# A phase 1/2 trial of zolucatetide (FOG-001), a first-in-class direct β-catenin:TCF inhibitor: updated safety and efficacy in patients with desmoid tumors

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# Declaration of Interests

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**Financial Interests**

Avacta Advisory Board, Personal
Ikena Oncology Advisory Board, Personal
Immunome Advisory Board, Personal
Kura Oncology Advisory Board, Personal
Orion Advisory Board, Personal
Parabilis Advisory Board, Personal
Springwork Therapeutics Advisory Board, Personal
Memorial Sloan Kettering Licensing Fees, Institutional
GODDESS Patient Reported Outcomes Instrument in Desmoid Tumors
UpToDate Royalties, Personal
Bristol Myers Squibb International Local PI, Institutional, Financial interest, Research Grant for conduct of study
Erasca Trial Chair, Institutional, Financial interest, Research Grant for conduct of study
Immunome Coordinating PI, Institutional, Financial interest, Research Grant for conduct of study
Kura Oncology Coordinating PI, Personal and Institutional, Financial interest, Research Grant for conduct of study
Neok Bio Local PI, Institutional, Financial interest, Research Grant for conduct of study
Orion Local PI, Personal and Institutional, Financial interest, Research Grant for conduct of study
Parabilis Local PI, Personal and Institutional, Financial interest, Research Grant for conduct of study
Springwork Therapeutics Coordinating PI, Personal and Institutional, Financial interest, Research Grant for conduct of study
Tango Local PI, Institutional, Financial interest, Research Grant for conduct of study
Vivace Therapeutics Local PI, Personal and Institutional, Financial interest, Research Grant for conduct of study

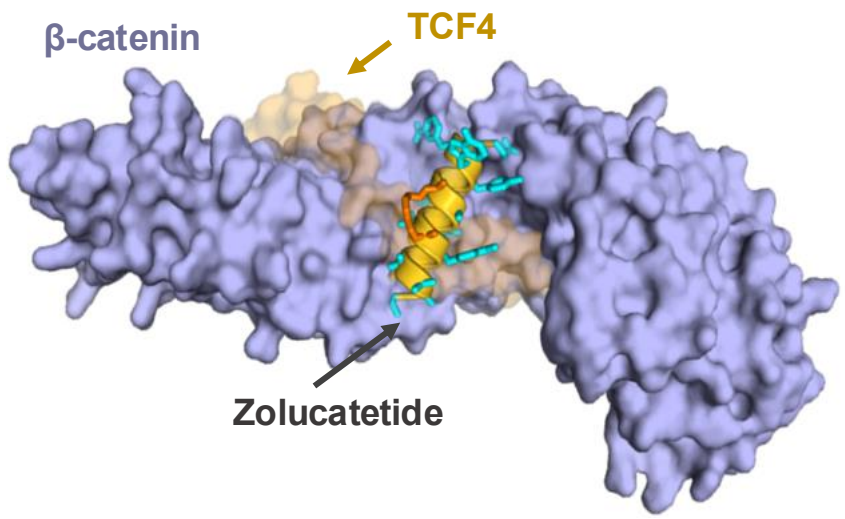
**Non-Financial Interests**

Chordoma Foundation Advisory Role
Desmoid Tumor Research Foundation Leadership Role, Scientific Director

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# Background

- Desmoid tumors (DT) are locally invasive, intermediate-grade, soft-tissue tumors that can cause significant morbidity for patients[1]
- Wnt/β-catenin pathway activating mutations (WPAM) are causal drivers of desmoid tumors, with nearly all harboring a mutation in either *CTNNB1* or *APC*[2,3]
- Currently available systemic therapy options do not target the causal Wnt/β-catenin pathway directly
- Zolucatetide is a Helicon™ peptide that selectively inhibits the β-catenin:TCF interaction, and directly targets the key molecular driver of the disease
- FOG-001-101 is a phase 1/2 dose-escalation and dose-optimization study of zolucatetide in DT and other WPAM+ tumors
- Here we present safety and efficacy data from a June 22, 2026 data cut of N=76 patients with DT from both dose escalation and dose optimization portions of the study




