Biomea Fusion Announces Positive Topline Results from Ongoing Phase II COVALENT-111 Study in Patients with Type 2 Diabetes

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- *Icovamenib met the primary endpoint, displaying a meaningful statistically significant placebo-corrected mean reduction in HbA1c in the prespecified per protocol patient population*
- *Best response achieved in target, beta-cell deficient patients on one or more antidiabetic agents at baseline, showing a placebo-adjusted mean reduction of 1.47% in HbA1c at Week 26 with statistical significance, after only 12 weeks of dosing icovamenib with 100 mg*
- *Icovamenib was well-tolerated, with no adverse-event related discontinuations, no hypoglycemic events and no serious adverse events*

REDWOOD CITY, Calif., Dec. 17, 2024 (GLOBE NEWSWIRE) -- Biomea Fusion, Inc. (“Biomea” or “Biomea Fusion” or “the Company”) (Nasdaq: BMEA), a clinical-stage biopharmaceutical company dedicated to discovering and developing oral covalent small molecules to improve the lives of patients with diabetes, obesity, and genetically defined cancers, today announced positive topline results from the ongoing COVALENT-111 study, evaluating the efficacy, safety and tolerability of icovamenib in patients with type 2 diabetes (T2D).

COVALENT-111 is a double-blinded, randomized, 3:1 placebo-controlled trial that has enrolled adult patients diagnosed with T2D within the last 7 years, who had HbA1c levels between 7.0% and 10.5%, and a body mass index (BMI) between 25 and 40 kg/m². At baseline, all participants were receiving treatment with diet and exercise and were uncontrolled with up to three antidiabetic medications. Icovamenib was investigated in three different dosing arms with a primary follow up after 26 weeks which we are reporting on today: Arm A at 100mg QD (once daily) for 8 weeks, Arm B at 100mg QD for 12 weeks, and Arm C at 100 mg QD for 8 weeks and 100mg BID (twice daily) for 4 weeks. The study enrolled a total of 225 patients that received at least one dose of icovamenib and were considered evaluable for the modified intent-to-treat population (mITT). Dosing was interrupted for many patients due to an interim clinical hold imposed by the U.S. Food and Drug Administration (FDA). This topline efficacy analysis focuses on those patients who had completed at least 80% of their dosing prior to the clinical hold and who at baseline were treated with one or more anti-hyperglycemic therapy, the Per Protocol Patient population (n=168).

The study showed positive topline results at Week 26, demonstrating statistically significant and clinically meaningful reductions in HbA1c, the gold standard for assessing glycemic control in T2D. In patients who completed dosing per protocol and were suboptimally controlled at baseline on one or more prior agent, icovamenib showed meaningful reductions in HbA1c with statistical significance in all major categories. Here icovamenib showed a mean reduction in HbA1c of 0.36% (p=0.022). The strongest performing arm was Arm B (icovamenib dosed at 100mg QD for 12 weeks) with a mean HbA1c reduction of 0.5% (p=0.012). In the analysis of the T2D phenotypes, icovamenib showed further improved reduction in the insulin deficient patients. Within the mild age-related diabetes (MARD) and severe insulin-deficient diabetes (SIDD) patients the mean HbA1c reduction was 0.73% (p=0.009) and in Arm B these patient subtypes reduced the mean HbA1c by 1.05% (p=0.004). Patients who were considered most severe insulin deficient, the SIDDs, demonstrated the best response with a mean HbA1c reduction in Arm B of 1.47% (p=0.022). Importantly, MARD and SIDD represent more than 50% of the US patient population. Of note, in the patients that failed on a GLP-1 based therapy an HbA1c reduction of 0.84% was demonstrated.

Throughout the 26-week period there were no serious adverse events or discontinuations due to adverse events observed. No drug-to-drug interactions were observed during the study. Overall, icovamenib was well tolerated and demonstrated a favorable safety profile in the COVALENT-111 study.

The company used clinical biomarker data to categorize participants into prespecified subtypes (SIDD, MARD, SIRD, and MOD) during screening:

- **SIDD**: Characterized by low insulin secretion, high HbA1c, and reduced beta-cell function (low HOMA-B)
- **MARD**: Characterized by mild age-related diabetes, typically older age at onset, with mild hyperglycemia and fewer metabolic disturbances
- **SIRD**: Defined by significant insulin resistance, high HOMA-IR, and potential complications like liver disease
- **MOD**: Identified by mild obesity, less severe insulin resistance, and relatively mild hyperglycemia

The study will further assess secondary endpoints (e.g., HbA1c reduction, fasting glucose, HOMA-B and HOMA-IR) within each pre-specified subtype to identify distinct patterns of response. Analysis of the full Phase II COVALENT-111 data is ongoing and Biomea Fusion plans to present detailed results at an upcoming medical conference in 2025.

"I am very excited about these initial results we are presenting today. We believe we now have a defined path to further develop icovamenib in diabetes. We have identified the optimal dose, the patient population to target, and most importantly, we now have strong efficacy and safety data," says Thomas Butler, CEO and Chair of Biomea Fusion. "These results validate our approach and highlight that icovamenib has the potential to address an aspect of diabetes that no other current therapy can. We are excited to continue advancing this promising molecule and bring a new

treatment option to patients who need it most."

Based on these initial results and the upcoming 52-week readout in the second half 2025, Biomea plans to engage with the FDA to discuss the data. This meeting will provide an opportunity to align with FDA on how to further advance icovamenib as a first-in-class menin inhibitor therapy for T2D.

