Late-Breaker Oral Presentation Showing New Analysis from the Escalation Portion of COVALENT-111 Presented at the 1st Annual Asian Conference on Innovative Therapies for Diabetes Management (ATTD-ASIA 2024)

November 18, 2024

Icovamenib Achieves a Mean Reduction in HbA1c Greater than 1% at Week 26 Following 4 Weeks of Dosing in Type 2 Diabetes Patients Characterized by Insulin Deficiency

- 32 patients from the 100mg and 200mg cohorts, doses selected for the expansion phase, were characterized based on baseline biomarkers and analyzed for efficacy. Patients identified as insulin deficient (approx. 50% of the broader patient population) and insulin resistant were compared to examine the mean reduction in HbA1c at Week 26, following 4 weeks of dosing.
- 83% of patients with insulin deficiency responded to icovamenib, and showed a greater mean HbA1c reduction at Week 26 compared to baseline, than those that were found to be more insulin resistant (-1.23% vs -0.48%, placebo-adjusted, 22 weeks after last dose of icovamenib).
- These two patient groups are pre-specified in the upcoming read out of the Phase IIb expansion portion of COVALENT-111 in December, reporting over 200 persons with type 2 diabetes (T2D) with 8 and 12 weeks of icovamenib treatment.

REDWOOD CITY, Calif., Nov. 18, 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 its presentations at the 1st Annual Asian Conference on Innovative Therapies for Diabetes Management (ATTD-ASIA 2024) taking place in Singapore, 18-20 November 2024.

Biomea will showcase the following three oral presentations and participate in one industry symposium:

- Trial in Progress COVALENT-111: A Phase 2 Trial of the Oral Menin Inhibitor Icovamenib (BMF-219) in Patients with Type 2 Diabetes
  Oral Presentation: November 19 at 12:45 – 12:50 SGT
- Late-Breaker: Assessment of Icovamenib (BMF-219) in Persons with Poorly Controlled Severe Insulin-Deficient (SIDD) Type 2 Diabetes (T2D): COVALENT-111 Case Studies
  Oral Presentation: November 19 at 12:50 – 12:55 SGT
- Unlocking the Potential of Menin Inhibition: Icovamenib and a Look into the Future of Diabetes Management
  Industry Symposium: November 19 at 17:10 – 18:10 SGT
- Trial in Progress COVALENT-112: A Phase 2 Trial of the Oral Menin Inhibitor Icovamenib (BMF-219) in Type 1 Diabetes
  Oral Presentation: November 20 at 11:25 - 11:35 SGT

All presentations will be available for viewing through the conference virtual platform; they will also be available on Biomea’s website under: https://investors.biomeafusion.com/news-events/events.

Data Highlights for Presentations at ATTD-Asia 2024
T2D is characterized by a progressive decline in beta-cell function while type 1 diabetes (T1D) is characterized by autoimmune destruction of beta cells leading to hyperglycemia. Preclinical data suggests investigational icovamenib may induce beta-cell proliferation and improve insulin secretion. In the multiple ascending dose portion of the Phase II COVALENT-111 trial, many T2D participants achieved clinically significant improvements in glycemic control up to 22 weeks after only 4 weeks of daily icovamenib. At ATTD-Asia the company will report the Phase II expansion design of COVALENT-111 (NCT05731544) evaluating icovamenib in adults with T2D and the Phase II design of COVALENT-112 (NCT06152042) evaluating icovamenib's efficacy and safety in adults with T1D.

T2D is a heterogenous disease, characterized by varying degrees of insulin resistance and insulin deficiency. Covalently inhibiting menin is a new proposed mechanism of action particularly relevant for diabetes patients with a depleted pool of beta cells. The severe insulin-deficient diabetes (SIDD) and mild age-related diabetes (MARD) subgroups, two of five identified by Ahlqvist et al., encompass approximately 50%-70% of patients with T2D[1], depending on the population, and are distinguished by significant insulin deficiency.

The company will present a review of insulin-deficient versus insulin-resistant patients based on T2D participants in the escalation portion of COVALENT-111, representative of exposure expected in the expansion portion. Here, after only 4 weeks of dosing and with a follow up 22 weeks after the last dose, the insulin-deficient diabetes patients (SIDD and MARD subgroups), showed a mean 1.23% placebo adjusted decline in HbA1c while the patients characterized by insulin resistance (severe insulin-resistant diabetes and mild obesity-related diabetes subgroups) demonstrated a mean 0.48% placebo adjusted decline. Subtyping diabetes patients may help identify specific subgroups for improved targeted treatment approaches in the future.