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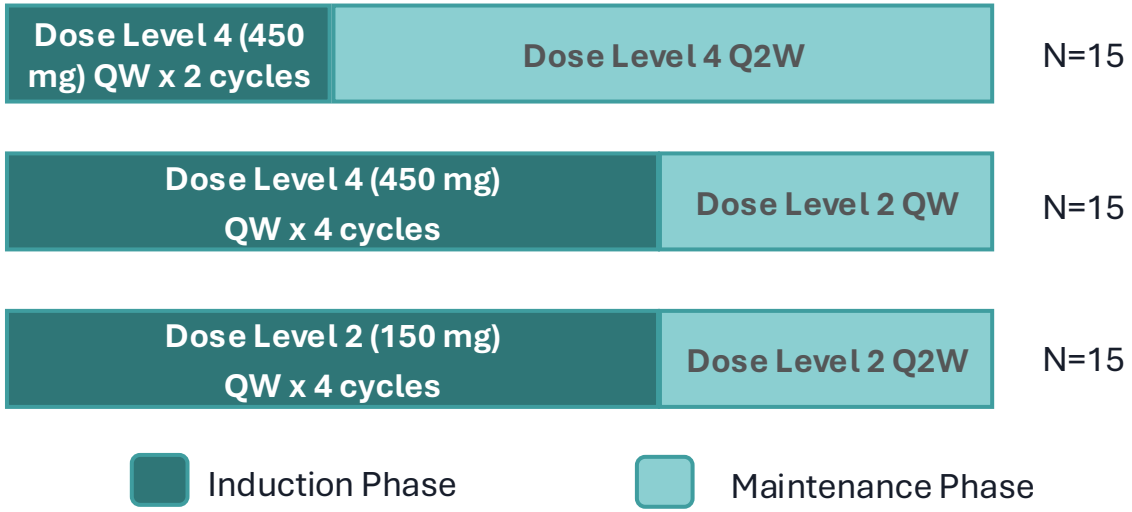
1. Penel N, et al. Curr Opin Oncol 2017;29:268–274
2. Timbergen MJM et al. Front Oncol 2019;9:397
3. Federman N. NPJ Precis Oncol 2022;6:62

# FOG-001-101 Study Cohorts for Patients with Desmoid Tumors

## Dose Escalation (N=31)*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Dose Level 2<br>150 mg QW | N=1 | Dose Level 3<br>300 mg QW | N=12 | Dose Level 4<br>450 mg QW | N=16 | Dose Level 6<br>900 mg QW | N=2 |

## Dose Optimization (N=45)




* IV weekly in 28-day cycles

Dose optimization arms designed to evaluate Phase 3 Induction and Maintenance dose and schedule, and to satisfy Project Optimus requirement

- **Induction:** Achieve rapid tumor reduction
- **Maintenance**: Sustain antitumor benefit and optimize tolerability for chronic administration

