
# **OGSIVEO** is the #1 prescribed systemic therapy for adults with desmoid tumors[1]

**The first and only FDA–approved targeted therapy for adult patients with progressing desmoid tumors who require systemic treatment**

**The DeFi study published in *The New England Journal of Medicine* was the largest (N=142) completed Phase 3 trial in adults with desmoid tumors.[2]**

**NCCN**
CATEGORY 1
**PREFERRED**

**NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma recommend nirogacestat (OGSIVEO) as a Category 1 Preferred systemic therapy option for patients with desmoid tumors (aggressive fibromatosis).[3]**

DeFi, Desmoid Fibromatosis; FDA, US Food and Drug Administration; NCCN, National Comprehensive Cancer Network® (NCCN®).

## Indication

OGSIVEO is indicated for adult patients with progressing desmoid tumors who require systemic treatment.

## Important Safety Information

### Warnings and Precautions

**Diarrhea:** Diarrhea, sometimes severe, can occur in patients treated with OGSIVEO. Diarrhea occurred in 84% of patients treated with OGSIVEO, and included Grade 3 events in 16% of patients. Median time to first diarrhea event was 9 days (range: 2 to 434 days). Monitor patients and manage using antidiarrheal medications. Modify dose as recommended.

**Please see Important Safety Information throughout and click here for full Prescribing Information.**

Ogsiveo®
(nirogacestat)
150 mg & 100 mg tablets

# Identifying the earliest signs of desmoid tumor progression is key for patient management

## NCCN Guidelines® recommendations for initiating treatment:[3,*]

**Symptoms** OR **Impairing or threatening in function** OR **Tumor growth documented on imaging (e.g., MRI or CT)**

**Surgery is no longer recommended by guidelines as first-line treatment for most clinical situations[3,4]**

**Up to 77% recurrence rates after surgical resection of desmoid tumors[5,6,†]**

*A course of ongoing observation is an appropriate option even for patients with disease progression, if the patient is minimally symptomatic and the anatomical location of the tumor is not critical. For tumors that are symptomatic, or impairing or threatening in function, patients should be offered therapy with the decision based on the location of the tumor and potential morbidity of the therapeutic option.[3]
†Based on retrospective, observational data. Factors associated with local recurrence postsurgery include tumor location, age of the patient, tumor size, margin status, and prior recurrence.[7,8]
CT, computed tomography; MRI, magnetic resonance imaging; NCCN, National Comprehensive Cancer Network® (NCCN®).

## Important Safety Information (cont'd)

### Warnings and Precautions

**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 of OGSIVEO 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 x 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:** OGSIVEO can cause fetal harm when administered to pregnant women. Oral administration of nirogacestat to pregnant rats during the period of organogenesis resulted in embryo-fetal toxicity and death 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.

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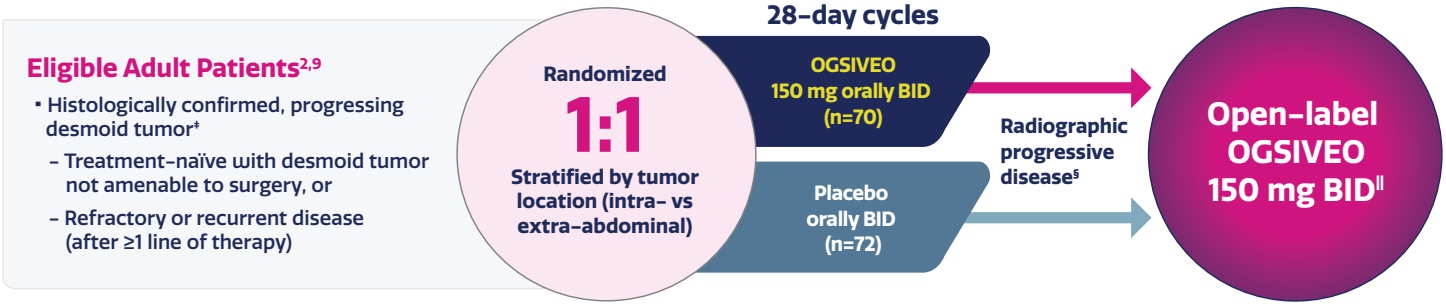
# **OGSIVEO** was studied in the landmark DeFi trial

DeFi: An international, multicenter, randomized (1:1), double-blind, placebo-controlled, Phase 3 study of OGSIVEO in patients with progressing desmoid tumors not amenable to surgery. Patients had treatment-naïve, refractory, or recurrent disease (N=142).[2,9]




