Biomea Fusion Presents Novel Preclinical Data at ADA 2022 Suggesting BMF-219's Potential as an Oral, Long-Acting Treatment for Type 2 Diabetes

June 4, 2022

- Menin acts as a 'brake' on beta cell regeneration; inhibiting menin function with BMF-219 may increase beta cell production and function, thereby increasing insulin levels and controlling high glucose levels
- BMF-219, a covalent menin inhibitor, showed strong, prolonged glycemic control, insulin sensitization, and hemoglobin A1C (HbA1c) reduction in the streptozotocin (STZ) beta-cell ablation and zucker diabetic fatty (ZDF) rat models while on drug and after washout, outperforming an agent used as standard of care
- Biomea plans to initiate a Phase I/II clinical trial of BMF-219 in type 2 diabetes in the second half of 2022, subject to investigational new drug (IND) submission and clearance
- Company to host virtual investor R&D event on Monday, June 6, 2022 at 4:05 PM EDT featuring BMF-219's potential to treat type 2 diabetes, including an overview of the data presented at American Diabetes Association (ADA) Scientific Sessions

REDWOOD CITY, Calif., June 04, 2022 (GLOBE NEWSWIRE) -- Biomea Fusion, Inc. (Nasdaq: BMEA), a clinical-stage biopharmaceutical company dedicated to discovering and developing novel covalent small molecules to treat and improve the lives of patients with genetically defined cancers and metabolic diseases, presented new data at the American Diabetes Association (ADA) Scientific Sessions demonstrating BMF-219's strong, prolonged glycemic control, insulin sensitization, and HbA1c reduction in two preclinical rat models of diabetes. These data suggest BMF-219's potential as an oral, long-acting treatment for type 2 diabetes. The preclinical presentations can be viewed on Biomea's website at https://biomeafusion.com/publications.

"Diabetes is a multi-factorial disease that typically requires daily treatment with multiple agents with various mechanisms of action in order to achieve glycemic control. The preclinical data that we have generated with BMF-219 appears nothing short of groundbreaking as we normalize glucose levels in ZDF rats, which have about four-fold their regular body size, and show in these animals a reduction in HbA1C of 3.5%, which was maintained after a scheduled follow up visit 15 pays post last dose," said Thomas Butler, Biomea's Chief Executive Officer and Chairman of the Board. "In addition, we were able to show in the STZ rat model, a model that displays a significant reduction in beta cell mass and where traditionally insulin has been the only effective single agent treatment, that BMF-219 showed remarkable glycemic control after 14 days of treatment. A therapy that has the ability to generate glucose responsive beta cells would be a major breakthrough for diabetes patients. We are excited about these results and look forward to submitting our IND in the second half of this year while continuing to explore the broad potential of menin in diabetes."

BMF-219 was tested preclinically in two separate ZDF rat models against pioglitazone (a thiazolidinedione) and liraglutide (a Glucagon like Peptide-1 agonist) and also against pioglitazone in a STZ rat model.

Notably, BMF-219 was superior to pioglitazone in an oral glucose tolerance test (OGTT), an assessment of glucose metabolism and processing, in the STZ beta cell ablation model during the treatment period. In this model, BMF-219 but not active comparator, pioglitazone, restored non-fasting glucose levels to near normal baseline by treatment day eight and significantly reduced blood glucose levels vs. vehicle and pioglitazone during an oral glucose tolerance test (OGTT) in STZ rats (mean AUC reduction of 41%, $p<0.05$) at day 17, suggesting that BMF-219 rapidly induced pancreatic beta cell regrowth and function.

BMF-219 also achieved glycemic control via similar assessments in both ZDF models at all timepoints, including superior glycemic control compared to pioglitazone after the washout period. In the ZDF model, BMF-219 and pioglitazone showed similar glycemic control during an OGTT while drug was present (AUC reduction of 54%, $p<0.001$) but only BMF-219 treated rats saw weight loss while on drug and maintained glycemic control two weeks after washout (AUC reduction of 40%, $p<0.05$), indicating prolonged glycemic control. A four-week BMF-219 treatment in ZDF rats resulted also in a significant reduction in HbA1C at Day 21, which reached 3.5% absolute reduction versus vehicle, compared to liraglutide (1.7% at Day 29), and remained reduced throughout the entire study, including post-treatment. At all BMF-219 doses, this significant reduction in HbA1C in ZDF rats was maintained during the 15-day washout period after the last dose. In addition to OGTT, blood glucose, insulin, C-peptide, HbA1c lipemic levels, and weight were also assessed. Collectively these data demonstrate the novel long-acting potential of BMF-219 as a single agent, oral treatment for type 2 diabetes.

Upcoming Webcast

A live webcast of Biomea's virtual investor R&D event on June 6th at 4:05 pm ET featuring the BMF-219 program in diabetes 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 for 14 days following the event.

