Parabilis Medicines' Zolucatetide, the First and Only Direct Inhibitor of the Elusive β-catenin:TCF Interaction, Receives FDA Orphan Drug Designation for the Treatment of Desmoid Tumors

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Latest milestone underscores accelerating regulatory momentum for the company's lead investigational Helicon peptide, following FDA Fast Track Designation in desmoid tumors

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Parabilis Medicines, a clinical-stage biopharmaceutical company committed to creating extraordinary medicines for people living with cancer using its Helicon ™ peptide platform to drug historically undruggable targets, today announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to zolucatetide (previously known as FOG-001), the company's lead investigational Helicon ™ peptide and the first and only direct inhibitor of the elusive β-catenin:TCF interaction, for the treatment of desmoid tumors. Zolucatetide has also received FDA Fast Track Designation in desmoid tumors.

"Patients living with desmoid tumors have lacked therapies that directly address the root biological cause of their disease because that biology, the β-catenin:TCF interaction, has long been considered 'undruggable,'" said Mathai Mammen, M.D., Ph.D., Chairman, CEO and President of Parabilis Medicines. "With Orphan Drug Designation and Fast Track Designation from the FDA, along with compelling early clinical data showing encouraging evidence of clinical activity, we are building momentum behind zolucatetide as a potential first-in-class therapy that we believe could help redefine the standard of care for patients with desmoid tumors and other tumors driven by the same elusive biology. We are committed to advancing this program with rigor and speed to deliver meaningful impact for patients."

Desmoid tumors are considered a rare condition involving locally invasive soft-tissue tumors that form in the connective tissues. While they do not metastasize, desmoid tumors can be aggressive and recurrent, often causing chronic and significant pain, limited mobility, disfigurement and organ dysfunction, and no existing therapies target the underlying biology of the disease.

Zolucatetide is an investigational first-in-class inhibitor of the Wnt/β-catenin pathway, which is the fundamental driver of desmoid tumor growth. Orphan Drug Designation follows early data, first released at the European Society for Medical Oncology (ESMO) Congress and Connective Tissue Oncology Society (CTOS) 2025 Annual Meeting, demonstrating that zolucatetide has shown evidence of clinically meaningful antitumor activity in desmoid tumors, including tumor reductions and 100% disease-control rate (DCR) in all 10 patients with at least one post-baseline scan and an 80% objective response rate (ORR) in the five patients with more than one post-baseline scan per RECIST 1.1.

The FDA grants Orphan Drug Designation to drugs and biologics that are intended for safe and effective treatment, diagnosis or prevention of rare diseases or conditions that affect fewer than 200,000 people in the U.S. Orphan Drug Designation provides certain incentives, such as tax credits towards the cost of clinical trials upon approval and prescription drug user fee waivers. Products with Orphan Drug Designation status are also entitled to a potential seven years of regulatory exclusivity following regulatory approval.

Beyond desmoid tumors, zolucatetide is being evaluated across a broad range of rare and common Wnt/β-catenin-driven tumor types. Clinical data presented at the AACR-NCI-EORTC 2025 meeting showed zolucatetide had single-agent activity in five low-complexity tumor types where Wnt/β-catenin mutations are the primary drivers of disease – including desmoid, adamantinomatous craniopharyngioma (ACP), ameloblastoma, salivary gland cancer, and solid pseudopapillary neoplasm (SPN) – with strong scientific rational for combination therapy in more complex cancers such as microsatellite-stable colorectal cancer (MSS CRC). Parabilis also shared early data indicating the potential of zolucatetide in hepatocellular carcinoma (HCC) and familial adenomatous polyposis (FAP) at the JP Morgan Healthcare conference earlier this year.

The company plans to share additional data readouts in 2026 from its ongoing Phase 1/2 trial of zolucatetide, in which more than 150 patients have been dosed to date.

About Zolucatetide (Previously FOG-001)

Zolucatetide 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, zolucatetide is intended to block the Wnt signaling pathway irrespective of the various APC and β-catenin mutations that typically drive disease.

Zolucatetide combines key features that distinguish it from previously reported Wnt/β-catenin pathway modulators: zolucatetide

acts inside the cell where it binds directly to the key oncogenic driver β-catenin; and zolucatetide 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.

Zolucatetide is currently being evaluated in a Phase 1/2 clinical trial in patients with locally advanced or metastatic solid tumors. Zolucatetide has received Fast Track Designation and Orphan Drug Designation for the treatment of desmoid tumors from the U.S. Food and Drug Administration (FDA).

About the Phase 1/2 trial of Zolucatetide

Zolucatetide is being evaluated in a 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 zolucatetide 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 Parabilis Medicines

Parabilis Medicines is a clinical-stage biopharmaceutical company dedicated to creating extraordinary medicines that unlock high-impact protein targets long-considered undruggable. Leveraging over a decade of proprietary data, laboratory innovations, and AI- and physics-based algorithms, 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, zolucatetide (previously known as 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 allosteric 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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