European Commission Grants Approval of OGSIVEO® (nirogacestat) for the Treatment of Adults with Desmoid Tumors

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OGSIVEO is the first and only therapy to receive marketing authorization in the EU for the treatment of desmoid tumors

STAMFORD, Conn., Aug. 18, 2025 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc., a healthcare company of Merck KGaA, Darmstadt, Germany, announced today that the European Commission (EC) granted marketing authorization for OGSIVEO® (nirogacestat), an oral gamma secretase inhibitor, as monotherapy for the treatment of adults with progressing desmoid tumors who require systemic treatment. OGSIVEO is the first and only therapy approved in the European Union (EU) to treat desmoid tumors.

“Desmoid tumors can have a profound impact on people’s lives and are difficult to manage due to their invasive nature and high rates of recurrence. Until now, there have been no approved medicines in Europe,” said Bernd Kasper, M.D., Ph.D., Professor, University of Heidelberg, Mannheim Cancer Center, Mannheim, Germany, and principal investigator of the DeFi trial. “OGSIVEO is a highly innovative therapy with efficacy data demonstrating both meaningful antitumor activity and a significant improvement in desmoid tumor symptoms, including a significant reduction in pain which is the most debilitating symptom reported by patients.”

“This approval is a long-awaited advance for desmoid tumor patients, their families and physicians in Europe,” said Lynne Hernandez, Executive Director of the Desmoid Tumor Research Foundation. “It is our hope that patients will benefit from greater awareness of desmoid tumors, faster diagnoses, and better outcomes now that there is an approved treatment.”

Desmoid tumors are rare, locally aggressive tumors that form in the connective tissues of the body.[1,2] Approximately 1,300 to 2,300 new cases of desmoid tumors are diagnosed annually in the EU.[3,4,5] These tumors can cause severe pain, limited function, loss of mobility, disfigurement and fatigue.[1,6-10] They are challenging to manage because of their unpredictable nature and high rate of recurrence, which can significantly impact an individual’s quality of life. [2,7,8,11,12] Desmoid tumor experts and treatment guidelines now recommend medical therapy as first-line intervention instead of surgery for most tumor locations requiring treatment.[13,14]

“We would like to extend our gratitude to the patients, families, investigators, and advocacy organizations who helped make this EC approval possible,” said Danny Bar-Zohar, MD, CEO of Healthcare and Executive Board Member at Merck KGaA, Darmstadt, Germany. “OGSIVEO is already established as the standard of care systemic therapy for desmoid tumors in the U.S., and our goal is to bring the same treatment benefits to patients in Europe. Following last month’s EC approval of our therapy for patients with NF1-PN, we are in the unique position of launching two innovative treatments -- underscoring our commitment to the rare tumor patient community.”

The EC approval of OGSIVEO is based on results from the Phase 3 DeFi trial, which enrolled 142 adult patients with progressing desmoid tumors and met the primary endpoint of improving progression-free survival (PFS). OGSIVEO demonstrated 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). OGSIVEO also demonstrated a significant improvement in objective response rate (ORR). The confirmed 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. Additionally, OGSIVEO demonstrated early and sustained improvement 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).[13]

OGSIVEO exhibited a manageable safety and tolerability profile. The most common adverse reactions reported in 88 patients receiving OGSIVEO across all studies (69 patients from DeFi and 19 patients from early phase studies) were diarrhea (85%), rash (65%), ovarian toxicity in women of childbearing potential (60%) nausea (59%), fatigue (50%), hypophosphataemia (50%), headache (40%) and stomatitis (40%).[13]

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, as assessed by blinded independent central review, or death by any cause. Secondary and exploratory endpoints included safety and tolerability measures, objective response rate, duration of response, changes in tumor volume assessed by magnetic resonance imaging (MRI), and changes in patient-reported outcomes. DeFi also included an open-label extension phase.

About Desmoid Tumors

Desmoid tumors are rare, locally aggressive tumors of the soft tissues that can be serious, debilitating, and, in rare cases when vital structures are impacted, life-threatening.[1,2]

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.[3,11] It is estimated that there are 1,300-2,300 new desmoid tumor cases diagnosed per year in the European Union. [3,4,5]

Although desmoid tumors do not metastasize, they can be associated with recurrence rates of up to 77% after surgical resection.[11,12] Desmoid tumor experts and treatment guidelines now recommend systemic therapies as first-line intervention for most tumor locations requiring treatment.[14,15]

About OGSIVEO® (nirogacestat)

OGSIVEO® (nirogacestat) is an oral, selective, small molecule gamma secretase inhibitor approved in the United States and European Union as monotherapy for the treatment of adult patients with progressing desmoid tumors who require systemic treatment.

The FDA and the EMA have granted Orphan Drug designation for OGSIVEO for the treatment of desmoid tumors.

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 SpringWorks Therapeutics

SpringWorks Therapeutics, a healthcare company of Merck KGaA, Darmstadt, Germany, is a commercial-stage biopharmaceutical company dedicated to improving the lives of patients with rare tumors. We developed and are commercializing the first and only FDA and EC approved medicine for adults with desmoid tumors and the first and only FDA and EC approved medicine for both adults and children with neurofibromatosis type 1 associated plexiform neurofibromas (NF1-PN). We are also advancing a portfolio of novel targeted therapy product candidates for patients with additional rare tumors and hematological cancers.

For more information, visit www.springworkstx.com and follow @SpringWorksTx on X, LinkedIn, Facebook, Instagram and YouTube.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. More than 62,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From providing products and services that accelerate drug development and manufacturing as well as discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2024, Merck KGaA, Darmstadt, Germany, generated sales of € 21.2 billion in 65 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as MilliporeSigma in life science, EMD Serono in healthcare and EMD Electronics in electronics. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

Contacts:

Media
Media@Springworkstx.com

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