Icovamenib Treatment in Patients with Severe Insulin-Deficient Diabetes Led to a Significant Improvement in Pancreatic Beta-cell Function with a 53% Mean Increase in C-peptide Levels 3 Months After Last Dose

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- *Therapeutic effects were sustained off treatment, with persistent reduction in HbA1c and improvement in beta-cell function 3 months after last dose, suggesting disease-modifying potential of icovamenib*
- *Strong correlation between C-peptide increase and HbA1c reduction (r = -0.73, p<0.0001) across all dosing groups (n=23) support the proposed mechanism of beta cell restoration*
- *Best response observed in prespecified, beta-cell deficient patients on one or more antihyperglycemic agents at baseline, achieving a statistically significant placebo-adjusted mean reduction in HbA1c of 1.47% at Week 26 (p=0.022), after only 12 weeks of 100 mg once daily icovamenib*
- *Preclinical in vivo experiments indicated that icovamenib enhanced the responsiveness of human islets to GLP-1-based medicines, consistent with the increase in expression levels (transcript and protein) of both the GLP-1 receptor and intracellular insulin*
- *Severe Insulin Deficient Diabetes represents an underserved patient population within type 2 diabetes and is estimated to be over 100 million people worldwide.*

REDWOOD CITY, Calif., March 24, 2025 (GLOBE NEWSWIRE) -- Biomea Fusion, Inc. ("Biomea") (Nasdaq: BMEA), a clinical-stage diabetes and obesity medicines company, today announced the presentation of preclinical and clinical data from studies assessing icovamenib at the *Advanced Technologies & Treatments for Diabetes (ATTD) 2025 Conference* in Amsterdam, The Netherlands. The new findings support icovamenib's potential as a first-in-class, disease-modifying therapy by targeting beta-cell restoration, enhancing insulin secretion, and sustaining glycemic improvements beyond icovamenib's treatment period.

"At ATTD, we presented data on icovamenib's ability to drive a significant increase in C-peptide production in patients who need it most, demonstrating a durable effect that lasted well beyond the treatment period. This is an exciting moment for icovamenib, but most importantly an exciting moment for patients who are in need of an alternative mechanism of action for their diabetes. This data validates the topline analysis reported last December, highlighting the impactful responses seen in those with poor beta cell function at baseline. With icovamenib, we look to increase the fundamental capability of our patients, enabling them to produce more insulin on their own and take back control of their diabetes. We look forward to providing further updates with this study as we continue to uncover the broad potential of icovamenib in type 2 diabetes," said Thomas Butler, Chief Executive Officer and Chairman of Biomea Fusion.

Icovamenib, an investigational, covalent menin inhibitor, is being evaluated for its ability to restore pancreatic beta-cell mass and function, which are key drivers of disease progression in insulin-deficient diabetes. The presentations provided comprehensive insights into icovamenib's mechanism of action, long-term clinical activity, biomarker responses, safety profile, and potential as a combination therapy with GLP-1-based medicines.

"These findings reinforce the potential role of icovamenib in improving beta-cell function even after treatment cessation. The significant increase in C-peptide levels observed in icovamenib-treated patients more than 3 months after stopping therapy supports the proposed mechanism of action, the restoration of beta cell mass and function," said Juan Pablo Frías, MD, Chief Medical Officer of Biomea Fusion. "Additionally, we have observed benefits consistent with a potential synergy between icovamenib and GLP-1-based medicines, highlighting icovamenib's potential to complement existing and broadly used therapies. We are eager to continue advancing this novel approach and are working towards bringing a first-in-class, potentially disease-modifying therapy to patients. The ability to restore beta-cell function, thereby improving insulin production and secretion, could be a game-changer for patients with severe insulin deficiency, a population that has long been underserved by current treatment options."

ATTD 2025 Conference Highlights:

- **First Large-Scale Analysis of C-Peptide Response:** The data represents the first large-scale assessment of C-peptide levels in icovamenib-treated patients, providing robust evidence supporting its proposed mechanism of action. C-peptide, a key biomarker of endogenous insulin production, demonstrated significant increases, indicating improved pancreatic

beta-cell function over 3 months after the final dose of icovamenib.

