

# **OGSIVEO®**

## **Category:**

Best Product for Orphan/Rare Diseases

## **Company Name:**

SpringWorks Therapeutics

## **Product/Solution Name:**

OGSIVEO®

## **Compound/Tech Name:**

nirogacestat

## **Trade Name:**

OGSIVEO®

## **Corporate Name:**

OGSIVEO®

## **Date of Approval:**

2023-11-27

## **Indications:**

OGSIVEO is a gamma secretase inhibitor indicated for adult patients with progressing desmoid tumors who require systemic treatment.

## **Therapeutic Areas:**

Rare Oncology

## **General Information File Document upload:**

N/A

## **Background information and need for drug / device:**

Desmoid tumors are rare, locally aggressive and invasive tumors that can form anywhere in the body where there is soft, connective tissue. While they are not metastatic, desmoid tumors are locally invasive and can pose serious health risks, that may lead to debilitating symptoms and, in rare cases where vital organs are impacted, desmoid tumors can be life-threatening. There are approximately 1,000 to 1,650 new patients diagnosed each year in the U.S. Desmoid tumors typically affect people in their prime life-building years, with the average age of diagnosis being between the ages of 20 to 44, and women are two to three times more likely to be affected by this disease than men. Desmoid tumors can cause severe pain (often leading to opioid use to manage pain), loss of physical function and mobility, disfigurement, amputation, and a diminished quality of life. The pain and symptom burden can also have psychological consequences, including anxiety, depression, fear of recurrence, and worries about altered appearance.

OGSIVEO® (nirogacestat) is the first and only FDA-approved therapy for the treatment of desmoid tumors. Historically, they were most often treated with surgical resection. Due to the invasive nature of these tumors, however, surgical resection is often associated with high rates of morbidity and tumor recurrence, with up to 77% of patients experiencing tumor regrowth following surgery. As desmoid tumor experts came to better understand the nature of the disease, treatment guidelines from the Desmoid Tumor Working Group and NCCN have evolved to recommend systemic treatment first for most tumor locations. Prior to OGSIVEO, there was a high unmet need since off-label therapies, such as chemotherapy and tyrosine kinase inhibitors, were (and still are) associated with tolerability challenges. The desmoid tumor community had been waiting decades for a safe and effective FDA-approved therapy developed specifically to treat their tumors. With OGSIVEO, adult patients now have a therapy that not only improves tumor response but also significantly and often rapidly improves pain (the most debilitating symptom reported by people living with desmoid tumors), physical and role functioning, and health-related quality of life. The FDA approval of OGSIVEO was a watershed moment for the desmoid tumor community and was 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 and deliver it to patients in desperate need of a treatment advance.

### **Background File Document upload:**

**[SpringWorks FDA Approval of OGSIVEO Press Release 1.pdf](#)**  
**[OGSIVEO Media Fact Sheet\\_vF 1.pdf](#)**  
**[FDA Press Release\\_ OGSIVEO Approval 1.pdf](#)**  
**[DTRFPRESSRELEASEFDAApprovalOGSIVEO 1.pdf](#)**  
**[DesmoidTumorcom 1.pdf](#)**  
**[Desmoid Tumor Media Fact Sheet\\_vF 1.pdf](#)**  
**[OGSIVEOcom 1.pdf](#)**

## **History of the development of the solution/product:**

The development journey of nirogacestat took a pivotal turn in 2012 when a poster presentation of a Phase 1 solid tumor trial sponsored by Pfizer Inc. caught the eye of Dr. Shivaani Kummar, who at the time was a physician researcher at the National Cancer Institute (NCI). The data included a small number of desmoid tumor patients who had a promising response to nirogacestat, including a 100% disease control rate, with 5 of 7 evaluable patients achieving objective responses, and a median duration of therapy of over 4 years. These results prompted Dr. Kummar to lead an open-label Phase 2 NCI-sponsored trial of nirogacestat in 17 adults with progressing desmoid tumors. Patients in the Phase 2 trial also had a 100% disease control rate, with benefit demonstrated irrespective of the number or type of prior lines of therapy. In both studies, the median progression-free survival (PFS) was not reached due to lack of tumor progression events.

While these results were very encouraging, Pfizer had already decided not to take nirogacestat forward. Patients, researchers and the Desmoid Tumor Research Foundation (DTRF) teamed up to advocate for nirogacestat's continued development, which led to the creation of SpringWorks Therapeutics in 2017. SpringWorks in-licensed nirogacestat from Pfizer and launched with a mission to push this promising science forward for a severely underserved patient population.