*All patients had histologically confirmed desmoid tumors that had progressed ≥20% by RECIST v1.1 within the past 12 months. Tumor imaging occurred every 3 months.[2,9]
†Imaging-based progression or completion of the primary analysis.[2]
‡Eligible patients were given the option to enroll in the open-label extension phase.[2]

# **OGSIVEO** demonstrated powerful efficacy in the DeFi study

| Primary End Point: Progression-Free Survival (PFS) | Key Secondary Efficacy End Point: Objective Response Rate (ORR) |
|---|---|
| **OGSIVEO significantly improved PFS[9,§]**<br>▪ **71% reduction in the risk of disease progression or death vs placebo** (HR=0.29; 95% CI: 0.15, 0.55; *P*<0.001)‖<br>▪ Median PFS in the OGSIVEO arm was not reached (95% CI: NR, NR) compared with 15.1 months (95% CI: 8.4, NR) in the placebo arm¶,#<br>– PFS events occurred in 12 patients (17%) in the OGSIVEO arm and 37 patients (51%) in the placebo arm | **OGSIVEO demonstrated significant improvement in ORR[9,**]**<br>▪ **41% (95% CI: 29.8, 53.8; n=29) objective response rate with OGSIVEO vs 8%** (95% CI: 3.1, 17.3; n=6) **with placebo**; *P*<0.001††,‡‡,§§<br>– Complete response: 7% (n=5) with OGSIVEO vs 0% (n=0) with placebo<br>– Partial response: 34% (n=24) with OGSIVEO vs 8% (n=6) with placebo |

§Progression-free survival was defined as the time from randomization until the date of imaging-based or clinical progression or death. Progression-free survival was based on RECIST v1.1 as assessed by blinded independent central review or on clinical progression by the investigator (and confirmed by independent review). Clinical progression required worsening of symptoms resulting in a global deterioration of health status causing the permanent discontinuation from trial treatment and the initiation of emergent treatment (e.g., radiotherapy, surgery, or systemic therapy including chemotherapy or tyrosine kinase inhibitors) for desmoid tumors.[2,9]
‖*P*-value was from a one-sided stratified log-rank test with placebo as reference.[9]
¶Data cut-off as of April 7, 2022 for PFS.[2]
#Obtained using Kaplan-Meier methodology.[9]
**Objective response rate was defined as complete response or partial response according to RECIST v1.1. Assessed by blinded independent central review. Partial response was defined as a ≥30% decrease in the sum of the longest diameters of target tumors. Complete response was defined as disappearance of all target and non-target tumors.[2,9]
††Obtained using exact method based on binomial distribution.[9]
‡‡*P*-value was from a two-sided Cochran-Mantel-Haenszel test.[9]
§§Desmoid tumors can have an unpredictable course and may exhibit spontaneous regression.[10]
BID, twice daily; CI, confidence interval; DeFi, Desmoid Fibromatosis; HR, hazard ratio; NR, not reached; RECIST, Response Evaluation Criteria in Solid Tumors.

## Important Safety Information (cont'd)

### Adverse Reactions

The most common (≥15%) adverse reactions were diarrhea (84%), ovarian toxicity (75% in the 36 females of reproductive potential), rash (68%), nausea (54%), fatigue (54%), stomatitis (39%), headache (30%), abdominal pain (22%), cough (20%), alopecia (19%), upper respiratory tract infection (17%), and dyspnea (16%).

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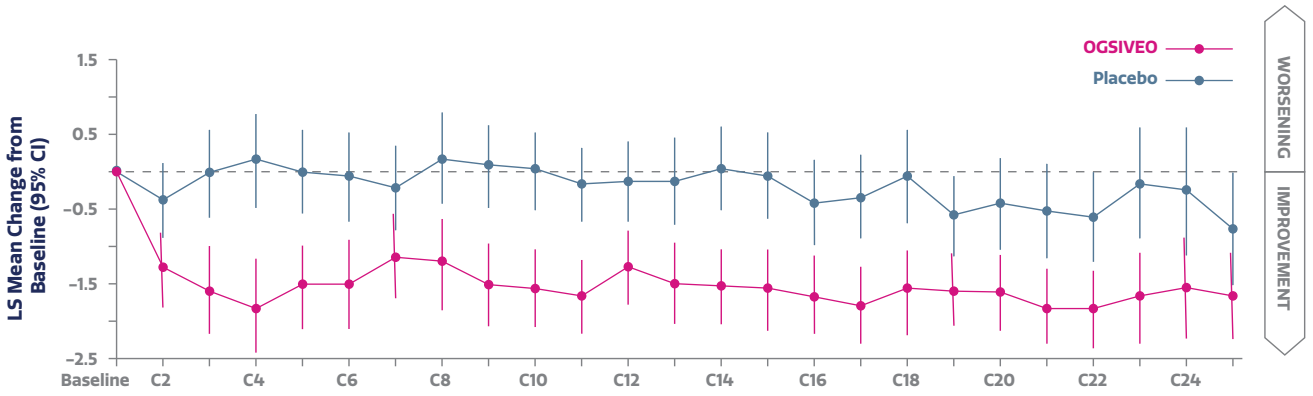
# **OGSIVEO** reduced patient-reported worst pain intensity