Two case studies from the escalation portion of COVALENT-111 are also being presented to highlight the potential of icovamenib in patients with poorly controlled insulin-deficient T2D. One of the patients, a 29-year-old man with a four-year history of T2D, experienced a 2.5% reduction in HbA1c (from 9.5% at baseline to 7.0%) at Week 26, dropping an additional 1.2% at Week 47 (down to 5.8%) leading to the discontinuation of metformin. Both HOMA-B (+190.0%) and C-peptide (+71.0%) increased significantly during the 26-week study period. The other insulin deficient patient, a 45-year-old man with a 10-year history of T2D, had a 1.1% reduction in HbA1c from baseline (8.6% to 7.5%) at Week 26 with increases in HOMA B (+1233.0%) and C-peptide (+59.0%). In both cases icovamenib was generally well tolerated, there were no adverse events, no dose discontinuations or modifications reported, and no symptomatic or clinically significant hypoglycemia was observed.

In addition, the company is hosting an industry symposium entitled “Unlocking the Potential of Menin Inhibition: Icovamenib and a Look into the Future of Diabetes Management,” chaired by Professor Juliana Chan and Dr. Juan Pablo Frías, to discuss beta-cell biology and introduce the novel therapeutic approach for diabetes through menin inhibition. Key topics discussed include the fundamentals of beta-cell biology and its critical role in glucose homeostasis; the pivotal role of menin in pancreatic beta-cell function and diabetes pathogenesis, and an overview of the COVALENT-111 (T2D) and COVALENT-112 (T1D) clinical studies. A focal point of the symposium will be an in-depth presentation on T2D subgroups, highlighting their distinct characteristics and phenotypes to enhance the understanding of T2D heterogeneity and its implications for personalized treatment strategies.

Upcoming COVALENT-111 Study Read-Out
The Phase IIb expansion portion of COVALENT-111 is designed to further explore icovamenib’s potential for long-term glycemic control, dosing patients for up to 12 weeks at various dosing levels with follow-up at Week 26 and 52. The study aims to identify the optimal dose for late-stage development and define biomarkers for patients who respond best to icovamenib alone. Key inclusion criteria are persons with T2D with a HbA1c greater than 7.0%, a BMI of 25 to 40, who have had diabetes onset within the last seven years and were failing their current treatments, which could include up to three anti-diabetic medications, including GLP-1 based therapies. We believe the study is designed to help understand the impact of dosing the broader patient population and determine icovamenib’s potential impact on insulin-deficient and insulin-resistant patients. The goal is to select the optimal dose, dose duration, and patient set to advance to late-stage clinical development. Inhibiting menin in patients with diabetes is a novel and investigative treatment modality, and the study will help define a study population to discuss with the Food and Drug Administration during a potential end of Phase II meeting in 2025.

"We’re pleased to present our case studies at ATTD-Asia and show the overall benefit we believe icovamenib may provide, particularly to insulin-deficient patients with T2D. We expect the upcoming topline results in December will provide critical insights into how icovamenib affects both insulin-deficient and insulin-resistant patients and help us identify the biomarkers for optimal patient selection. I am very excited about icovamenib’s potential and look forward to reporting our study results," stated Juan Pablo Frias, MD, Biomea Fusion’s Chief Medical Officer.

About COVALENT-111
COVALENT-111 is a multi-site, randomized, double-blind, placebo-controlled Phase I/II study. In the completed Phase I portion of the trial, healthy patients were enrolled in single ascending dose cohorts to evaluate safety at the prospective dosing levels for T2D patients. Phase II consists of multiple ascending dose cohorts and includes adult patients with T2D uncontrolled by standard of care medicines. Once the escalation portion of COVALENT-111 was completed, the study advanced into an expansion portion consisting of multiple cohorts dosing T2D patients up to 12 weeks with either icovamenib or placebo, followed by a 40-week off treatment period. To date, approximately 200 patients completed their respective dosing. Additional information about this Phase I/II clinical trial of icovamenib in T2D can be found at ClinicalTrials.gov using the identifier NCT05731544.

About COVALENT-112
COVALENT-112 is a multi-site, randomized, double-blind, placebo-controlled Phase II study in adults with stage three T1D. This stage describes the period following clinical diagnosis of T1D when symptoms are present due to significant beta cell loss. COVALENT-112 includes an open-label portion for adults with T1D up to 15 years since diagnosis. The open-label portion (n=40) examines the efficacy, safety, and durability of icovamenib at two oral dose levels, 100 mg and 200 mg over a 12-week treatment period followed by a 40-week off treatment period. To date, approximately 20 patients completed 8 weeks of dosing in the open label portion. Additional information about the Phase II clinical trial of icovamenib in T1D can be found at ClinicalTrials.gov using the identifier NCT06152042.

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, 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; the anticipated availability of data from our clinical trials, anticipated milestones, 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 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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References:

[1]Ahlqvist E, et al. Lancet Diabetes Endocrinol. 2018;6:361-369