Callers are encouraged to utilize the free webcast at https://investors.biomeafusion.com/news-events/events. Those who plan on participating in the Q&A or do not have internet available may access the call by dialing (844) 717-9653 (U.S. domestic) or +1 (213) 320-2545 (international).

Poster Presentation Details:

Oral Menin Inhibitor, BMF-219, Displays a Significant and Durable Reduction in HbA1c in a Type 2 Diabetes Mellitus Rat Model

Full Text:
Menin is an epigenetic regulatory protein that plays a key role in beta-cell proliferation and function, as previously demonstrated though increased beta-cell mass generation in Men1 knockout mice (Ja et al., 2021;13(5):e13524). Here, we demonstrate the marked potential of an oral menin inhibitor, BMF-219, in durable glycemic control following a short course treatment in a Type 2 Diabetes Mellitus (T2DM) Zucker Diabetic Fatty Rat model. Rats were treated daily with BMF-219, liraglutide or vehicle for 28 days and monitored for an additional 28 days post-treatment. All animals tolerated BMF-219 well throughout the study. Notably, BMF-219 treatment resulted in a significant reduction in HbA1C at Day 21, which reached 3.5% absolute reduction in HbA1C versus vehicle, compared to liraglutide (1.7% reduction) at Day 29 and remained reduced throughout the entire study, including post-treatment. The high-dose arm of BMF-219 showed a strong reduction in 4-hour fasting blood glucose during the treatment up to Day 29. Both BMF-219 dose groups showed improved glycemic control by oral glucose tolerance test (OGTT) on day 25, in contrast to vehicle and liraglutide-treated animals. Additionally, insulin levels, HOMA-IR, HOMA-B, OGTT, HbA1C, and C-peptide levels measured at Day 57 across all groups will be reported. Collectively, these data demonstrate the novel long-acting potential of BMF-219 as an oral treatment for T2DM, in maintaining glycemic control after short-term dosing.

Oral Long-Acting Menin Inhibitor Normalizes Type 2 Diabetes Mellitus (T2DM) in Two Rat Models

Full Text:
Menin is a scaffold protein that has been recognized for its role in T2DM as a key regulator of β-cell proliferation. Menin inhibition has previously been shown to improve glycemic control in diabetic mice. Herein, we report the first evidence that BMF-219, an orally bioavailable, selective, irreversible menin inhibitor, restores glycemic control in Zucker Diabetic Fatty (ZDF) Rat and Streptozotocin-induced Rat (STZ) models of T2DM. Rats were treated daily with BMF-219, vehicle, or pioglitazone for 16 days. BMF-219 was well tolerated throughout the conduct of the study. BMF-219 treatment resulted in a significant 50% reduction in fasting and non-fasting blood glucose levels, reduced serum insulin and c-peptide levels ($p<0.05$), and reduced HOMA-IR ($p<0.001$) after two weeks of treatment in ZDF rats. BMF-219 decreased glucose levels at all timepoints during an oral glucose tolerance test at Day 15 (AUC reduction of 54%, $p<0.001$) and at Day 29 (AUC reduction of 40%, $p<0.05$, ~2 weeks after the last dose) in the ZDF model, indicating prolonged glycemic control. Strikingly, BMF-219, but not pioglitazone, reduced blood glucose levels during an OGTT in STZ animals (AUC reduction of 41%, $p<0.05$, see figure). Significant reductions in blood lipemic levels ($p<0.01$) and body weight were observed in both models. Collectively, our data indicate the novel and marked potential of BMF-219 as an oral, long-acting treatment for T2DM.

About Menin 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 type 2 diabetes (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 are diminished, leading to insufficient insulin secretion and hyperglycemia. Menin is thought to act as a brake on beta-cell turnover / beta-cell 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 explored the potential for menin inhibition as a viable therapeutic approach to permanently halt or reverse progression of type 2 diabetes.

About Biomea Fusion

Biomea Fusion is a clinical stage biopharmaceutical company focused on the discovery and development of covalent small molecules to treat patients with genetically defined cancers and metabolic diseases. 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. The company is utilizing its proprietary FUSION™ System to advance a pipeline of covalent-binding therapeutic agents against key oncogenic drivers of cancer and metabolic diseases. Biomea Fusion's goal is to utilize its capabilities and platform to become a leader in developing covalent small molecules in order to maximize the clinical benefit when treating various cancers and metabolic diseases.

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 our cash runway, the clinical and therapeutic potential of our product candidates and development programs, including BMF-219, the potential of BMF-219 as a treatment for various types of cancer and diabetes, our research, development and regulatory plans, including our pursuit of BMF-219 in metabolic diseases, 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 we may encounter delays or unforeseen results in preclinical development, IND-filing and acceptance, patient enrollment and in the initiation, conduct and completion of our planned clinical trials and other research, development and regulatory 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 (the "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.

Contact:

Van Sandwick
Director, Investor Relations & Corporate Development
vsandwick@biomeafusion.com
(650) 460-7759