid tumors (sometimes referred to as aggressive fibromatosis, or desmoid fibromatosis) 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.[4,9] It is estimated that there are 1,000-1,650 new cases diagnosed per year in the United States.[9-11]

Although they do not metastasize, desmoid tumors are associated with recurrence rates of up to 77% after surgical resection.[4-6] Desmoid tumor experts and treatment guidelines now recommend systemic therapies as first-line intervention instead of surgery for most tumor locations requiring treatment.[6]

About SpringWorks Therapeutics

SpringWorks is a commercial-stage biopharmaceutical company applying a precision medicine approach to developing and delivering life-changing medicines for people with severe rare diseases and cancer.

Founded in 2017, SpringWorks has a diversified targeted oncology pipeline spanning solid tumors and hematological cancers, including clinical trials in rare tumor types and highly prevalent, genetically defined cancers. OGSIVEO™, approved in the United States for the treatment of adult patients with progressing desmoid tumors who require systemic treatment, is SpringWorks' first FDA-approved therapy. SpringWorks' strategic approach and operational excellence in clinical development have enabled it to rapidly advance its lead product candidates into late-stage trials and enter into multiple collaborations 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 and commercialization plans, our preclinical and clinical results, the potential for OGSIVEO to become an important new treatment for patients with desmoid tumors, the potential for a Marketing Authorisation Application for nirogacestat, as well as statements 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 of our commercialization efforts with respect to OGSIVEO, (ii) our limited experience as a commercial company, (iii) our ability to obtain or maintain adequate coverage and reimbursement for OGSIVEO, (iv) the success and timing of our product development activities, including the initiation and completion of SpringWorks' clinical trials, (v) our expectations regarding the potential clinical benefit of OGSIVEO for patients with desmoid tumors, (vi) the potential for OGSIVEO to become the new standard of care for patients with desmoid tumors, (vii) our expectations concerning the market potential for OGSIVEO, (viii) our expectations regarding when OGSIVEO will be available, (ix) 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, (x) the success and timing of our collaboration partners' ongoing and planned clinical trials, (xi) 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), the European Medicines Agency (EMA) and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; (xii) whether FDA, 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, (xiii) our ability to obtain regulatory approval of any of our product candidates or maintain regulatory approvals granted for our products, (xiv) our plans to research, discover and develop additional product candidates, (xv) our ability to enter into collaborations for the development of new product candidates, (xvi) our ability to establish and maintain manufacturing capabilities, and our and our collaboration partners' abilities to manufacture our products and product candidates and scale production, (xvii) our ability to maintain adequate patent protection and successfully enforce patent claims against third parties, and (xviii) 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 September 30, 2023, as well as discussions of potential risks, uncertainties and other important factors in SpringWorks' other filings with the Securities and Exchange Commission.

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References

[1] OGSIVEO. Prescribing Information. SpringWorks Therapeutics, Inc.

[2] Sbaraglia M, Bellan E, Dei Tos AP. The 2020 WHO Classification of Soft Tissue Tumours: news and perspectives. *Pathologica*. 2021;113(2):70-84. doi:10.32074/1591-951X-213.

[3] Penel N, Chibon F, Salas S. Adult desmoid tumors: biology, management and ongoing trials. *Curr Opin Oncol*. 2017;29(4):268-274. doi:10.1097/CCO.0000000000000374.

[4] Skubitz KM. Biology and treatment of aggressive fibromatosis or desmoid tumor. *Mayo Clin Proc*. 2017;92(6):947-964. doi:10.1016/j.mayocp.2017.02.012.

[5] Easter DW, Halasz NA. Recent trends in the management of desmoid tumors. Summary of 19 cases and review of the literature. *Ann Surg*. 1989;210(6):765-769. doi:10.1097/00000658-198912000-00012.

[6] Gronchi A, Kasper B, et al. Desmoid Tumor Working Group. The management of desmoid tumours: a joint global consensus-based guideline approach for adult and paediatric patients. *Eur J Cancer*. 2020;127:96-107. doi:10.1016/j.ejca.2019.11.013.

[7] Gounder M, Ratan R, Alcindor T, et al. Nirogacestat, a Gamma-Secretase Inhibitor for Desmoid Tumors. *N Engl J Med.* 2023;388:898-912. doi:10.1056/NEJMoa2210140.

[8] Data on file. SpringWorks Therapeutics, Inc.

[9] 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. doi:10.1245/s10434-015-4632-y.

[10] Orphanet Report Series: Rare Diseases collection. Prevalence and incidence of rare diseases: bibliographic data. Number 1, January 2022. Accessed November 24, 2023. https://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf.

[11] U.S. Department of Commerce. News Blog. U.S. population estimated at 332,403,650 on Jan. 1, 2022. Accessed November 24, 2023. https://www.commerce.gov/news/blog/2022/01/us-population-estimated-332403650-jan-1-2022#:~: