Parabilis Medicines Presents Updated Phase 1/2 Data for Zolucatetide Demonstrating Compelling Efficacy and Favorable Safety and Tolerability Profile in Patients with Desmoid Tumors

October 24, 2026

- *Objective response rate of 72.2% among response-evaluable patients receiving a starting dose of ≥450 mg at 32-week landmark*
- *Disease control rate of 100% across all response-evaluable patients receiving a starting dose of ≥450 mg, with no disease progression and no treatment discontinuations due to TRAEs*
- *Data informed FDA-aligned dose and regimen selection for upcoming PEDESTAL Phase 3 registrational trial, with initiation planned in the first half of 2027 and topline results anticipated in 2029*
- *Company to host investor webcast on Saturday, October 24, 2026, at 18:00 CEST (12:00 p.m. EDT)*

CAMBRIDGE, Mass., Oct. 24, 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 updated safety and efficacy data for zolucatetide, the first and only direct inhibitor of the β-catenin:TCF interaction, in patients with desmoid tumors. The data were presented today in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2026, taking place October 23–27, 2026, in Madrid, Spain.

The updated results, based on a June 22, 2026, data cutoff, include data from both the dose escalation and dose optimization portions of the ongoing Phase 1/2 trial and reinforce the strong efficacy and favorable safety and tolerability profile observed with zolucatetide. Among response-evaluable patients who began treatment at a starting dose of ≥450 mg, zolucatetide demonstrated an objective response rate (ORR) of 72.2% (13/18) in a 32-week landmark analysis. A disease control rate (DCR) of 100% was observed across all 46 response-evaluable patients who received a starting dose of ≥450 mg, with no disease progression.

Data from a three-arm randomized dose optimization trial supported selection of a 450 mg weekly induction regimen administered for four cycles, followed by 300 mg every two weeks for long-term maintenance. Following productive end-of-Phase 2 discussions, Parabilis has reached alignment with the U.S. Food and Drug Administration (FDA) on the selected dose and regimen, on the use of a placebo-controlled study design, and on progression-free survival (PFS) as the primary endpoint for registrational development.

Parabilis plans to initiate the randomized, double-blind PEDESTAL Phase 3 trial (**P**hase 3 **E**valuation of **DES**moid **T**umor **A**ctivity with zo**L**ucatetide) in the first half of 2027, with topline results anticipated in 2029.

“Desmoid tumors are chronic and life-altering for patients, often affecting people at a young age, and patients need treatments that can deliver rapid, deep and durable tumor responses with a tolerability profile suited for long-term treatment,” said Mathai Mammen, M.D., Ph.D., Chairman, CEO and President of Parabilis Medicines. “We designed zolucatetide to directly inhibit β-catenin:TCF, a historically undruggable target at the heart of the biology driving these tumors. The depth and consistency of responses we are seeing, together with the favorable safety and tolerability profile observed to date, reinforce our conviction that zolucatetide has the potential to deliver a truly differentiated medicine and meaningfully expand the number of patients who can benefit from treatment. We are very pleased with the clarity of the FDA’s feedback on our registrational development strategy, and with our Phase 3 regimen selected, we are moving with urgency to bring this medicine to patients.”

Updated Phase 1/2 Results
As of the June 22, 2026, data cutoff, 76 patients with desmoid tumors had been enrolled and treated across all dose levels in the dose escalation and dose optimization portions of the trial. Median age was 37 years (range 19–80), and 69.7% of patients were female. The population included both patients who had previously been treated with and failed gamma-secretase inhibitors (GSIs) and patients naive to GSIs.

A total of 48 patients began treatment at a starting induction dose of ≥450 mg, prior to down-dosing for maintenance. Two patients were started at 900 mg, but had an average dose of 400–500 mg over the first four months of treatment. Of these 48 patients, 46 were response-evaluable, and 18 had scans at 32 weeks. Median time on treatment for this cohort was 4.7 months (range 0.5–22.3), reflecting recent enrollment of a substantial portion of the cohort.