## PFS results were supported by change from baseline in patient-reported worst pain intensity favoring the OGSIVEO arm[9]

- Change from baseline at Cycle 10 in patient-reported worst pain intensity was a prespecified secondary end point in the DeFi study[2]
- Patient-reported outcome questionnaires for the BPI-SF were completed at baseline and the start of every treatment cycle[2]
- Assessment of pain at time points other than Cycle 10 was not prespecified in the DeFi study
- A positive change from baseline indicated worsening of patient-reported worst pain intensity[2]

### BPI-SF Average Worst Pain Intensity Score[2,*,†]




**Number of Patients Completing the Assessment[†††]**

| | Baseline | C2 | C4 | C6 | C8 | C10 | C12 | C14 | C16 | C18 | C20 | C22 | C24 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OGSIVEO | 69 | 61 | 43 | 46 | 39 | 40 | 40 | 35 | 38 | 32 | 33 | 32 | 31 |
| Placebo | 71 | 61 | 43 | 46 | 35 | 31 | 26 | 25 | 25 | 21 | 17 | 19 | 15 |

*Patient-reported worst pain intensity was assessed daily using item 3 of the BPI-SF, an 11-point numerical rating scale ranging from 0 ("no pain") to 10 ("pain as bad as you can imagine") and averaged over 7 days prior to each visit. Each cycle was 28 days. Cycle 10 was chosen as the time point for patient-relevant end point analysis to allow adequate time for a treatment response to be observed.[2,9]

†Scheduled visits with at least 10 patients in each arm were included in the analysis.[2]

‡The PRO questionnaire was considered to be completed if the patients met the minimum requirements for scoring. Some patients discontinued and were not expected to complete the PRO questionnaire but did complete the minimum requirements for scoring.[2]

BPI-SF, Brief Pain Inventory-Short Form; C, cycle; CI, confidence interval; DeFi, Desmoid Fibromatosis; LS, least squares; PFS, progression-free survival; PRO, patient-reported outcome.

### Analysis Limitations

- Definitive conclusions cannot be made about the BPI-SF results due to low questionnaire completion rate, asymmetric questionnaire completion between treatment arms, and the fact that analysis of results at time points other than Cycle 10 was not prespecified
- These data are not included in the OGSIVEO Prescribing Information

## Important Safety Information (cont'd)

### Adverse Reactions

Serious adverse reactions occurred in 20% of patients who received OGSIVEO. 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.

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# **OGSIVEO** safety information and dose modifications

- **Warnings and Precautions:** diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, embryo-fetal toxicity[9]
- **The most common adverse reactions** (≥15%) in patients receiving OGSIVEO in the DeFi study were diarrhea (84%), ovarian toxicity (75% in the 36 females of reproductive potential), rash (68%), nausea (54%), fatigue (54%), stomatitis (39%), headache (30%), abdominal pain (22%), cough (20%), alopecia (19%), upper respiratory tract infection (17%), and dyspnea (16%)[9]
- **Serious adverse reactions** occurred in 20% of patients who received OGSIVEO. Serious adverse reactions occurring in ≥2% of patients were ovarian toxicity (4%)[9]

**Recommended dose modifications for adverse reactions[9]**

| Adverse Reaction | Severity | OGSIVEO Dosage Modifications |
|---|---|---|
| **Diarrhea persisting for ≥3 days despite maximal medical therapy** | **Grades 3 or 4** | Withhold OGSIVEO until resolved to Grade ≤1 or baseline, then restart at a dose of 100 mg twice daily. |
| **ALT or AST increased** | **Grade 2 (≥3 to 5 x ULN)** | Withhold OGSIVEO until ALT, AST, or both are resolved to <3 × ULN or baseline, then restart at a dose of 100 mg twice daily. |
| | **Grades 3 or 4 (>5 x ULN)** | Permanently discontinue. |
| **Hypophosphatemia persisting for ≥3 days despite maximal replacement therapy** | **Grades 3 or 4** | Withhold OGSIVEO until resolved to Grade ≤1 or baseline, then restart at a dose of 100 mg twice daily. |
| **Hypokalemia despite maximal replacement therapy** | | |

For other severe adverse reactions, life-threatening adverse reactions, or persistent intolerable Grade 2 adverse events, withhold drug until resolved to Grade ≤1 or baseline. Only restart at a dose of 100 mg twice daily after considering the potential benefit and likelihood of recurrence of the adverse reaction. Permanently discontinue OGSIVEO for recurrence of severe or life-threatening adverse reaction upon rechallenge at the reduced dose.[9]

**Medical interventions and lifestyle changes may also help manage certain side effects***

*Prior to use of any concomitant medication, please refer to Section 7 (Drug Interactions) of the OGSIVEO Prescribing Information.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; DeFi, Desmoid Fibromatosis; ULN, upper limit of normal.

