CLOSER LOOK

MEMORANDUM

Biomea Fusion FY2025 – Phase 2 trial results of icovamenib in T1D expected in 2Q26; two phase 2 trials of icovamenib in T2D initiated; phase 1 GLP-1 RA study enrolling – March 25, 2026

Redwood City, California-based Biomea Fusion reported its full year 2025 results yesterday – see the press release. As background, in January 2025, Biomea repositioned itself as a company focused on diabetes and obesity treatment. It is currently developing icovamenib (an oral menin inhibitor) for T1D and T2D and BMF-650 (an oral GLP-1 RA) for obesity.

Cash, cash equivalents, and restricted cash totaled $56 million at the end of 2025, down 4% from 2024 and providing a projected cash runway into 1Q27. Additionally, the company reported a net loss of $62 million in 2025, down 55% from the $138 million loss reported in 2024. R&D expenses totaled $62 million in 2025, representing a 47% decrease from 2024, attributable to the company's cessation of its oncology programs.

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52-week follow-up data for icovamenib in T2D announced in October 2025

Results from the year-long phase 2 COVALENT-111 trial (n=414) of icovamenib, an oral covalent menin inhibitor promoting beta-cell proliferation and function, in T2D were announced in October 2025.

- **After 12 weeks of daily dosing,** icovamenib demonstrated an average A1c reduction of 1.2% (p=0.01) at Week 52 among participants with severe insulin-deficient T2D (SIDD) – characterized by insulin deficiency and rapid disease progression. Moreover, icovamenib conferred a statistically significant A1c reduction of 1.3% (p=0.05) in participants who were on GLP-1 RAs and were not achieving glycemic targets at baseline (n=11). Glycemic effects were consistent across dosing arms and were sustained through Week 52.
- **These results follow the topline 26-week results announced in December 2024,** in which icovamenib conferred a meaningful A1c reduction of 0.36% in people with T2D.

Two phase 2 studies initiated in 2025, with readouts planned for 4Q26

Following positive COVALENT-111 results, Biomea initiated two phase 2 randomized, double-blind, placebo-controlled studies of icovamenib for T2D in 4Q25:

- **COVALENT-211** for patients with insulin-deficient T2D who are not achieving glycemic targets despite standard of care therapy; and
- **COVALENT-212** for patients with T2D who are not achieving glycemic targets while on a GLP-1 RA therapy.

Both studies, while not yet listed on ClinicalTrials.gov, anticipate topline data on a 26-week primary endpoint in 4Q26.

Follow-up data for icovamenib in T1D expected in 2Q26

52-week results from the phase 2 COVALENT-112 trial (n=37) of icovamenib in T1D are expected in 2Q26 – though the trial is listed as "discontinued" on ClinicalTrials.gov with a notably lower enrollment compared to the previous estimand (n=190). Patients who completed at least 80% of planned dosing will be reviewed for the 52-week follow-up data, per study protocol.

- **COVALENT-112 was designed to test the durability, efficacy, tolerability, and safety of icovamenib** in adults with stage 3 T1D and an A1c between 6.5% and 10% at baseline. In June 2024, the study was placed on a full clinical hold due to hepatotoxicity concerns from COVALENT-111 (for T2D), but was later allowed to resume after a review by the FDA in October 2024. Key efficacy endpoints will include change from baseline in stimulated C-peptide, total daily insulin dose, and change in A1c from baseline. The study will also include a CGM component to characterize any changes in TIR, hypoglycemia, or other glycemic patterns.

Enrollment ongoing for first-in-human phase 1 study of oral, non-peptide GLP-1 RA BMF-650

The first-in-human, phase 1 trial of BMF-650, an oral, non-peptide GLP-1 RA, in people with overweight or obesity who are otherwise healthy (n=80) began in October 2025. As disclosed on ClinicalTrials.gov, the trial will consist of two distinct parts, with Part 1 comprising a single ascending dose study and Part 2 being a multiple ascending dose study that includes a 28-day dosing period for weight-loss assessment. The primary objectives are to assess safety and tolerability over a six-week period in Part 1 and over an 11-week period in Part 2. Biomea also hopes to characterize BMF-650's pharmacokinetics and food effect in fed versus fasted states.

The key early efficacy readout, expected in 2Q26, will be 28-day weight-reduction at the highest MAD dose. Biomea dosed its first patient in October 2025.

In preclinical studies (n=15), BMF-650 conferred 12% and 15% weight loss in primates with obesity after 28 days of treatment with the 10 mg/kg and 30 mg/kg doses, respectively. Additionally, BMF-650 demonstrated significant glucose-lowering and appetite suppression effects, resulting in dose-dependent reductions in daily food intake.

Close Concerns' Questions

1. How many patients does Biomea plan to enroll in COVALENT-211 and COVALENT-212?
2. How will Biomea position its non-peptide GLP-1 RA in a highly competitive anti-obesity medication market?
3. Why was the COVALENT-112 trial listed as discontinued?

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