Efficacy

- ORR per RECIST 1.1 was 72.2% (13/18) among all patients evaluable at the 32-week landmark

- A disease control rate (DCR) of 100% was observed across all 46 response-evaluable patients
- Responses were observed irrespective of prior gamma-secretase inhibitor (GSI) exposure or CTNNB1 or APC mutation status
- No evidence of disease progression or resistance

Safety

- Zolucatetide continued to demonstrate a favorable safety and tolerability profile at the selected doses for Phase 3 registrational development
- Treatment-related adverse events (TRAEs) were predominantly low-grade; the most commonly reported TRAEs were fatigue, alopecia and nausea
- No patients discontinued treatment due to TRAEs
- Not associated with ovarian toxicity or high-grade gastrointestinal or skin toxicities commonly reported with GSIs

“The early clinical results with zolucatetide are encouraging, particularly the magnitude and apparent rapidity of tumor responses observed to date,” said Mrinal Gounder, M.D., Sarcoma Medical Oncologist and Early Drug Development Specialist at Memorial Sloan Kettering Cancer Center, and presenting author of the study. “Desmoid tumors can impose a substantial physical and emotional burden on patients, and therapies capable of achieving meaningful tumor shrinkage while maintaining acceptable tolerability remain an important clinical goal. These findings support further investigation of zolucatetide in the planned Phase 3 trial.”

The Phase 1/2 trial is ongoing in patients with desmoid tumors and a range of other tumor types driven by alterations in the Wnt/β-catenin pathway, and follow-up is continuing. Zolucatetide has received Fast Track and Orphan Drug Designations from the FDA for the treatment of desmoid tumors.

These findings provide further clinical validation of the potential of the Company's Helicon™ platform to unlock disease-driving targets historically considered undruggable.

Investor Webcast
Parabilis will host an investor webcast on Saturday, October 24, 2026, at 18:00 CEST (12:00 p.m. EDT) to discuss the updated zolucatetide data that will be presented at ESMO Congress 2026. The webcast will be available on the Investors section of the Parabilis website at https://investors.parabilismed.com. Both the presentation and a replay of the webcast will be available following the event.

About Desmoid Tumors
Desmoid tumors are locally invasive soft-tissue tumors that arise in connective tissues and can be aggressive and recurrent, often causing chronic pain, limited mobility, disfigurement and organ dysfunction. An estimated 30,000 people in the U.S. alone are living with desmoid tumors, including approximately 11,000 who are actively managed, with significant unmet need globally as well. Desmoid tumors typically present in young adults, predominantly females, with many patients requiring prolonged or intermittent treatment. Wnt/β-catenin pathway-activating mutations are the causal driver of desmoid tumors, yet no approved therapies directly target this underlying biology of the disease.

About Zolucatetide
Zolucatetide is an investigational first-in-class and first and only direct inhibitor of the interaction between β-catenin and the T-cell factor (TCF) family of transcription factors, a genetically validated driver of numerous cancers and other serious diseases that has long been considered undruggable. Developed using Parabilis’ Helicon™ peptide platform, zolucatetide is designed to prevent the activation of disease-driving genes by directly targeting β-catenin:TCF, a key downstream node in the Wnt/β-catenin pathway. This approach has the potential to address aberrant Wnt/β-catenin signaling regardless of the upstream APC or β-catenin mutations driving pathway 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.

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, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical fact are forward-looking statements. These include, without limitation, statements regarding: the design, initiation, enrollment and timing of the planned PEDESTAL Phase 3 trial of zolucatetide in desmoid tumors, including expected initiation in the first half of 2027 and topline results anticipated in 2029; our interactions with the U.S. Food and Drug Administration (FDA) regarding the dose and regimen, trial design and primary endpoint for registrational development; the ongoing Phase 1/2 trial of zolucatetide, including continued follow-up of participants; the potential therapeutic benefit, safety, tolerability and differentiation of zolucatetide, and its potential to expand the number of patients who may benefit from treatment; the potential benefits of Fast Track and Orphan Drug Designations; the development of zolucatetide in additional indications, including FAP, ACP, HCC and other Wnt-driven tumors; our strategy, plans and objectives.

Words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are based on management's current expectations and assumptions. They are subject to risks, uncertainties and other important factors that could cause actual results to differ materially from those expressed or implied. These include, among others: the Phase 1/2 data described in this press release are interim, based on a June 22, 2026 data cutoff, and involve a limited number of patients, and may change as patients continue to be followed. Results of earlier clinical trials may not be predictive of results of later trials, including the PEDESTAL trial; FDA feedback on our development plans is not binding, may change and may not be sufficient to support marketing approval; the risk of delays or difficulties in initiating or enrolling clinical trials; the risk of unexpected adverse events or safety findings as more patients are treated for longer periods; Fast Track and Orphan Drug Designations may not lead to faster development, regulatory review or approval.

For a further discussion of these and other risks, see "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement in this press release speaks only as of the date of this press release. Except as required by law, we undertake no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

Disclosure: *Dr. Gounder has financial interests related to Parabilis Medicines.*

Contacts

Media Contact
Jessica Freifeld
media@parabilismed.com

Investor Contact
Tom Kotarakos
investors@parabilismed.com