"The topline data from the COVALENT-111 Phase II study are incredibly promising, showing that icovamenib delivers significant and clinically meaningful reductions in HbA1c. We now understand the duration of dosing and target patient population. This study confirms the potential of menin inhibition as a novel mechanism for treating type 2 diabetes. Achieving a HbA1c reduction of this magnitude without chronic treatment is paradigm shifting in diabetes therapy," said Dr. Juan Pablo Frias, Chief Medical Officer of Biomea Fusion.

Conference Call and Webcast Details
Webcast of Biomea's investor update on Tuesday, December 17, 2024, at 8:00 am EST will be available to registered attendees under the Investors and Media section of the company's website at https://investors.biomeafusion.com/news-events/events. A replay of the presentation will be archived on Biomea's site following the event.

The clinical hold which was placed on icovamenib was due to data FDA had observed during the Escalation Phase, when higher dosages of icovamenib were tested. The clinical hold led to a disruption for patients enrolled in the COVALENT-111 study. It had a more profound impact on the ongoing Phase II COVALENT -112 study in type 1 diabetes, where over 90% of the targeted patient population were not able to complete dosing due to the clinical hold. We are therefore planning to continue the enrollment in COVALENT-112 so we can provide a more complete update in this patient population in 2025.

About Icovamenib
Icovamenib is an investigational, orally bioavailable, potent, and selective covalent inhibitor of menin. The molecule was built using Biomea Fusion's FUSION™ System and is designed to regenerate insulin-producing beta cells with the aim to cure diabetes. Icovamenib's proposed mechanism of action in diabetes is to enable the proliferation, preservation, and reactivation of a patient's own healthy, functional, insulin-producing beta cells. As the potentially first disease-modifying therapy for T1D and T2D, icovamenib could become an important addition and complement to the diabetes treatment landscape once it has successfully completed its ongoing clinical studies.

About Menin's Role in Diabetes
Loss of functional beta cell mass is a core component of the natural history in both types of diabetes — type 1 diabetes (mediated by autoimmune dysfunction) and T2D (mediated by metabolic dysfunction). Beta cells are found in the pancreas and are responsible for the synthesis and secretion of insulin. Insulin is a hormone that helps the body use glucose for energy and helps control blood glucose levels. In patients with diabetes, beta cell mass and function have been observed to be diminished, leading to insufficient insulin secretion and hyperglycemia. Menin is thought to act as a brake on beta cell turnover and growth, supporting the notion that inhibition of menin could lead to the regeneration of normal, healthy beta cells. Based on these and other scientific findings, Biomea is exploring the potential for icovamenib-mediated menin inhibition as a viable therapeutic approach to potentially halt or reverse progression of T2D.

About Type 2 Diabetes
Diabetes is considered a chronic health condition that affects how the body turns food into energy and results in excessive glucose in the bloodstream. Over time, this can cause serious health problems and damage vital organs. Most people with diabetes have a shorter life expectancy than people without this disease. The Centers for Disease Control and Prevention estimates about two in five adults in the United States are now expected to develop diabetes during their lifetime. More than 37 million people of all ages (about 11% of the US population) have diabetes today. 96 million adults (more than one in three) have pre-diabetes, blood glucose levels that are higher than normal but not high enough to be classified as diabetes. Diabetes is also one of the largest economic burdens on the United States health care system with one dollar out of every four dollars in US health care costs spent on caring for people with diabetes. Despite the current availability of many diabetes medications, there remains a significant need in the treatment and care of patients with diabetes.

About Biomea Fusion
Biomea Fusion is a clinical-stage biopharmaceutical company focused on the discovery and development of oral covalent small molecules to improve the lives of patients with diabetes, obesity, and genetically defined cancers. A covalent small molecule is a synthetic compound that forms a permanent bond to its target protein and offers a number of potential advantages over conventional non-covalent drugs, including greater target selectivity, lower drug exposure, and the ability to drive a deeper, more durable response.

We are utilizing our proprietary FUSION™ System to discover, design and develop a pipeline of next-generation covalent-binding small-molecule medicines designed to maximize clinical benefit for patients. We aim to have an outsized impact on the treatment of disease for the patients we serve. We aim to cure.

Visit us at biomeafusion.com and follow us on LinkedIn, X, and Facebook.

Forward-Looking Statements
Statements we make in this press release may include statements which are not historical facts and are considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact, including statements regarding the clinical and therapeutic potential of our product candidates and development programs, their mechanism of action, and their potential relative to approved products marketed by third parties; the potential benefits to future trial design and program development of subtyping diabetes patients; our research, development and regulatory plans, the progress of our ongoing and upcoming clinical trials and the timing of such events may be deemed to be forward-looking statements. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. Any forward-looking statements in this press release are based on our current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, including the risk that preliminary or interim results of preclinical studies or clinical trials may not be predictive of future or final results in connection with future clinical trials that our analysis of

preliminary or interim data in subsets of patients may not be predictive of our product candidate in a broader patient population, and the risk that we may encounter delays in preclinical or clinical development, patient enrollment and in the initiation, conduct and completion of our ongoing and planned clinical trials and other research and development activities. These risks concerning Biomea Fusion's business and operations are described in additional detail in its periodic filings with the U.S. Securities and Exchange Commission (SEC), including its most recent periodic report filed with the SEC and subsequent filings thereafter. Biomea Fusion explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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