Parabilis Medicines Presents Clinical Data Demonstrating First-Ever Drugging of Key Cancer Driver with FOG-001

October 17, 2025

Wnt/β-catenin pathway, first identified as a key cancer driver over 30 years ago and implicated in millions of cancer cases annually, is not addressed by any currently approved therapies

Oral presentation at ESMO 2025 shows FOG-001 – Parabilis's lead investigational Helicon™ peptide, targeting the β-catenin:TCF interaction – demonstrated tumor reductions in 100% of desmoid patients with an 80% objective response rate in patients with more than one post-baseline scan

Additional presentations at AACR-NCI-EORTC, PCF, CTOS, and SNO will expand on FOG-001's potential across a range of rare and common Wnt/β-catenin-driven solid tumors

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Parabilis Medicines, a clinical-stage biopharmaceutical company committed to creating extraordinary medicines for people living with cancer, today announced at the ESMO Congress 2025 the first-ever clinical data showing that its investigational FOG-001 therapy has successfully drugged β-catenin:TCF – a key cancer-driving node in the Wnt/β-catenin pathway, until now considered "undruggable."

In the ongoing Phase 1/2 trial of FOG-001 in patients with a range of Wnt/β-catenin-driven tumors, as of mid-August 2025, 12 patients with desmoid tumors had been dosed across three dose levels. Of the 10 patients who had at least one post-baseline scan, tumor reductions were observed at all dose levels with a 100% disease-control rate (DCR). Of the five patients with more than one post-baseline scan, an objective response rate (ORR) of 80% (4/5) was observed, per RECIST 1.1. Responses were seen in both gamma secretase-naive and –treated patients, and FOG-001 demonstrated clinically meaningful anti-tumor activity alongside acceptable safety and tolerability profiles.

FOG-001 achieves its effect by blocking the interaction between β-catenin and the T-cell factor (TCF) family of transcription factors, the key driver of tumorigenesis in Wnt pathway-activated cancer cells. The data support further development of FOG-001 in patients with desmoid tumors, and suggest that FOG-001, unlike other available therapies for this disease, directly addresses the underlying mechanism of disease through inhibition of β-catenin.

"For decades, scientists had said that the Wnt/β-catenin:TCF interaction couldn't be drugged, but our data prove otherwise," said Mathai Mammen, M.D., Ph.D., Chairman, CEO and President of Parabilis Medicines. "FOG-001 shows what bold science can achieve — taking on one of cancer's most important drivers and opening the door to an entirely new class of therapies. This milestone validates the power of Parabilis's distinctive Helicon peptides and marks an important step forward in our mission to create extraordinary medicines for patients."

The Wnt/β-catenin pathway was first identified over 30 years ago as a fundamental driver of cancer and is implicated in millions of cases each year, across both common cancers — including gastrointestinal cancers like colorectal, hepatocellular, and gastric cancers — as well as many rare cancers such as desmoid tumors and adamantinomatous craniopharyngioma (ACP). Attempts to target the β-catenin:TCF interaction, the key downstream node within the Wnt pathway, have repeatedly failed until now with FOG-001.

Parabilis's Helicon™ platform has overcome limitations of traditional small molecule therapeutics by designing stabilized α-helical peptides that gently penetrate cells and bind tightly to proteins with relatively flat binding surfaces. With FOG-001, Parabilis has achieved what decades of cancer research could not: directly drugging the "undruggable" β-catenin:TCF interaction.

Beyond ESMO, additional clinical data on FOG-001 across a range of Wnt/β-catenin-driven tumors will be presented at several additional upcoming scientific meetings, including the AACR-NCI-EORTC International Conference on Molecular Targets (October 22-26, Boston, MA), the Connective Tissue Oncology Society (CTOS) 2025 Annual Meeting (November 12-15, Boca Raton, FL), and the Society for Neuro-Oncology (SNO) 2025 Annual Meeting (November 19-23, Honolulu, HI). The company will also share new preclinical data on its allosteric active androgen receptor (AR^{ON}) and ERG degrader discovery programs for the treatment of prostate cancer at AACR-NCI-EORTC and the Prostate Cancer Foundation (PCF) Scientific Retreat (October 23-25, Carlsbad, CA).

Details of the presentations are as follows:

ESMO mini oral information:

Presentation Title: "A Phase 1/2 trial of FOG-001, a first-in-class direct β-catenin:TCF4 inhibitor: Safety and preliminary antitumor

activity in patients with desmoid tumors”
Date and Time: Friday, October 17, 2025, 4:00 – 5:30 p.m. CEST
Session: Mini oral session: Sarcoma
Location: Essen Auditorium, Hall 7.2A

AACR-NCI-EORTC oral and poster information:

Title: “A Phase 1/2 trial of FOG-001, a first-in-class direct β-catenin inhibitor, preliminary safety and efficacy in patients with solid tumors bearing Wnt pathway-activating mutations (WPAM+)”
Oral Presentation
Date and Time: Friday, October 24, 2025, 10:00 – 11:40 a.m. EDT
Session: Plenary Session 4: Clinical Trials Plenary Session
Location: Level 3, Ballroom AB
Poster Presentation
Date and Time: Friday, October 24, 2025, 12:30 – 4:00 p.m. EDT
Session: Poster Session B
Location: Level 2, Exhibit Hall D

