Biomea Fusion Announces Preliminary Data from Ongoing COVALENT-103 Study of Investigational Covalent FLT3 Inhibitor BMF-500 in Relapsed or Refractory Acute Leukemia

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- Preliminary data supports BMF-500's potential as a transformative therapy for patients with FLT3 mutated relapsed or refractory (R/R) acute leukemia
- BMF-500 showed a favorable safety and tolerability profile, with no dose-limiting toxicities observed across all dose levels
- Pharmacokinetic and pharmacodynamic data confirmed on-target FMS-like tyrosine kinase 3 (FLT3) inhibition, demonstrating dose-proportional activity and good compartmental penetration
- Preliminary Phase I data for BMF-500 in R/R acute leukemia patients with FLT3 gene mutations having failed gilteritinib indicated clinical activity with evidence of responses, including a first complete response with incomplete hematologic recovery (CRi) and reductions in bone marrow blasts in 5 of 6 of the evaluable FLT3 mutated patients

REDWOOD CITY, Calif., Dec. 09, 2024 (GLOBE NEWSWIRE) -- Biomea Fusion, Inc. ("Biomea" or "the company") (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, today announced preliminary data from the ongoing Phase I COVALENT-103 study evaluating BMF-500, the company's investigational covalent FLT3 inhibitor developed using the proprietary FUSION™ System.

"These early findings from the COVALENT-103 study announced today highlight the potential of BMF-500 to deliver meaningful clinical benefits for patients with acute leukemia harboring a FLT3 mutation. BMF-500 is an exceptionally potent molecule and the second covalent inhibitor we have developed in-house and advanced to the clinic and has shown high target selectivity and inhibition," said Thomas Butler, CEO of Biomea Fusion. "Our early results are particularly exciting as FLT3 gene mutations are common in AML patients and are associated with a very poor prognosis. Patients with such mutations who have failed gilteritinib have a median overall survival of less than 2 months. We hope to provide a significant improvement in the outcome for these patients with BMF-500. Given the safety profile demonstrated to date, and the lack of myelosuppression, we think BMF-500 could be an excellent combination partner used in standard of care."

As of the data cut off, November 20, 2024, 20 patients with R/R acute leukemia had been enrolled in the dose-escalation portion of the study, all of whom received at least one dose of BMF-500. Among these, the study enrolled 13 patients with confirmed FLT3-mutations, of which 10 harbored FLT3-ITD mutations and 3 had FLT3-TKD mutations. All patients with FLT3-mutations had progressed following treatment with gilteritinib, and 5 had received at least 2 prior FLT3 inhibitors. The study enrolled 5 patients with wild-type FLT3 and 2 patients with an unknown FLT3 mutation status. The median number of prior lines of therapies among the enrolled patients was 4. No QT prolongations or related cytopenias were observed and no dose-limiting toxicities (DLTs) were reported as of the data cut off. BMF-500 was generally well tolerated, and dose escalation is continuing per protocol.

Pharmacokinetic/pharmacodynamic data confirmed on-target FLT3 inhibition, as BMF-500 and its metabolites showed bone marrow penetration and near complete FLT3 inhibition as early as Day 1 of dosing, as well as dose-proportional FLT3 inhibition.

Preliminary data supports BMF-500's potential as a transformative therapy for patients with FLT3 mutated R/R acute leukemia. During dose escalation, BMF-500 achieved a first CRi at the end of Cycle 2, in 1 of 2 (50%) FLT3 mutated patients dosed at 100 mg twice daily (BID), while the other patient experienced a clearance of peripheral blasts, greater than 50% reduction in bone marrow blasts and reduced transfusion frequency. The majority (5 of 6) of efficacy evaluable FLT3-mutated patients experienced a reduction of their bone marrow blasts. Other evidence of clinical activity such as: clearance or reduction of peripheral blasts, reduction of transfusion frequency, reduction in use of hydroxyurea were observed.

