Biomea Fusion Presents Achievement of Minimal Residual Disease Negativity (MRD-neg) in First Complete Responder from Ongoing Phase I Study (COVALENT-101) of BMF-219 in Patients with Relapsed or Refractory (R/R) Acute Myeloid Leukemia (AML) at the 2023 ASH

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- BMF-219 demonstrated early signs of clinical activity and ability to achieve durable and sustained complete responses (CRs) with minimal residual disease negativity (MRD-neg) in acute myeloid leukemia (AML) patients
- Pharmacodynamic data further supports the mechanism of action of BMF-219 as a menin inhibitor; in-line with preclinical models, BMF-219 downregulated key leukemogenic genes (e.g. HOXA9, MEIS1) as well as MEN1
- BMF-219, the first and only investigational covalent oral menin inhibitor in clinical development for AML, was generally well tolerated with no dose-limiting toxicities observed and without adverse event (AE) related treatment discontinuations
- Clinical data to date support protocol enhancements to COVALENT-101 to include focusing exclusively on patients with menin sensitive mutations such as MLL-r and NPM1 mutant acute leukemias and higher dose levels for CYP3A4 inhibitor Arm (Arm B)

REDWOOD CITY, Calif., Dec. 11, 2023 (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 positive clinical data for BMF-219, an investigational covalent menin inhibitor, in relapsed / refractory AML patients with menin-dependent mutations at the 65th American Society of Hematology (ASH) Annual Meeting. The poster can be viewed at Biomea's website at https://biomeafusion.com/publications.

"We are very excited to present the clinical update at ASH on our targeted, covalently binding menin inhibitor, BMF-219, achieving durable and sustained CRs in patients with menin inhibitor-sensitive acute leukemia, even at suboptimal dosing levels. The gene expression data we presented here validates the proposed mechanism of action of BMF-219 and is in-line with our preclinical models," said Steve Morris, M.D., Chief Development Officer at Biomea.

As of the October 31, 2023, out of 29 patients dosed in the Phase I of COVALENT-101, nearly half (45%) of the participants received prior Hematopoietic Stem Cell Transplant (HSCT) and the median prior lines of therapy was 3. A total of 7 patients were selected as evaluable for efficacy. The efficacy evaluable population includes AML patients who meet the following criteria: dosed at or near predicted efficacious dose (500 mg or above [Arm A – non-CYP inhibitor Arm]; 125 mg or above [Arm B]), had known menin-dependent mutations, and completed at least two cycles of therapy. Within this patient population 2 Complete Responses (CRs) (CR rate 2/7 = 29%) were observed with a mean time to response of 1.8 months (1 CR patient had a NUP-98 mutation and 1 CRi patient had a NPM1 mutation).

In the CYP inhibitor arm, BMF-219 showed increasing plasma pharmacokinetic (PK) exposure with escalating dose levels, and the ability to achieve systemic exposures predicted to be efficacious based on preclinical acute leukemia models. Further dose escalation is still needed to achieve target AUC.

Pharmacodynamic data from a case study of an AML patient containing NUP98-NSD1 mutation showed suppression of key leukemogenic genes (e.g. HOXA9, MEIS1) as well as downregulation of MEN1, without noticeable increases in differentiation markers (e.g. CD14, ANPEP, ITGAM) in contrast to non-covalent menin inhibitors.

Across all patients enrolled in the trial as of the data cutoff date (n=29), BMF-219 was generally well-tolerated with no dose-limiting toxicities observed and without treatment discontinuations due to toxicity. Four participants experienced Differentiation Syndrome (DS) ≤ Grade 3, with onset 1-3 weeks after initiation of therapy and an average duration of 10 days, managed by cytoreductive therapy (hydroxyurea and steroids). Two participants recovered without dose modification or interruption, and none of the participants discontinued due to DS.

Initially, patients were enrolled agnostic to mutational status; subsequently, the study protocol was amended to enrich for patients with AML harboring menin-dependent mutations. Dose Level 4 is the first dose level which focused primarily on enrolling patients with known menin-dependent mutations. Biomea is planning to amend the dosing protocol to explore higher dosing levels in Arm B. Dose escalation is to be followed by a dose optimization/expansion to determine the recommended phase 2 dose.

About BMF-219

BMF-219 is a covalently binding inhibitor of menin, a protein known to play an essential role in oncogenic signaling in genetically defined leukemias as well as in diabetes. Preclinically, BMF-219 has demonstrated in well-established acute leukemia cell lines robust downregulation of key leukemogenic genes in addition to menin itself. Additionally, BMF-219 has shown anticancer activity in multiple in vitro, in vivo, and ex vivo models of acute leukemia,

multiple myeloma, diffuse large B-cell lymphoma and chronic lymphocytic leukemia. BMF-219 is currently being evaluated in first-in-human clinical trials enrolling patients with specific menin-dependent mutations in liquid and solid tumors as well as patients with diabetes.

About COVALENT-101

COVALENT-101 is a Phase I, open-label, multi-center, dose-escalation and dose-expansion study designed to assess the safety, tolerability, and pharmacokinetics/pharmacodynamics of oral dosing of BMF-219 in patients with relapsed/refractory (R/R) acute leukemias — including subpopulations where menin inhibition is expected to provide therapeutic benefit (e.g., patients with MLL1/KMT2A gene rearrangements or NPM1 mutations). The study is designed to enroll subsets of acute leukemia patients who are receiving a CYP3A4 inhibitor and also those not receiving a CYP3A4 inhibitor. COVALENT-101 is also investigating the dosing of BMF-219 in other patient populations where preclinical studies have shown high menin dependence, such as multiple myeloma, diffuse large B-cell lymphoma, and chronic lymphocytic leukemia. Additional information about this Phase I clinical trial of BMF-219 can be found at ClinicalTrials.gov using the identifier NCT05153330.

About Acute Myeloid Leukemia (AML)

AML is the most common form of acute leukemia in adults and represents the largest number of annual leukemia deaths in the U.S. and Europe. AML originates within the white blood cells in the bone marrow and can rapidly move to the blood and other parts of the body, including the spleen, central nervous system, and other organs. Approximately 30,000 people in the U.S. and Europe are diagnosed with AML each year, and the five-year overall survival rate in adults is roughly 29%. Among patients with relapsed/refractory disease, the need is greatest, as the overall survival is only approximately 3 to 9 months. It is estimated that upwards of 45% of AML patients have menin-dependent genetic drivers (MLL1-r, NPM1 mutant, and certain additional less common but recurrent gene mutations).

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 is a leader in advancing next-generation covalent small molecule medicines designed to maximize clinical benefit to treat 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, our research, development and regulatory plans, including the progress of our ongoing COVALENT-101 clinical trial of BMF-219, the availability of data from the trial, 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 in the initiation, conduct and completion of preclinical studies, including IND-enabling studies, the submission and clearance of IND applications, and 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 (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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