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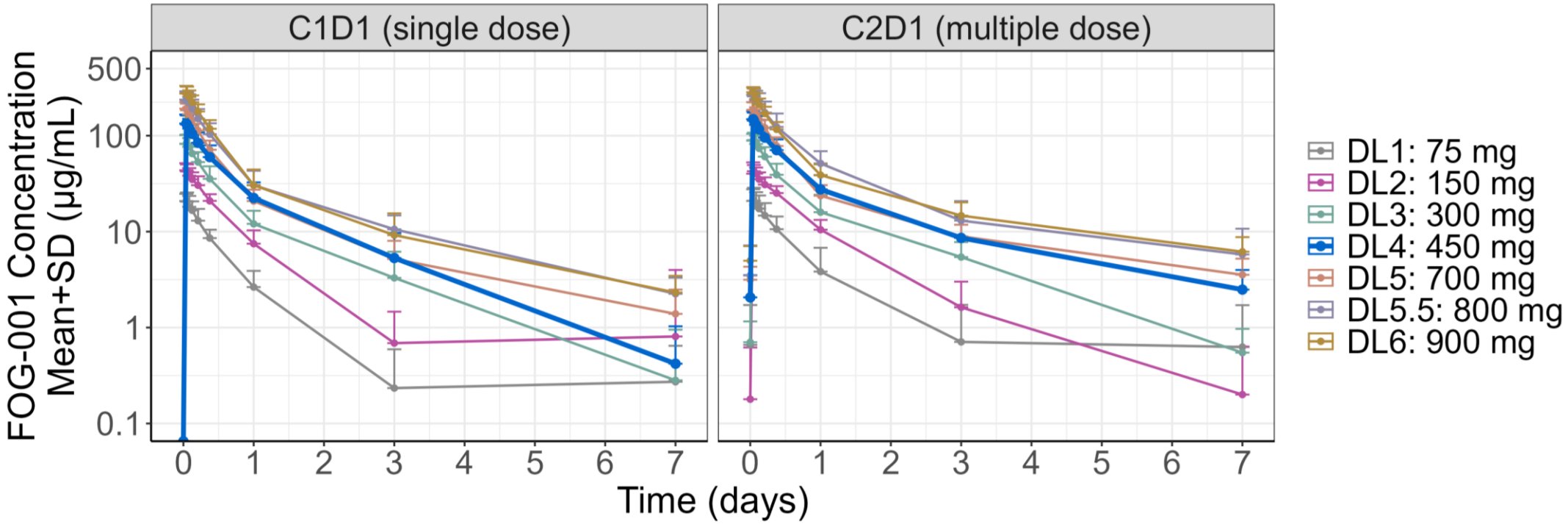
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# Demographics and Baseline Characteristics

| Characteristics | All patients (N=76) |
|---|---|
| **Median age**, years (range) | 37 (19–80) |
| **Sex,** n (%) | |
| Female | 53 (69.7) |
| Male | 23 (30.3) |
| **Wnt pathway activating mutation**, n (%) | |
| *APC* | 10 (13.2) |
| *CTNNB1* | 46 (60.5) |
| Not available | 20 (26.3) |
| **Tumor location**, n (%) | |
| Intra-abdominal | 15 (19.7) |
| Extra-abdominal | 61 (80.3) |
| **Prior DT treatment**, n (%) | 65 (85.5) |
| **Treatment-naïve**, n (%) | 11 (14.5) |
| **Median number of prior therapies** (range) | 2 (0–13) |
| **Prior therapies**, n (%) | |
| Surgery | 30 (39.5) |
| Radiation | 9 (11.8) |
| Systemic | 60 (78.9) |
| **Median number of prior systemic therapies** (range) | 2 (0–7) |
| **Prior systemic therapies**, n (%) | |
| Nirogacestat | 54 (71.1) |
| Sorafenib | 34 (44.7) |
| **Median target lesion size per RECIST**, mm (range) | 102 (26 - 468) |

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# Zolucatetide Pharmacokinetics




**Zolucatetide Displays Favorable PK Characteristics**

- Dose proportional exposure
- Low inter-patient variability

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Data cutoff: 22-Jun-2026

DL - Dose level; PK = pharmacokinetic; SD = standard deviation

# Safety Summary

| TRAEs in ≥20% of Study Patients | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **TRAEs, n (%)** | **150 mg (n=16)** | | **300 mg (n=12)** | | **450 mg (n=46)** | | **900 mg (n=2)** | | **All patients (N=76)** | |
| | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** | **All Grade** | **Grade ≥3** |
| **Any TRAE** | 15 (93.8) | 1 (6.3) | 8 (66.7) | 0 | 44 (95.7) | 6 (13.0) | 2 (100) | 2 (100) | 69 (90.8) | 9 (11.8) |
| **TRAEs (any grade) in ≥20% of pts** | | | | | | | | | | |
| Fatigue | 7 (43.8) | 0 | 4 (33.3) | 0 | 27 (58.7) | 1 (2.2) | 2 (100) | 0 | 40 (52.6) | 1 (1.3) |
| Alopecia | 5 (31.3) | 0 | 1 (8.3) | 0 | 21 (45.7) | 0 | 2 (100) | 0 | 29 (38.2) | 0 |
| Nausea | 4 (25.0) | 0 | 3 (25.0) | 0 | 21 (45.7) | 0 | 1 (50.0) | 0 | 29 (38.2) | 0 |
| Epistaxis | 4 (25.0) | 0 | 1 (8.3) | 0 | 16 (34.8) | 0 | 0 | 0 | 21 (27.6) | 0 |
| AST increased | 1 (6.3) | 0 | 0 | 0 | 17 (37.0) | 1 (2.2) | 2 (100) | 1 (50.0) | 20 (26.3) | 2 (2.6) |
| Blood bilirubin increased | 1 (6.3) | 0 | 0 | 0 | 15 (32.6) | 1 (2.2) | 2 (100) | 1 (50.0) | 18 (23.7) | 2 (2.6) |
| Myalgia | 3 (18.8) | 0 | 0 | 0 | 15 (32.6) | 0 | 0 | 0 | 18 (23.7) | 0 |
| **Any serious TRAE** | | | | | | | | | 2 (2.6)[1] | |
| **TRAE leading to discontinuation of treatment** | | | | | | | | | 0 | |
| **TRAEs leading to death (Grade 5)** | | | | | | | | | 0 | |

