Parabilis Medicines Initiates Dose-Ranging Clinical Study of Zolucatetide in Familial Adenomatous Polyposis

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New dose-ranging cohort in FAP builds on compelling early clinical evidence observed with zolucatetide in patients with FAP and concomitant desmoid tumors

Zolucatetide directly inhibits β-catenin:TCF, targeting the APC-mutation biology that drives precancerous adenomatous polyp formation in patients with FAP

CAMBRIDGE, Mass., Oct. 14, 2026 (GLOBE NEWSWIRE) -- Parabilis Medicines (Nasdaq: PBLS), a clinical-stage biopharmaceutical company dedicated to creating extraordinary medicines for patients with serious diseases by unlocking historically undruggable targets, today announced the initiation of a dose-ranging clinical cohort evaluating zolucatetide in patients with familial adenomatous polyposis (FAP) as part of the company's ongoing Phase 1/2 clinical trial. Zolucatetide is Parabilis' lead investigational Helicon™ peptide and the first and only direct inhibitor of the β-catenin:TCF interaction, a key driver of a range of cancers and tumor types.

"People with FAP face a lifetime of surveillance, repeated procedures and major surgeries, all while living with the persistent risk of cancer," said Mathai Mammen, M.D., Ph.D., Chairman, CEO and President of Parabilis Medicines. "We believe a medicine that addresses the underlying biology of the disease has the potential to change that trajectory. FAP is driven by loss of APC and the resulting persistent activation of Wnt/β-catenin signaling, making direct inhibition of the β-catenin:TCF interaction the most direct therapeutic approach to reversing the causal biology of the disease. We are highly encouraged by the significant reductions in precancerous duodenal polyp burden we have observed with zolucatetide in our first patients with FAP. The initiation of this dose-ranging study reflects our growing confidence in zolucatetide's potential to fundamentally change the treatment of FAP and is an important step toward defining the dose and schedule we intend to take into registrational development for this devastating disease."

Early clinical proof-of-concept data reported to date from patients with FAP and concomitant desmoid tumors enrolled in the ongoing Phase 1/2 trial support the therapeutic potential of zolucatetide in FAP. In two patients who underwent routine endoscopic evaluation while receiving zolucatetide, significant reductions in polyp burden were observed, from Spigelman Stage IV to a near-normal duodenum and from Spigelman Stage II to Stage I, respectively. Zolucatetide has demonstrated a favorable safety and tolerability profile to date.

The dedicated FAP cohort is part of Parabilis' ongoing Phase 1/2 clinical trial of zolucatetide, a multicenter, open-label study evaluating zolucatetide across Wnt/β-catenin-driven diseases. The cohort will evaluate zolucatetide monotherapy in adults with FAP and a documented APC mutation who have undergone colectomy and have measurable duodenal polyp burden.

Parabilis anticipates disclosing additional data in the first quarter of 2027 from patients with FAP and concomitant desmoid tumors currently enrolled in the ongoing Phase 1/2 trial.

Beyond FAP, zolucatetide is being evaluated across a broad range of Wnt/β-catenin-driven tumor types, including desmoid tumors; adamantinomatous craniopharyngioma (ACP); hepatocellular carcinoma (HCC); and multiple other tumor indications.

About FAP
FAP is a genetic disease caused in all cases by germline loss-of-function mutations in the *APC* gene, resulting in persistent activation of Wnt/β-catenin signaling that drives the development of hundreds to thousands of precancerous gastrointestinal polyps. Without intervention, people with FAP face the near certainty of developing colorectal cancer. Prophylactic colectomy is often required to reduce that risk, but even after removal of the colon, patients remain at risk of developing precancerous polyps and cancer elsewhere in the gastrointestinal tract, particularly in the duodenum, as well as other manifestations of FAP. There are currently no approved systemic therapies for FAP, leaving patients reliant on lifelong surveillance, repeated procedures and major surgeries to manage the disease, while the persistent risk of cancer creates a significant lifelong psychological and emotional burden for patients and their families.

About Zolucatetide
Zolucatetide is an investigational first-in-class and first-and-only direct inhibitor of the β-catenin:TCF interaction, a genetically validated driver of numerous cancers and other serious diseases that has long been considered undruggable. Designed using Parabilis' Helicon™ peptide platform, zolucatetide inhibits the interaction between β-catenin and the T-cell factor (TCF) family of transcription factors, preventing activation of disease-driving genes. By targeting this key downstream node, zolucatetide is designed to address aberrant Wnt/β-catenin signaling irrespective of the various upstream APC and β-catenin mutations that drive its activation, potentially overcoming a key limitation of approaches targeting earlier steps in the pathway.

Zolucatetide is currently being evaluated in an ongoing Phase 1/2 clinical trial (NCT05919264) across a range of indications, including desmoid tumors, familial adenomatous polyposis (FAP), adamantinomatous craniopharyngioma (ACP), hepatocellular carcinoma (HCC) and additional Wnt-driven tumor types. A Phase 3 registrational trial in desmoid tumors is planned.

About Parabilis Medicines
Parabilis Medicines (Nasdaq: PBLS) is a clinical-stage biopharmaceutical company dedicated to creating extraordinary medicines for patients with serious diseases by unlocking biologically important targets long considered undruggable. The company has pioneered a new class of alpha-helical peptides – Helicons™ – capable of modulating intracellular proteins that have historically been beyond the reach of conventional medicines. The company's lead investigational medicine, zolucatetide, is the first and only direct inhibitor of the β-catenin:TCF interaction, a central node in the Wnt/β-catenin pathway that has eluded drug developers for decades. Zolucatetide is being evaluated in the clinic across multiple Wnt/β-catenin-driven diseases, including desmoid tumors, familial adenomatous polyposis (FAP), adamantinomatous craniopharyngioma (ACP), hepatocellular carcinoma (HCC) and a range of other rare and common solid tumor indications. Beyond zolucatetide, Parabilis is pursuing a follow-on β-catenin degrader program and advancing additional Helicon-based programs focused on other challenging targets, including ERG and allosteric AR^{ON} in prostate cancer, where we believe our medicines could have life-altering impact. For more information, visit www.parabilismed.com or follow us on LinkedIn.

Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, express or implied statements regarding: the clinical development of zolucatetide for the treatment of FAP, desmoid tumors, ACP, HCC and other Wnt-driven tumors, including the initiation, timing, progress, results and future data releases of our ongoing and planned clinical trials; the design, enrollment, conduct and timing of the dose-ranging cohort in FAP within the ongoing Phase 1/2 trial; the expected timing of additional data from patients with FAP and concomitant desmoid tumors; the Company's plans to define the dose and schedule for registrational development of zolucatetide in FAP; the expected enrollment and timing of certain patient cohorts in Wnt-driven diseases; and expectations regarding the efficacy, tolerability, safety, and commercial potential of zolucatetide.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks and uncertainties that could negatively affect the Company's business, operating results, financial condition and stock value. Factors that could cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release include, without limitation: risks relating to the Company's ability to execute on its strategy, including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to clinical development activities; the Company's dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; risks related to regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; risks related to establishing and maintaining the Company's intellectual property protections; and risks related to the competitive landscape for the Company's product candidates; as well as other risks and uncertainties described in greater detail in "Risk Factors," in the Company's most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in the Company's subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent the Company's views only as of today and should not be relied upon as representing its views as of any subsequent date. The Company expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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