Parabilis Medicines Presents Clinical and Preclinical Data Demonstrating Broad Potential of Helicon™ Peptides at AACR-NCI-EORTC 2025

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FOG-001, the first and only direct β-catenin:TCF inhibitor, shows early clinical activity in a range of Wnt/β-catenin–driven tumors — reinforcing clinical development opportunities across both rare and common cancers

Preclinical data from ERG and allosteric AR^{ON} degrader discovery programs in prostate cancer underscore Helicon platform's ability to repeatedly address "undruggable" cancer-driving targets

Parabilis Medicines, a clinical-stage biopharmaceutical company committed to creating extraordinary medicines for people living with cancer, today announced preliminary clinical and preclinical findings across its Helicon™ peptide pipeline at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston, Massachusetts.

The findings reinforce the broad potential of FOG-001, the company's lead investigational therapy and the first-ever direct Wnt/β-catenin:TCF inhibitor, to act across a range of rare and more prevalent solid tumors linked by the same dysregulated biology of the Wnt/β-catenin pathway. Single-agent activity resulting in tumor shrinkage by at least 30% (partial response (PR)) was observed in five low-complexity tumor types, with strong scientific support as well for FOG-001's potential in combination therapy for more complex tumors, including microsatellite-stable colorectal cancer (MSS CRC).

Together with positive preclinical read-outs demonstrating pharmacologic proof of concept for the company's discovery-stage Helicon peptides in prostate cancer targeting the ERG and active androgen receptor (AR^{ON}) targets, these data highlight how the company's Helicon platform can repeatably target high-impact "undruggable" targets long considered inaccessible to conventional therapeutic approaches.

"Just one week after presenting the first clinical proof that β-catenin:TCF can be drugged, we are showing the breadth of what this breakthrough could mean for science and for patients," said Mathai Mammen, M.D., Ph.D., Chairman and CEO of Parabilis Medicines. "FOG-001 is demonstrating meaningful signs of clinical activity across multiple Wnt/β-catenin-driven tumors, supporting its continued development in both simpler and more biologically complex Wnt-driven cancers through both monotherapy and combination therapy approaches."

He added, "Together with our preclinical advances in prostate cancer, the data illustrate the potential of Helicons to take on some of the toughest problems in oncology and bring forward transformative medicines that could meaningfully improve outcomes for patients."

FOG-001 Clinical and Preclinical Findings

The Wnt/β-catenin pathway — first identified as a key cancer driver over 30 years ago — is implicated in millions of cancer cases annually, spanning many rare and prevalent solid tumors as well as diseases like familial adenomatous polyposis (FAP) that predispose individuals to certain cancers, including colorectal cancer and desmoid tumors. Despite its central role in cancer biology, the pathway's critical β-catenin:TCF transcription complex has long been considered "undruggable."

Preliminary data from the ongoing Phase 1/2 trial of FOG-001 (NCT05919264), as of mid-August 2025, show that the therapy is well tolerated with no Grade 4/5 treatment-related adverse events or discontinuations and exhibits a favorable pharmacokinetic profile. As of this early data cut, an **objective response rate (ORR) of 43%** and a **disease control rate (DCR) of 83%**, per RECIST 1.1, were observed in non-CRC patients with Wnt pathway activating mutations (WPAM). Evidence of single-agent activity was observed across numerous Wnt/β-catenin–driven tumors, particularly in those with low mutational burden, including desmoid, adamantinomatous craniopharyngioma (ACP), ameloblastoma, salivary gland cancer, and solid pseudopapillary neoplasm (SPN).

In MSS CRC, a **50% DCR** was achieved within the efficacious monotherapy dose range, with molecular data confirming on-target pathway inhibition and reprogramming of the tumor microenvironment toward a more immune-active state. Complementary preclinical studies demonstrated that FOG-001 enhances the effects of standard and emerging therapies for MSS CRC—showing in these preclinical models additive or synergistic activity with each of 5-fluorouracil and anti-VEGF regimens, synergy with anti–PD-1 therapy, and combination benefit with pan-RAS and KRAS G12D inhibitors.

Together, these findings highlight FOG-001's broad pipeline potential — warranting continued development in Wnt pathway–activated low-complexity tumors, and as a backbone for rational combination regimens in more complex cancers. The Phase 1/2 study remains ongoing across a wide range of Wnt-driven rare and common cancers, with additional data readouts expected over the coming months.

Prostate cancer pipeline expansion

Parabilis also presented preclinical data advancing its prostate cancer franchise, focused on two long-standing oncogenic drivers that currently lack effective therapies. ERG-degrading Helicon peptides potently and durably reduced ERG protein levels —overexpressed in 40–50% of prostate cancers — showing *in vivo* pharmacologic proof-of-concept demonstrating tumor growth inhibition and efficacy comparable to or exceeding standard of care in challenging prostate cancer models.

In parallel, allosteric AR^{ON} Helicon degraders that bind a conserved site distinct from the androgen ligand pocket, were designed to selectively target the active, agonist-bound androgen receptor. These Helicon degraders block proliferation in AR-amplified prostate cancer cells, offering a strategy to overcome resistance driven by AR mutations or amplification. Importantly, this approach also allows for effective combinations with approved and emerging treatments that target the testosterone ligand pocket. Together, these data demonstrate the repeatability of the Helicon platform in addressing high-value, historically undruggable targets in oncology.

“Our Helicons are delivering against three of the most challenging and compelling targets in oncology, from β-catenin:TCF to ERG to AR^{ON},” said Fawzi Benzaghou, M.D., Chief Medical Officer of Parabilis Medicines. “By pursuing bold science that makes the undruggable druggable, we’re opening new therapeutic possibilities for patients with few or no options. These data reinforce the power of our α-helical peptide platform to repeatedly unlock difficult targets and advance medicines with the potential for extraordinary patient impact.”

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.

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