[1]Events were one each of grade 1 fever and grade 2 peripheral sensory neuropathy

- **Most commonly reported TRAEs are low-grade, reversible, and manageable with monitoring and supportive care**
- **No TRAEs resulting in treatment discontinuation or death**
- **No high-grade gastrointestinal or skin toxicities**
- **Not associated with ovarian toxicity**
- **Bilirubin elevations were attributable to OATP transporter inhibition and not to hepatocellular injury or cholestasis**

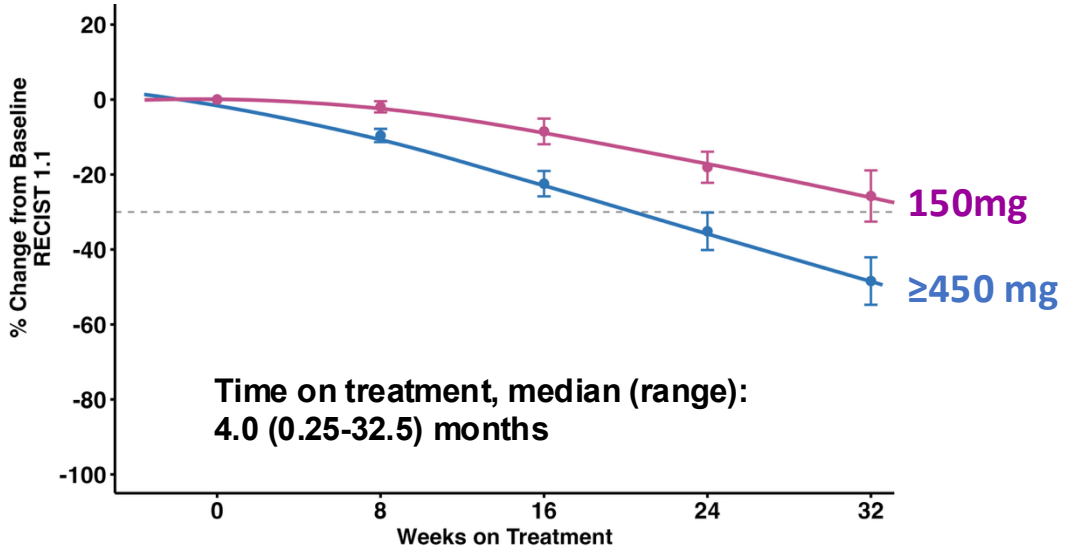
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AST – Aspartate aminotransferase; TRAE – Treatment-related adverse event

# Zolucatetide Efficacy in Patients with Desmoid Tumors

## Tumor Shrinkage Over Time by Starting Dose




Dots represent mean values of % change from baseline; errors bars represent standard errors. Trendline represents regression by locally estimated scatterplot smoothing (LOESS) fitted to the individual observations.

