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2026
ANNUAL MEETING

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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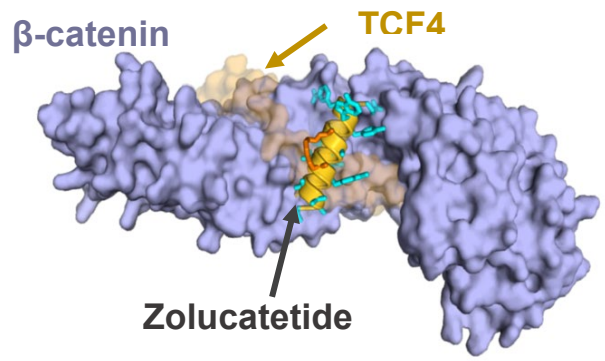
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Background

- Wnt/β-catenin pathway activating mutations (WPAM) are causal drivers of desmoid tumors (DT), with nearly all harboring a mutation in either *CTNNB1* or *APC*[1-2]
  - *APC* mutations, associated with concurrent familial adenomatous polyposis (FAP), account for ~10% of DT
- 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 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





1. Timbergen MJM et al. Front Oncol 2019;9:397
2. Federman N. NPJ Precis Oncol 2022;6:62

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)

Data cutoff: 22-Jun-2026



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	



- **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**

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

Data cutoff: 22-Jun-2026

Zolucatetide Efficacy in Patients with Desmoid Tumors

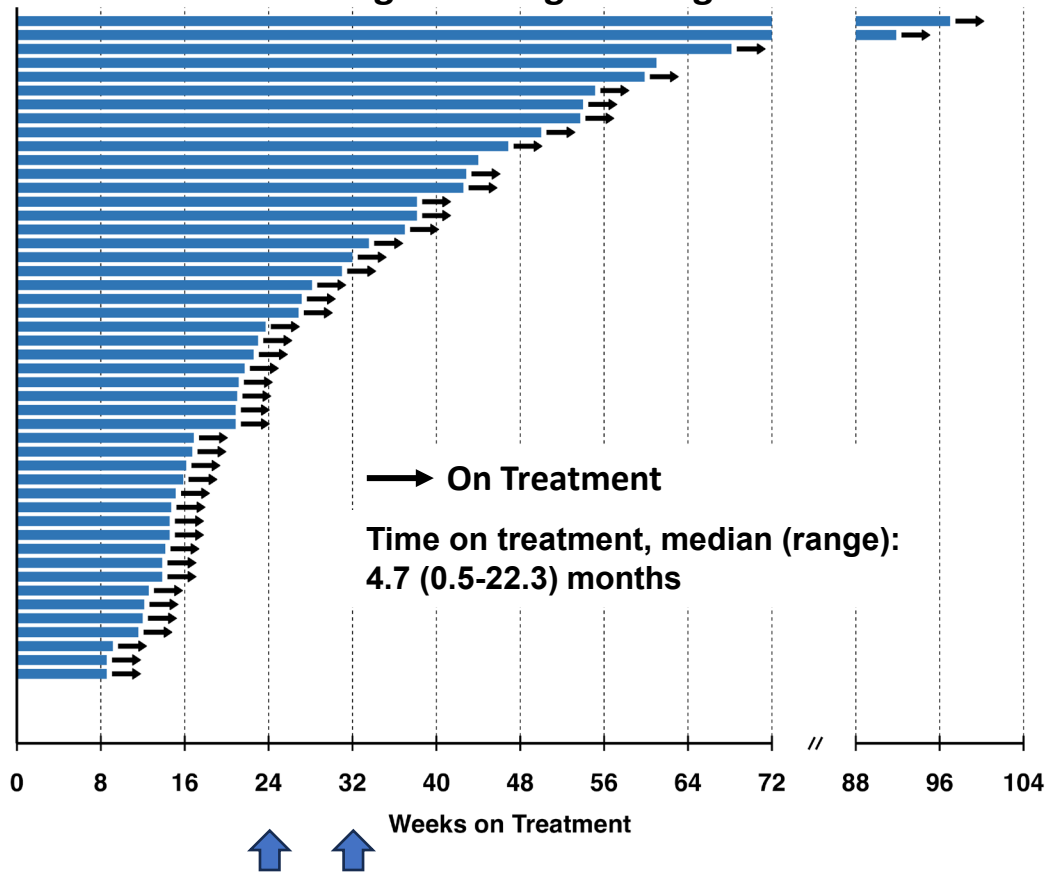
Landmark ORR by RECIST 1.1		
Starting Dose	**24 Weeks**	**32 Weeks**
≥ 450 mg	**61.9%** (13/21)	**72.2%** (13/18)
150 mg	0% (0/4)	33.3% (1/3)

