Biomea Fusion Announces Two Poster Presentations at Upcoming ASH Annual Meeting 2023

November 2, 2023

- **First presentation of clinical data from ongoing COVALENT-101 trial of covalent menin inhibitor BMF-219 as a treatment for patients with liquid tumors**
- **Trial in progress presentation featuring study design of ongoing COVALENT-103 trial of covalent FLT3 inhibitor BMF-500**

REDWOOD CITY, Calif., Nov. 02, 2023 (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 that abstracts related to BMF-219, a novel, investigational covalent menin inhibitor, currently in Phase 1 clinical study across multiple liquid and KRAS-mutated solid tumors, and BMF-500, a novel, investigational covalent FMS-like tyrosine kinase 3 (FLT3) inhibitor currently in Phase 1 clinical study in FLT3-mutated acute leukemias, have been accepted for presentation at the upcoming American Society of Hematology (ASH) Annual Meeting, to be held in San Diego from December 9-12, 2023. Both BMF-219 and BMF-500 were originated in-house with Biomea’s proprietary FUSION™ system platform, which discovers and designs next-generation covalent-binding small molecule product candidates.

“We look forward to our first presentation of clinical data of BMF-219 from our ongoing, extensive study of this novel covalent menin inhibitor across a broad spectrum of mutation-specific liquid and solid tumors in patients with significant unmet needs,” said Steve Morris, M.D., Chief Development Officer at Biomea. “The upcoming presentation at ASH follows our initial reporting earlier this year of topline data from our ongoing COVALENT-101 trial, which demonstrated two complete responses out of five relapsed/refractory acute myeloid leukemia patients with menin-dependent mutations.”

Details for the abstracts are listed below and can be viewed online at the ASH conference website.

Publication Number: 2916
Title: Covalent Menin Inhibitor BMF-219 in Patients with Relapsed or Refractory (R/R) Acute Leukemia (AL): Preliminary Phase 1 Data from the COVALENT-101 Study
Session Name: 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster II
Session Date: Sunday, December 10, 2023
Presentation Time: 6:00 PM - 8:00 PM
Location: San Diego Convention Center, Halls G-H

Full Text of Abstract

Background: Menin, a protein involved in transcriptional regulation, plays a role in the genesis of multiple cancers. Preclinical data from BMF-219, an investigational, highly selective, oral small-molecule inhibitor of menin, show sustained potent abrogation of menin-dependent oncogenic signaling.

BMF-219 is the first and only covalent menin inhibitor in clinical development and is being evaluated in multiple hematologic malignancies, solid tumors, and diabetes mellitus. COVALENT-101 (NCT05153330) is a Phase I dose-escalation and -expansion study of BMF-219 in R/R AL (Cohort 1), DLBCL (Cohort 2), MM (Cohort 3), and CLL (Cohort 4). Here we report preliminary safety, PK and anticancer activity data from Cohort 1 (AL).

Methods: Doses of BMF-219 are escalated independently for each indication, initially in single-subject cohorts followed by a “3 + 3” design.

Eligible patients (pts) include adults with R/R AL ineligible for standard therapy. Initially pts were enrolled agnostic to molecular status. A subsequent amendment introduced quotas for KMT2Ar (MLL1r), NPM1 and other known menin-dependent mutations: CEBP/A, MLL1-PTD, MN1, NUP98, NUP214, PICALM-AF10, SETBP1. Prior exposure to reversible menin inhibitor therapy is permitted.

Subjects receive BMF-219 daily for continuous 28-day cycles until progression/intolerability. There are 2 parallel dose-escalation arms: pts not taking (Arm A) or taking (Arm B) moderate or strong CYP3A4 inhibitors. The study is ongoing and accruing in the escalation. Expansion cohorts will enroll pts to obtain further safety and efficacy data at the OBD/RP2D.

Results: As of data cutoff of 7/24/2023, 26 pts with R/R AL (24 AML; 2 ALL) are enrolled; 7 remain on study treatment. Baseline characteristics include 17(65%) males and 9(35%) females with a median age of 57.5 years (range 33-84). There is a median of 4 (range 1-8) prior lines of therapy and 11 (42%) with prior HSCT(s). Six pts (23%) had KMT2Ar, 3 (12%) KMT2A-PTD, 4 (15%) NPM1, and 13 (50%) WT for KMT2A and NPM1.

Dosing began with single-patient cohorts at 100 mg QD (Arm A) and 25 mg QD (Arm B) and has been escalated through 4 dose levels. Thus far, pts have been dosed up to 500 mg QD (Arm A) and 125 mg QD (Arm B).

BMF-219 exposures were comparable between arms, with ~2-4-fold higher exposures observed with co-administration of a moderate or strong CYP3A4 inhibitor. At the highest dose (DL4) in which PK was evaluated, Arm A (500 mg QD) and Arm B (125 mg QD), pts on average achieved ~50%

of target exposure (2000 ng*hr/mL) with some pts surpassing it. Higher QD dosing or corresponding BID dosing is expected to achieve desired exposure.

BMF-219 has generally been well tolerated with no DLTs observed and no discontinuations due to treatment-related toxicities. No related QTc prolongation was observed. At the time of data cutoff, 23 of 26 pts were included in the safety population. Common TRAEs (≥10%) include vomiting 13% (3) and Differentiation Syndrome (DS) 13% (3). No Grade 5 TRAEs were reported. The only common Grade ≥3 TRAE (≥5%) was DS 13% (3).