## Landmark ORR by RECIST 1.1

| Starting Dose | 24 Weeks | 32 Weeks |
|---|---|---|
| **≥ 450 mg** | **61.9%** (13/21) | **72.2%** (13/18) |
| **150 mg** | 0% (0/4) | 33.3% (1/3) |

Efficacy evaluable population including both confirmed and unconfirmed responses; all patients with opportunity for confirmation of initial PR were confirmed

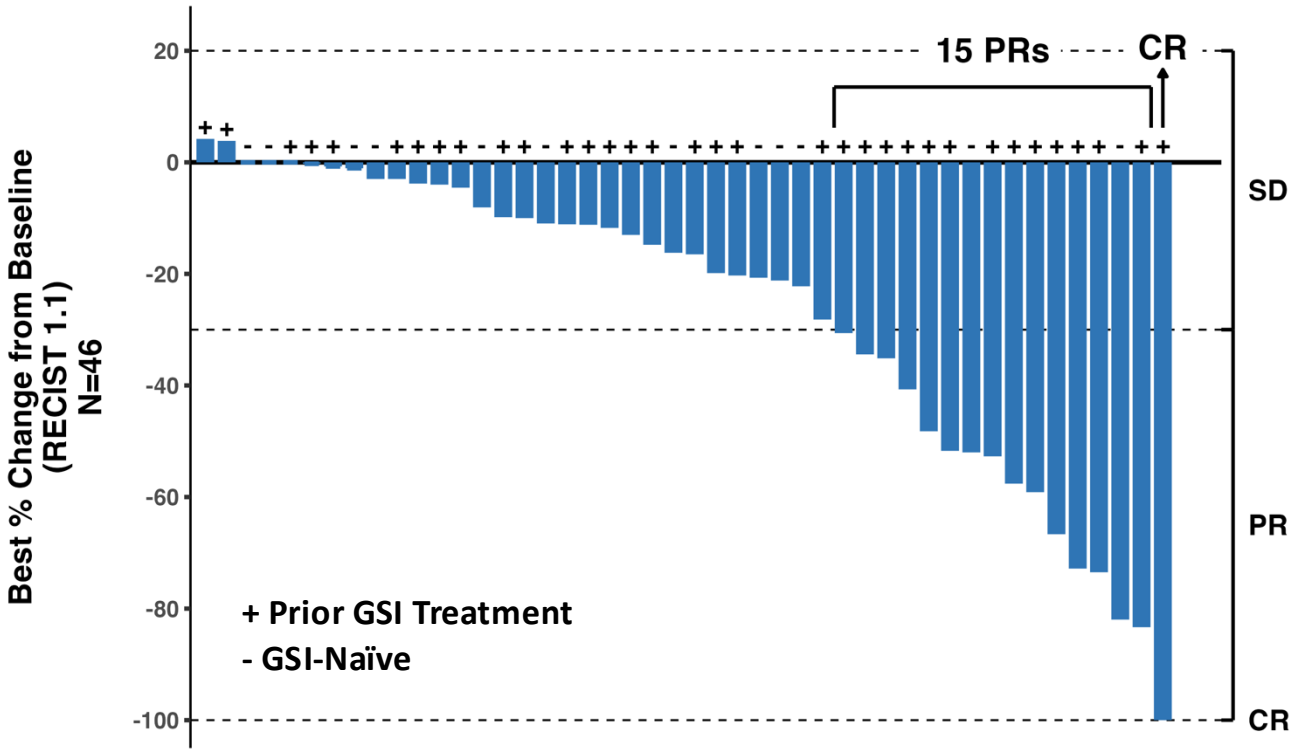
- **Dose-dependent antitumor activity with faster and more pronounced responses at higher doses, that continue to deepen over time**
- **Longer-term follow-up is ongoing (median follow-up at data-cut for all dosed patients: 4 months)**
- **These data reflect patients starting at ≥450 mg for induction followed by a lower-dose maintenance regimen, which informed the chosen recommended phase 3 regimen of 450 mg QW induction for 4 cycles followed by 300 mg Q2W (AUC-matched to 150 mg QW).**