- **OGTT-Based Beta-Cell Function Assessment:** An oral glucose tolerance test (OGTT) was conducted at baseline and six timepoints over 26 weeks, providing a detailed evaluation of beta-cell insulin secretory capacity. This test is considered a robust and well-validated method of assessing beta cell insulin secretory capacity via assessment of the C-peptide index, the ratio of plasma C-peptide per unit of glucose. This offers critical insights into icovamenib's impact on pancreatic beta-cell function.
- **C-Peptide Increases in Insulin-Deficient Subgroups:** Patients with insulin deficient diabetes (n=45) experienced a mean increase in C-peptide index levels. In particular the severe insulin-deficient diabetes patients who received icovamenib (n=23) experienced the largest mean increase in C-peptide index levels by Week 26 (53% mean increase from baseline).
- **Long-Term Beta-Cell Restoration Potential:** Insulin deficient patients who received icovamenib (n=45) demonstrated a persistent increase in C-peptide levels beyond the active treatment period, over 3 months after the final dose of icovamenib, suggesting a durable effect on insulin secretion and reinforcing our belief in icovamenib's potential to drive long-term improvements in beta-cell function.
- **Strong Correlation between C-peptide and HbA1c:** An analysis of the severe insulin-deficient diabetes subgroup of participants (n=23) who were uncontrolled on at least one prior antihyperglycemic therapy revealed a strong correlation between changes in C-peptide index and HbA1c at Week 26 (r=-0.73). The strong correlation between the improvement in HbA1c and the increase in C-peptide index, 14 weeks after cessation of icovamenib therapy, supports the proposed mechanism of action of icovamenib, a durable improvement in beta-cell function. These data suggests that icovamenib fundamentally impacted the disease, potentially restoring the patient's ability to produce more insulin, after a short treatment period.
- **Precision Medicine Potential:** Analysis across different diabetes subtypes demonstrated that icovamenib preferentially increased insulin secretion in insulin-deficient patients, highlighting its potential as a targeted therapy for individuals with severe insulin deficiency, a population with limited treatment options and the highest risk profile.
- **Enhanced Impact of GLP-1 based Therapeutic Agents with Icovamenib Combination:** Icovamenib enhanced responsiveness of human islets to the GLP-1-based medicines, semaglutide and tirzepatide. Enhancement in beta-cell function was correlated with an increase in the expression levels of the GLP-1 receptor as well as intracellular insulin – both transcript and protein levels were increased. These effects induced by icovamenib may allow lower doses of GLP-1-based medicines to achieve glycemic targets, potentially improving tolerability of these agents.

ATTD 2025 Presentations:
All abstracts will be published in the peer-reviewed Journal of Diabetes Technology & Therapeutics. All presentations and the symposium slides are also available on Biomea Fusion's Investor Relations Page under the Events section https://investors.biomeafusion.com/news-events.

Global Experts across the Diabetes Field have also Recognized the Significance of these Findings:
"Icovamenib's recent data has shown an impressive restoration of beta cell function as demonstrated by significant elevations in C-peptide even after the treatment period ended. This data validates the proposed mechanism of action of this menin inhibitor as a disease modifying agent and helps address the poor adherence and persistence commonly seen in type 2 diabetes."
Steve Edelman, M.D., Endocrinologist, Professor of Medicine UCSD / VA San Diego.

"We do not have an agent today that addresses one of the root causes of diabetes – beta cell dysfunction – icovamenib, if approved, would be the first. Patients in the COVALENT-111 trial have achieved lasting benefits without continuous chronic dosing, suggesting that icovamenib may be disease-modifying. I am very impressed."
Alice Cheng, M.D., Endocrinologist, Associate Professor of Medicine, University of Toronto.

"The C-peptide data which was presented during ATTD is a meaningful update, as we now have insight into why insulin-deficient patients may respond better to icovamenib treatment. The potential to restore endogenous insulin production capacity is an exciting development in the treatment of type 2 diabetes."
Jeremy Pettus, M.D., Endocrinologist, Professor of Medicine UCSD.

"Icovamenib is a very interesting molecule that acts quite differently than anything I have seen before. We are observing glucose controlled and beta cell-specific proliferation and an increase in stimulated C-peptide secretion leading to patient benefits that continued after the icovamenib dosage ended. I am very excited to further explore the many opportunities that icovamenib driven inhibition of menin will provide to patients."
Rohit N. Kulkarni, M.D., Ph.D., Professor of Medicine at Harvard Medical School.

"Great foray into precision medicine. We need to be addressing patients in a much more individualized manner. By addressing insulin-deficient diabetes patients with icovamenib, we have seen post treatment that the beta cell pool is being restored and producing a higher level of insulin, as measured by C-peptide. This indicates a fundamental and potentially lasting impact on the disease and validates the mechanism of action of menin inhibition."
Melanie Davies, M.D., Diabetologist, Professor of Diabetes Medicine at the University of Leicester

"The icovamenib data looks exciting. After 26 weeks there have been statistically significant and clinically relevant reductions in HbA1c and excellent tolerability in a prespecified insulin-deficient type 2 diabetes cohort. The data presented today help to confirm icovamenib's mechanism of action. A robust increase in insulin secretion, as measured by C-peptide, was demonstrated 3 months after the icovamenib dosing period and this improvement appears to be continuing. We have not previously seen data like this with any antihyperglycemic agent. As more trials are conducted, I believe that inhibition of menin may lead to benefits across all subtypes of diabetes. I applaud Biomea for developing a potential new treatment option that may be disease modifying for patients with diabetes."
Ralph DeFronzo, MD, Endocrinologist, Professor of Medicine and Chief of the Diabetes Division at UT Health Science Center, San Antonio

About Menin's Role in Diabetes
Loss of functional beta-cell mass and function is a core component of the natural history in both types of diabetes – type 1 diabetes ("T1D") (mediated by autoimmune dysfunction) and type 2 diabetes ("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-ell 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 United States 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 United States 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 Icovamenib
Icovamenib is an investigational, orally bioavailable, potent, and selective covalent inhibitor of menin. The molecule was built using Biomea'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 and received regulatory approval.

About Biomea Fusion
Biomea is a clinical-stage diabetes and obesity medicines company focused on the discovery and development of oral covalent small molecules to improve the lives of patients with diabetes, obesity, and metabolic disease. 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, including BMF-219, the potential of BMF-219 as a treatment for T1D and T2D, our research, development and regulatory plans, the progress of our ongoing and planned clinical trials, including COVALENT-111, the availability of data from our 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.

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