



SpringWorks Therapeutics Announces Initiation of Phase 3 Trial (DeFi) of Nirogacestat in Adult Patients with Desmoid Tumors

STAMFORD, Conn – May 20, 2019 – SpringWorks Therapeutics, a clinical-stage biopharmaceutical company focused on developing life-changing medicines for patients with severe rare diseases and cancer, today announced that the first patient has been dosed in the Phase 3 “DeFi” (**Desmoid/Fibromatosis**) trial evaluating nirogacestat, an oral, selective, small molecule gamma-secretase inhibitor, in adult patients with progressing desmoid tumors.

Desmoid tumors are rare and often debilitating and disfiguring soft-tissue tumors that can aggressively invade surrounding healthy tissues, including joints, muscles, blood vessels, nerves and internal organs. Depending on their size and location, desmoid tumors can cause significant morbidities, including severe pain, disfigurement, internal bleeding, debilitating loss of range of motion, and, in rare cases, desmoid tumors can be fatal.¹ It is estimated that 1,000 to 1,500 new cases of desmoid tumors are diagnosed each year in the United States.^{2,3} There are currently no therapies approved by the U.S. Food and Drug Administration (FDA) for the treatment of desmoid tumors.

“For patients living with these debilitating tumors, the DeFi trial marks a meaningful step forward in what we hope will result in the first approved treatment for this underserved patient community,” said Saqib Islam, Chief Executive Officer of SpringWorks Therapeutics. “I am grateful for the persistence of our partners, colleagues and the patient advocacy community, whose collective efforts made it possible for SpringWorks to advance nirogacestat into our Phase 3 DeFi trial. We look forward to enrolling patients to confirm the clinical benefits of nirogacestat for people with desmoid tumors.”

In June 2018, the FDA granted Orphan Drug designation for nirogacestat for the treatment of desmoid tumors, and in November 2018, the FDA granted Fast Track designation for nirogacestat for the treatment of adult patients with progressive, unresectable, recurrent or refractory desmoid tumors or deep fibromatosis.

About the DeFi Trial

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 will enroll approximately 100 adult patients, who will receive 150 mg of nirogacestat or placebo twice daily. Key eligibility criteria include 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 (PFS), defined as the time from randomization until the date of assessment of progression or death by any cause using RECIST 1.1. Secondary endpoints include safety and tolerability measures, as well as overall response rate, tumor volume changes as assessed by MRI, and changes in baseline in patient-reported outcomes.

More information about the DeFi trial is available at www.clinicaltrials.gov under the identifier NCT03785964.

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 aggressively invade surrounding healthy tissues, including joints, muscles, blood vessels, nerves and internal organs. While they can arise in any part of the body, the most common sites are the upper and lower extremities, abdominal walls, thoracic areas, and the head and neck. The severity of desmoid tumors and associated symptoms varies based on their size, location and the aggressiveness of the growth pattern. Desmoid tumors can cause significant morbidities, including severe pain, disfigurement, internal bleeding, debilitating loss of range of motion, and, in rare cases, desmoid tumors can be fatal.¹

Desmoid tumors can affect children and adults, and are more commonly diagnosed in young adults between 20-30 years of age, with a two-to-three-fold predominance in females.^{1,4} It is estimated that desmoid tumors affect 2 to 5 per million people worldwide, and that there are 1,000 to 1,500 new cases diagnosed per year in the United States.^{2,3}

Historically, desmoid tumors were treated with surgical resection or in severe cases, amputation, but even with these interventions, high rates of tumor regrowth have been observed.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. 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.

Nirogacestat has been investigated in 24 patients with desmoid tumors across Phase 1 and Phase 2 clinical trials. In these studies, treatment with nirogacestat demonstrated 100% disease control rate as measured by RECIST criteria, and median PFS was not reached by the time of publication in either trial due to lack of tumor progression events. Nirogacestat also showed an encouraging tolerability profile in these earlier studies, with many patients remaining on treatment for years and only one patient in the combined trials discontinuing due to an adverse event. The most common adverse events in prior studies were diarrhea, skin disorders and hypophosphatemia.

About SpringWorks Therapeutics

At SpringWorks Therapeutics, a clinical-stage biopharmaceutical company, we are driven to develop life-changing medicines for patients with severe rare diseases and cancer. Since our launch in 2017, we have worked to identify and advance promising science, beginning with our licensed clinical therapies from Pfizer Inc. We pioneer efficient pathways for drug development, leveraging shared-value partnerships with patient advocacy groups, innovators in industry and academia, and investors so that together, we can unlock the potential of science and bring new therapies to underserved patients. Nirogacestat, our gamma secretase inhibitor for the treatment of desmoid tumors is currently in a Phase 3 clinical trial, and SpringWorks Therapeutics expects to initiate a Phase 2b study of PD-0325901, our MEK 1/2 inhibitor for neurofibromatosis type 1 patients with plexiform neurofibromas, in the third quarter of 2019. PD-0325901 also holds promise as the backbone for combination therapies to treat metastatic solid tumors. At SpringWorks, we ignite the power of promising science to unleash new possibilities for patients. For more information, please visit www.springworkstx.com.

Follow SpringWorks Therapeutics on social media: [@SpringWorksTx](https://twitter.com/SpringWorksTx) and [LinkedIn](https://www.linkedin.com/company/springworkstx).

References

- 1 Gounder, M. M., Thomas, D. M., & Tap, W. D. (2017). Locally Aggressive Connective Tissue Tumors. *Journal of Clinical Oncology*, 36(2), 202-209. doi:10.1200/JCO.2017.75.8482.
- 2 Reitamo, J J; Häyry, P; Nykyri, E; Saxén, E. (1982). The desmoid tumor. I. Incidence, sex-, age- and anatomical distribution in the Finnish population. *American Journal of Clinical Pathology*, 77(6), 665-673. doi: 10.1093/AJCP.77.6.665
- 3 van Broekhoven, D. L., Grünhagen, D. J., den Bakker, M. A., van Dalen, T., & Verhoef, C. (2015). Time trends in the incidence and treatment of extra-abdominal and abdominal aggressive fibromatosis: a population-based study. *Annals of surgical oncology*, 22(9), 2817–2823. doi:10.1245/s10434-015-4632-y
- 4 Skubitz, K. M. (2017). Biology and Treatment of Aggressive Fibromatosis or Desmoid Tumor. *Mayo Clinic Proceedings*, 92(6), 947-964. doi:10.1016/j.mayocp.2017.02.012
- 5 Scaramussa, F.S. & Castro, U. B. (2016). Desmoid Tumor in Hand: A Case Report. *SM Journal of Orthopedics*, 2(3),1036.

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