SpringWorks quickly advanced nirogacestat into the Phase 3 DeFi trial and received important regulatory designations that underscored the significant unmet need: Orphan Drug designation (June 2018), Fast Track designation (November 2018), and Breakthrough Therapy designation (August 2019). The trial was fully enrolled within two years, despite the global COVID-19 pandemic. In September 2022, the DeFi data were presented as a late-breaking oral presentation during a Presidential Symposium at the European Society for Medical Oncology (ESMO) Congress. Data showed that treatment with nirogacestat demonstrated highly significant and clinically meaningful improvements on the primary endpoint of PFS (a 71% reduction in the risk of disease progression compared to placebo, translating to a hazard ratio of 0.29 and a p value of  $< 0.001$ ) and all key secondary endpoints, including pain, physical functioning and overall quality of life.

These data were published in The New England Journal of Medicine in March 2023 and served as the basis for the New Drug Application submitted to the FDA. On November 27, 2023, OGSIVEO became the first FDA-approved treatment for adults with progressing desmoid tumors who require systemic treatment. OGSIVEO is also the first approved gamma secretase inhibitor for any type of disease. News of the approval was an emotional moment for patients and was celebrated by desmoid tumor experts around the world.

The development journey of OGSIVEO is a testament to how the patient community, academia and the biopharmaceutical industry can work together to advance promising science. SpringWorks is honored to have brought the first FDA-approved therapy to adults with desmoid tumors. OGSIVEO is established as the systemic standard of care and its innovation makes it a deserving candidate to receive a Prix Galien award.

### **Development File Document upload:**

**[SpringWorks Phase 3 DeFi Trial Evaluating Data Release\\_ESMO 2022 1.pdf](#)**

**[SpringWorks NEJM DeFi Trial Press Release 1.pdf](#)**

**[SpringWorks ASCO 2023 Press Release 1.pdf](#)**

**[Phase 3 DeFi Trial NEJM Publication 1.pdf](#)**

**[Kummar et al\\_Journal of Clinical Oncology 1.pdf](#)**

**[Current Management of Desmoid Tumors\\_JAMA Oncology 1.pdf](#)**

**[MOA slide.pptx](#)**

### **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

OGSIVEO is the first and only FDA-approved treatment for adults with desmoid tumors, which are rare, locally aggressive soft-tissue tumors that can have a significant impact on people's lives and are difficult to manage due to their invasive nature and high rates of recurrence.

Prior to OGSIVEO, patients were treated with off-label therapies such as chemotherapy and tyrosine kinase inhibitors that often have inconsistent efficacy and tolerability challenges. Additionally, surgical resection, once a primary intervention, has fallen out of favor due to the high rates of post-surgical recurrence (up to 77%).

OGSIVEO is an innovative therapy with efficacy data demonstrating both meaningful antitumor activity resulting in tumor shrinkage (as measured by blinded independent central review of both RECISTv1.1 and volumetric MRI) and a significant improvement in desmoid tumor symptoms. The FDA approval of OGSIVEO in November 2023 represented a significant advance for this rare disease community. For the first time, patients have an approved therapy, in the form of an oral pill, that can reduce the size of their tumor and their debilitating pain, and improve their overall quality of life.

In addition, the pivotal study for OGSIVEO, the Phase 3 DeFi trial, has greatly contributed to future research. DeFi was the first randomized, controlled study to use a novel assessment tool to capture patient reported data. Specifically, the desmoid tumor-specific GODDESS tool, which was developed by the DTRF and Memorial Sloan Kettering Cancer Center, collected desmoid tumor-specific patient reported outcomes

such as pain, physical and role functioning and other quality of life measures that were not fully captured in traditional oncology study endpoints previously. Data from the DeFi trial were used to validate the GODDESS tool indicating it is a reliable, valid, responsive, and interpretable clinical trial endpoint in desmoid tumors.

Desmoid tumor experts have called the DeFi data "practice-changing," referred to OGSIVEO as a "game-changer," and said that they are thrilled to finally have an FDA-approved therapy for their patients. Patients have sent SpringWorks emotional emails describing what the approval of OGSIVEO means to them and DTRF has called the approval "an extraordinary victory in the area of rare disease" and "one that cannot be overstated."

Since its launch only a year and a half ago, OGSIVEO is now the most prescribed systemic therapy for adults with desmoid tumors - a testament to the impact it has had on patients and the benefits of the treatment as seen by doctors. Based on feedback from patients, we have seen OGSIVEO change the outlook for those patients who were previously underserved with surgery and off-label systemic therapies, while real-world experience reinforces its transformative benefits for patients, including significant reductions in pain.

### **Innovation File Document upload:**

**[Dr Loggers\\_ovarian function DeFi presentation ASCO 2024 1.pdf](#)**  
**[GODDESS\\_Quality of Life Research Journal.pdf](#)**

### **Please provide appropriate references (PubMed, Abstract, Website):**

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  15. Data on File.

## References File Document upload:

N/A