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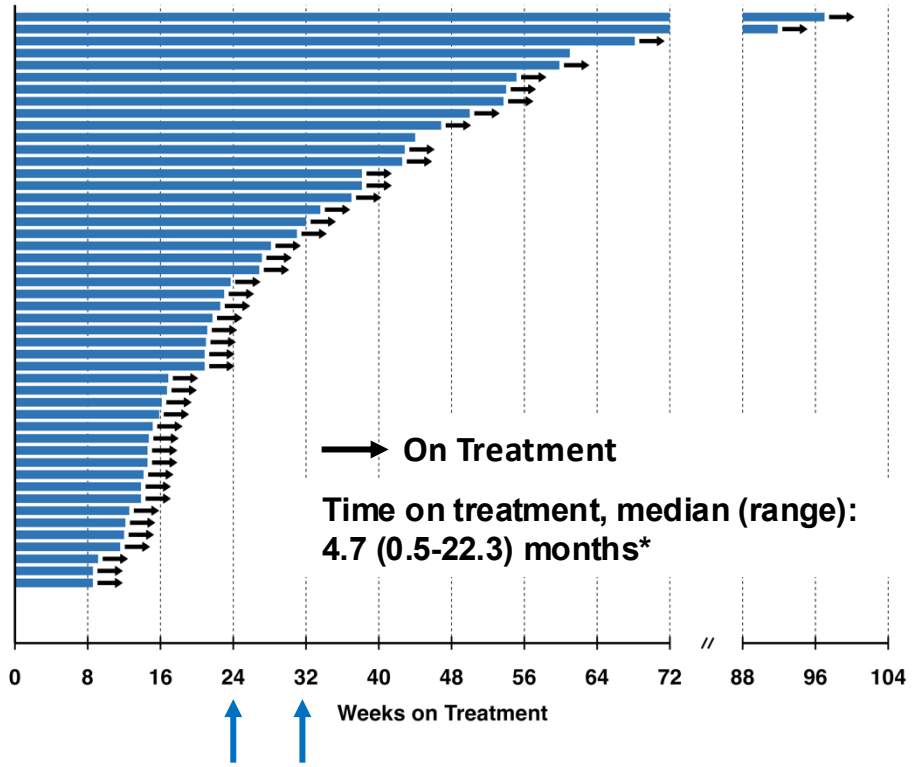
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DL - Dose level; RECIST – Response Evaluation Criteria in Solid Tumors;

# Zolucatetide Depth of Response and Duration of Exposure at ≥450 mg Starting Dose

## Best Percent Change by RECIST 1.1 in Patients (N=46) Receiving ≥ 450 mg Starting




## Duration of Exposure in Patients (N=48*) Receiving ≥ 450 mg Starting Dose




Arrows indicate timing of landmark analyses

**46 patients with a starting dose ≥ 450 mg are RECIST-evaluable (≥1 post-baseline scan)**

- Disease control rate (SD+PR+CR) 100%
- No patients have discontinued treatment due to PD
- Responses seen irrespective of prior GSI exposure or *CTNNB1*/*APC* mutation type

* One patient is not efficacy evaluable due to early resection of their desmoid tumor prior to completing a post-baseline scan, without subsequent dosing. A second patient has not had a first, 8-week scan.

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CR – complete response, DL - dose level, PD – progressive disease, PR – partial response, SD – stable disease; RECIST – Response Evaluation Criteria in Solid Tumors

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# Conclusions – Zolucatetide (FOG-001) in Desmoid Tumors

- **Zolucatetide is a Helicon™ peptide that directly and selectively inhibits the β-catenin:TCF interaction**

As of the data cut-off of June 22, 2026:

- **Encouraging anti-tumor activity that deepens over time**
  - Responses seen in 72% and 62% of patients at 32 and 24 week landmarks, respectively, among patients treated at ≥450 mg starting dose
  - Disease control rate of 100%
  - Irrespective of prior exposure to gamma secretase inhibitors or mutations in *CTNNB1* or *APC*
  - No patients have discontinued treatment due to progressive disease
- **Favorable safety profile, consisting mainly of low-grade and reversible AEs**
  - No treatment discontinuations due to AEs
- **A Phase 3 registrational study of zolucatetide in desmoid tumors is planned**
  - 450 mg QW for 4 cycles (induction phase) followed by 300 mg Q2W (maintenance phase) selected as the recommended Phase 3 regimen

**Enrollment in desmoid tumor-specific cohorts is ongoing (NCT05919264)**

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