**References: 1.** Data on file. SpringWorks Therapeutics, Inc. Based on analysis of Veeva Compass claims data from February 1, 2024, through July 31, 2024. **2.** Gounder M, Ratan R, Alcindor T, et al. Nirogacestat, a gamma-secretase inhibitor for desmoid tumors. *N Engl J Med.* 2023;388(10):898-912. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed December 2, 2024. 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. **4.** Kasper B, Baldini EH, Bonvalot S, et al; Desmoid Tumor Working Group. Current management of desmoid tumors: a review. *JAMA Oncol.* 2024;10(8):1121-1128. **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. **6.** Skubitz KM. Biology and treatment of aggressive fibromatosis or desmoid tumor. *Mayo Clin Proc.* 2017;92(6):947-964. **7.** Crago AM, Denton B, Salas S, et al. A prognostic nomogram for prediction of recurrence in desmoid fibromatosis. *Ann Surg.* 2013;258(2):347-353. **8.** Tsagozis P, Stevenson JD, Grimer R, Carter S. Outcome of surgery for primary and recurrent desmoid-type fibromatosis. A retrospective case series of 174 patients. *Ann Med Surg (Lond).* 2017;17:14-19. **9.** OGSIVEO. Prescribing Information. SpringWorks Therapeutics, Inc. **10.** Penel N, Chibon F, Salas S. Adult desmoid tumors: biology, management and ongoing trials. *Curr Opin Oncol.* 2017;29(4):268-274. **11.** Data on file. SpringWorks Therapeutics, Inc.

## Important Safety Information (cont'd)

### 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.

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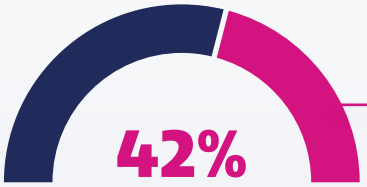
# Setting expectations at treatment initiation may help patients stay on track with therapy

**OGSIVEO 150 mg BID until disease progression or unacceptable toxicity**




**In patients who received OGSIVEO in the DeFi trial:**

**42% had dose reductions due to an adverse reaction[9,*]**

51% had dose interruptions (median days interrupted per interruption: 8 days; range: 1 to 132 days) and 20% permanently discontinued due to an adverse reaction.[9,11,*]

*Adverse events that led to dose reduction, interruption, or discontinuation of OGSIVEO included: diarrhea, ovarian toxicity, increased ALT/AST, rash, stomatitis, hypophosphatemia, fatigue, folliculitis, nausea, and hidradenitis.[9]

**For patients who were dose-reduced to 100 mg BID, no notable differences in PFS or ORR were observed[11]**

### Analysis Limitations

- Based on a post hoc analysis comparing PFS and ORR in patients treated with OGSIVEO in the DeFi study who dose-reduced versus those who did not
- DeFi was not powered to assess statistical differences between subgroups and this analysis should be considered descriptive only
- Therefore, the results require cautious interpretation and could represent chance findings
- These data are not included in the OGSIVEO Prescribing Information

**Proactive monitoring and management can help support patients receiving OGSIVEO**

## Personalized support services and resources

**Commercial Copay Program:** Eligible patients with commercial insurance may **pay as little as a $0 copay for OGSIVEO.†**

For further information on all SpringWorks CareConnections™ programs or questions about enrolling your patients, visit **www.springworkstxcares.com/hcp**

SpringWorks CareConnections™

†Terms and conditions apply. Copay program is subject to an annual benefit maximum. Full terms and conditions provided during enrollment process and are available upon request by contacting SpringWorks CareConnections at 844-CARES-55 (844-227-3755).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; DeFi, Desmoid Fibromatosis; ORR, objective response rate; PFS, progression-free survival.

## Important Safety Information (cont'd)

### Use in Specific Populations

Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with OGSIVEO and for 1 week after the last dose.

**Please see Important Safety Information throughout and click here for full Prescribing Information.**

SpringWorks THERAPEUTICS



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