Poster Title: “Distinct aspects of β-catenin biology drive multiple biologically rational FOG-001 combinations for MSS colorectal cancer”
Date and Time: Saturday, October 25, 2025, 12:30 – 4:00 p.m. EDT
Session: Poster Session C
Location: Level 2, Exhibit Hall D

Poster Title: “Degradation of the ETS transcription factor ERG by stabilized helical peptide (Helicon™) degraders enable pharmacological validation in ERG-fusion prostate cancer models”
Date and Time: Friday, October 24, 2025, 12:30 – 4:00 p.m. EDT
Session: Poster Session B
Location: Level 2, Exhibit Hall D

Poster Title: “Discovery of Helicon peptides for the selective degradation of the agonist-bound conformation of androgen receptor (AR^{ON}) in prostate cancer”
Date and Time: Friday, October 24, 2025, 12:30 – 4:00 p.m. EDT
Session: Poster Session B
Location: Level 2, Exhibit Hall D

PCF presentation and poster information:

Poster Title: “Discovery of Helicon peptides for the selective degradation of the agonist-bound conformation of androgen receptor (AR^{ON}) in prostate cancer”
Date and Time: Thursday, October 23, 2025, 7:30 – 10:30 PM PDT
Location: Costa De La Luna Ballroom

Presentation Title: “Discovery and Optimization of ERG Bifunctional, Stapled Peptide Degraders using Generative AI–Driven Multi-Property Modeling”
Date and Time: Saturday, October 25, 2025, 12:45 – 1:00 PM PDT
Location: Costa Del Sol Ballroom

CTOS poster information:

Poster Title: “A Phase 1/2 trial of FOG-001, a first-in-class direct β-catenin inhibitor: Safety and preliminary antitumor activity in patients with desmoid tumors (DT)”
Date and Time: Thursday, November 13, 2025, 5:30 – 6:30 p.m. EST
Session: Poster Reception: Soft Tissue Tumors

SNO mini oral information:

Presentation Title: “A Phase 1/2 trial of FOG-001, a first-in-class direct β-catenin:TCF4 inhibitor: Safety and preliminary antitumor activity in adamantinomatous craniopharyngioma (ACP) patients”
Abstract Number: CTNI-10
Date and Time: Friday, November 21, 2025, 11:30 – 12:30 p.m. HST
Session: Rapid Orals
Location: Hawaii Convention Center, Kamehameha Exhibit Hall II & III

About the Phase 1/2 trial of FOG-001
FOG-001 is being evaluated in a first-in-human Phase 1/2 multicenter, open-label study (NCT05919264) assessing its safety, tolerability, pharmacokinetics, pharmacodynamics, and antitumor activity. The trial includes dose-escalation and dose-expansion phases and is testing FOG-001 both as a monotherapy and in combination with other anticancer agents in patients with advanced

or metastatic solid tumors likely or known to harbor a Wnt pathway–activating mutation (WPAM).

About FOG-001
FOG-001 is an investigational first-in-class competitive inhibitor of β-catenin interactions with the T-cell factor (TCF) family of transcription factors and is currently in clinical development. By directly targeting the β-catenin:TCF protein-protein interaction, FOG-001 is intended to block the Wnt signaling pathway irrespective of the various APC and β-catenin mutations that typically drive disease.

FOG-001 combines key features that distinguish it from previously reported Wnt/β-catenin pathway modulators: FOG-001 acts inside the cell where it binds directly to the key oncogenic driver β-catenin; and FOG-001 blocks the Wnt pathway at the key downstream node, disrupting the interaction between β-catenin and the TCF transcription factors, thereby abrogating the signal transmission by which Wnt pathway mutations are believed to drive oncogenesis.

FOG-001 is currently being evaluated in a first-in-human Phase 1/2 clinical trial in patients with locally advanced or metastatic solid tumors.

About Parabilis Medicines
Parabilis Medicines is a clinical-stage biopharmaceutical company dedicated to creating extraordinary medicines that unlock high-impact protein targets long-considered undruggable. The company has developed a new class of stabilized, cell-penetrant alpha-helical peptides – Helicons™ – capable of modulating intracellular proteins that are inaccessible to traditional drug modalities.

Headquartered in Cambridge, Mass., Parabilis is advancing a focused pipeline of multiple first-in-class therapies across both rare and common cancers. Its lead candidate, FOG-001, is the first direct inhibitor of the interaction between β-catenin and the T-cell factor (TCF) family of transcription factors, implicated in colorectal cancer, desmoid tumors, and a range of other Wnt/β-catenin-driven tumors. Parabilis is also advancing investigational degraders of ERG and AR^{ON} for the treatment of prostate cancer, as well as other preclinical programs.

Learn more about how the company is advancing a new generation of precision cancer medicines with the potential to meaningfully alter the trajectory of disease for patients in need: www.parabilismed.com.

Contacts

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