Case Study Highlights of Patient with Complete Response (CRi)

- 61-year-old patient with R/R AML, post allogenic transplant, with six co-occurring mutations (FLT3-ITD, ASXL1, IDH2, PHF6, RUNX1, SRSF2)
- 4 prior treatment regimens including venetoclax and gilteritinib
- Confirmed CRi at 100 mg BID dosing
- Progressive improvement in normal white blood cells, neutrophils, and monocytes despite ongoing transfusion needs

Webcast and Conference Call Details

Biomea Fusion will host a webcast and conference call today, Monday, December 9 at 4:30 pm EST. Interested parties will be able to join the webcast and view the related presentation under the Investors and Media section of the company's website at https://investors.biomeafusion.com/news-events/events. A replay of the webcast and conference call will be archived on Biomea's website following the event.

About COVALENT-103

COVALENT-103 is a multicenter, open-label, non-randomized trial seeking to evaluate the safety and efficacy of BMF-500, a twice daily oral treatment, in adult patients with relapsed or refractory acute leukemia with FMS-like tyrosine kinase 3 (FLT3) wild-type and FLT3 mutations. The Phase I COVALENT-103 study aims to evaluate the safety and tolerability of BMF-500, determine the optimal biologic dose and recommended Phase II dose. Additional information about the Phase I clinical trial of BMF-500 can be found at ClinicalTrials.gov using the identifier, NCT05918692.

About BMF-500

BMF-500, an investigational, novel, orally bioavailable, highly potent and selective covalent small molecule inhibitor of FLT3, was discovered and developed in-house at Biomea using the company's proprietary FUSION™ System and has demonstrated encouraging potential based on extensive preclinical studies. The kinase inhibitory profile of BMF-500 showed high target selectivity, suggesting the potential for reduced off-target liabilities. BMF-500 was designed to have a therapeutic profile to allow for combinations with standard of care and/or novel targeted agents like icovamenib, Biomea's investigational covalent menin inhibitor currently in clinical development for solid and liquid tumors as well as diabetes.

Previous data presented at the 2022 American Society of Hematology Annual Meeting showed BMF-500's picomolar affinity for inhibition of activating FLT3 mutations, including FLT3-ITD and various tyrosine kinase domain (TKD) mutations. BMF-500 demonstrated multi-fold higher potency and increased cytotoxicity as compared to the commercially available non-covalent FLT3 inhibitor gilteritinib. These data also showed complete tumor regression in mouse models of FLT3-ITD acute myeloid leukemia (AML), with no tumor regrowth even after treatment cessation.

Data presented at the 2023 American Association for Cancer Research (AACR) Annual Meeting demonstrated the potential utility of combination strategies to achieve higher antileukemic cell killing with reduced concentrations of BMF-500 and icovamenib. Additionally, Biomea has shown the potential of combinatorial approaches of BMF-500 and icovamenib with MEK and BCL2 blockade in other preclinical studies. These data provide preclinical evidence for combining pathway-specific inhibitors as a potential therapeutic strategy for further investigation in acute leukemia.

About FLT3 in AML

FLT3 is a receptor tyrosine kinase (RTK) that plays a central role in the survival, proliferation, and differentiation of immature blood cells. FLT3 gene mutations are common in patients with AML and are associated with a poor prognosis. Nearly 40% of AML patients have a FLT3 mutation, representing more than 7,000 incident patients in the U.S. each year. Once failing the only approved agent in the R/R setting, gilteritinib, patients typically have a poor prognosis and very short survival (median overall survival ~1.8 months). Academic literature suggests that up to 50% of AML patients with an NPM1 mutation also harbor a FLT3 mutation. While FLT3-specific and pan-tyrosine kinase inhibitors are approved by the FDA across various lines of therapy in AML, these agents have produced relatively low rates of durable responses and overall survival remains an unmet need.

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, 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 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, and the risk that preliminary or interim data from our clinical trials will not be predictive of future results of such trials. 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.

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