The efficacy evaluable population includes AML pts who meet the following criteria: dosed at or near predicted efficacious dose (500 mg or above [Arm A]; 125 mg or above [Arm B]), had known menin-dependent mutations, and completed at least one scheduled response assessment (or had a minimum of 7 doses if discontinued prematurely). Thus far, 2 of 5 efficacy evaluable patients achieved a complete remission (1 CR; 1 CRi) and both continue BMF-219 treatment.

- Patient A: 39/M, NUP98-NSD1, ECOG=0, 500 mg QD, Arm A, 4 prior lines of treatment including intensive chemotherapy and allo-HSCT. At C1D27, marrow blasts were reduced to 6% from 13% at study entry. The patient achieved CR at C2D28 with 0% blasts.
- Patient B: 70/F, NPM1m, ECOG=1, 125 mg QD, Arm B, 1 prior line of treatment with decitabine and an investigational agent. At C1D28, marrow blasts were reduced to 34% from 52% at study entry. The patient achieved CRi with 3% blasts at C2D28.

Conclusion: BMF-219 is generally well tolerated with no DLT observed (and able to be taken with and without CYP3A4 inhibitors) with no pts discontinuing therapy due to toxicity. BMF-219 dose escalation is ongoing and approaching target exposure. BMF-219 demonstrates early signs of clinical activity in different genomic subgroups. The trial is ongoing and includes enrollment for pts diagnosed with AL, DLBCL, MM and CLL.

Publication Number: 1546
Title: COVALENT-103: A Phase 1, Open-Label, Dose-Escalation, and Dose-Expansion Study of BMF-500, an Oral Covalent FLT3 Inhibitor, in Adults with Acute Leukemia (AL)
Session Name: 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster I
Session Date: Saturday, December 9, 2023
Presentation Time: 5:30 PM - 7:30 PM
Location: San Diego Convention Center, Halls G-H

Full Text of Abstract

Background: FLT3 mutations occur in 25-35% of patients with AML and are associated with poor prognosis. FLT3 mutations are most frequently the result of an internal tandem duplication (ITD) of amino acids in the juxtamembrane region of FLT3 or point mutations in the tyrosine kinase domain (TKD). FLT3-ITD mutations are associated with increased incidence of relapse, shorter duration of remission, and decreased disease-free and overall survival.

BMF-500 is a novel orally bioavailable, highly potent and selective covalent inhibitor of FLT3 including wildtype (WT), ITD, TKD, as well as a variety of additional resistance-conferring mutations such as the gatekeeper F691. BMF-500 has demonstrated high affinity for FLT3, lack of cKIT inhibition, and sustained cell-killing capacity despite drug washout (Law et al., ASH 2022 Abstract 2756). BMF-500 has shown sustained tumor regression and improved survival in both subcutaneous and disseminated xenograft models of mutant FLT3-driven AML.

Study Design: COVALENT-103 (NCT05918692) is an open-label, non-randomized, multicenter, first-in-human Phase I study evaluating the safety, tolerability, and clinical activity of escalating doses of twice daily oral BMF-500 in patients with relapsed or refractory (R/R) AL, including AML, ALL, or MPAL, with or without FLT3 mutations.

The trial has 2 arms that will undergo dose escalation in parallel: Arm A (without) and Arm B (with) concomitant use of a moderate or strong CYP3A4 inhibitor. Utilizing an accelerated titration design (ATD), doses of BMF-500 will be escalated in single-subject cohorts until 1 subject experience either a Grade 2 or higher related-adverse event or dose-limiting toxicity (DLT). At that point, the cohort will switch to a classical “3 +3” design. Patients with WT FLT3 AL may be enrolled, up to a limit of 33% per arm. Treatment will continue in 28-day cycles until progression or intolerability. Expansion cohorts will enroll additional patients to obtain further safety and efficacy data.

Patients must be refractory, relapsed or must have progressed on or following discontinuation of the most recent anti-cancer therapy or be ineligible for any approved standard of care therapies, including HSCT. Participants with FLT3-mutant AML must have received treatment with a FLT3 inhibitor approved for treatment of relapsed or refractory FLT3-mutant AML.

Key inclusion criteria include ECOG PS ≤ 2, adequate organ function, and documented FLT3 mutation status. Key exclusion criteria include known CNS disease involvement, clinically significant cardiovascular disease, and WBC count >50,000/µL (uncontrollable with cytoreductive therapy).

Objectives: The primary objective of the study is to evaluate safety and tolerability and to determine the optimal biological dose (OBD)/ recommended Phase 2 dose (RP2D) of BMF-500 oral monotherapy based on evaluation of available PK/ PD, safety and efficacy data. Secondary objectives include characterization of the pharmacodynamics and pharmacokinetics of BMF-500, and assessment of its antitumor activity per modified Cheson (2003) criteria or the NCCN Clinical Practice Guidelines (ALL Version 1.2022) as determined by the investigator. Endpoints include best overall response rate (ORR), complete remission (CRc), duration of response (DOR), relapse-free survival (RFS) and overall survival (OS).

The study was initiated in July 2023 and will enroll ~110 participants at approximately 30 sites.

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 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. Additional information about the Phase I clinical trial of BMF-500 can be found at ClinicalTrials.gov using the identifier NCT05918692.

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.

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 with various cancers and metabolic diseases, including diabetes. 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, Twitter 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 and BMF-500, the potential of BMF-500 as an FLT3 inhibitor and as a treatment for various types of cancers, the potential of BMF-219 as a treatment for various types of cancer, our research, development and regulatory plans, the progress of our ongoing and upcoming clinical trials, including COVALENT-101 and COVALENT-103, 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 preclinical or clinical development, the preparation, filing and clearance of INDs, 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 (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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