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**
- **Disease control rate (SD+PR+CR) 100%**
- **No patients have discontinued treatment due to PD**
- **Supports moving forward with Phase 3 dose and regimen (R3PD) of:**
  - **Induction: 450 mg QW for four 28-day cycles**
  - **Maintenance: 300 mg Q2W thereafter**



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



Arrows indicate timing of landmark analyses

Data cutoff: 22-Jun-2026

Activity in Patient Subgroups Treated at RP3D-Equivalent Dose*

- Robust response rate in GSI-exposed patients and those with multiple prior lines of systemic therapy
- Antitumor activity observed in high-risk patient subgroups (large or intra-abdominal tumors)

Patient Population		Week 32 Landmark ORR
Whole population		72.2% (13/18)
Prior Treatment		
Prior GSI exposure		75.0% (12/16)
Prior Lines of Systemic Therapy	0-1	62.5% (5/8)
	≥2	80.0% (8/10)
Clinical Subgroup		
Age	>30 years	71.4% (10/14)
	≤30 years	75.0% (3/4)
Tumor Size	≥10 cm	75.0% (6/8)
	<10 cm	70.0% (7/10)
Tumor Location	Intra-abdominal	100% (3/3)
	Extra-abdominal	66.7% (10/15)

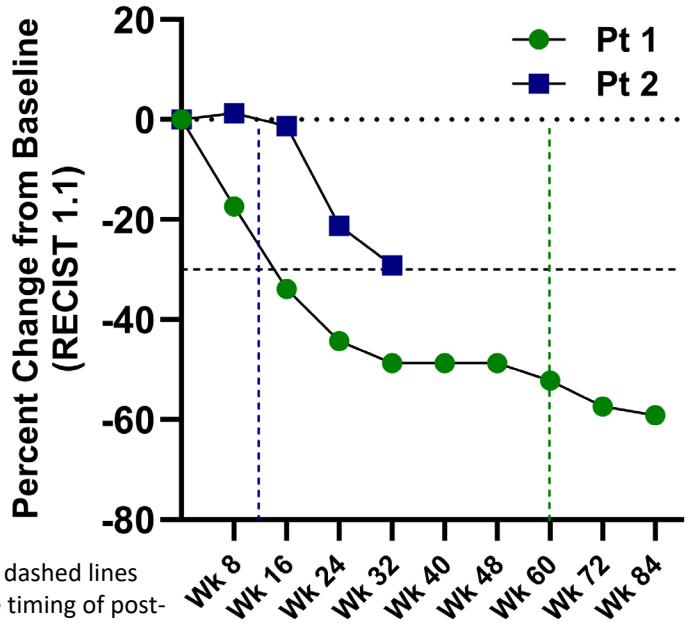


*Patients treated at ≥450 mg starting dose

Data cutoff: 22-Jun-2026

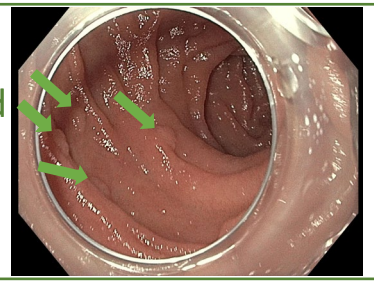
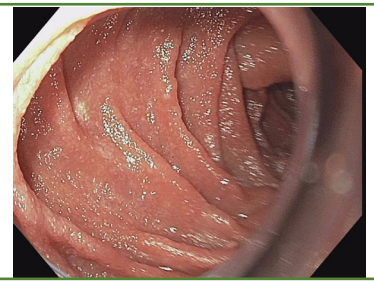
Activity in Patients with Desmoid Tumor and FAP Due to *APC* Mutations

Desmoid Tumor Shrinkage over Time



Vertical dashed lines indicate timing of post-treatment endoscopy

Marked Reduction in Duodenal Polyp Burden

	Baseline	After Zolucatetide	
Patient 1 29-year-old male			Improved from Spigelman Grade II to Grade I
Patient 2 29-year-old female			Improved from Spigelman Grade IV to normal mucosa within 12 weeks of treatment

- Zolucatetide treatment exerts substantial treatment effect on desmoid tumors and duodenal polyposis (both patients are post-colectomy)
- Now enrolling patients in an FAP-specific dose-ranging cohort of the ongoing Phase 1/2 trial (NCT05919264)



Conclusions

- **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%; no patients have discontinued treatment due to progressive disease
  - Robust antitumor activity regardless of clinical risk group or prior treatment exposures, including in post-GSI patients
- **Marked reductions in duodenal polyps and desmoid tumors in two patients with desmoid tumor/FAP**
- **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**

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

