Biomea Fusion to Present Preclinical Data for BMF-500, an Investigational Oral Covalent FLT3 Inhibitor, at the 64th American Society of Hematology (ASH) Annual Meeting

November 3, 2022

- BMF-500, an investigational third generation covalent FLT3 inhibitor, has demonstrated preclinically that it may be the most potent and selective inhibitor of FLT3 evaluated to date:
    - Greater Cytotoxicity: In acute myeloid leukemia (AML) cell lines, three-hour treatment with BMF-500 followed by washout produced higher cell killing at 96 hours than continuous exposure to the non-covalent FLT3 inhibitor gilteritinib
    - Sustained FLT3 Inhibition: BMF-500 elicited complete tumor regression of FLT3-ITD in mouse tumor models and maintained its effect without continued exposure
    - Highly Selective: Kinase panel assay displayed potential best in class selectivity towards FLT3
    - FLT3 mutant efficacy profile displayed significant benefit over existing FLT3 inhibitors
- Approximately one third of patients diagnosed with AML have a FLT3 mutation, which is associated with poor outcomes
- Biomea Fusion remains on track to file an IND for BMF-500 in the first half of 2023

REDWOOD CITY, Calif., Nov. 03, 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, today announced it will present preclinical data of investigational covalent FLT3 inhibitor, BMF-500, at the 64th ASH Annual Meeting, which will be held from December 10-13, 2022, at the Ernest N. Morial Convention Center in New Orleans, Louisiana.

BMF-500 was discovered and developed in-house at Biomea using the company's proprietary FUSION™ System and designed to have a therapeutic profile to allow for combinations with standard of care and/or novel targeted agents like BMF-219, Biomea's investigational covalent menin inhibitor. The company is on track to submit an investigational new drug (IND) application for BMF-500 in the first half of 2023 and, subject to the successful clearance of an investigational new drug (IND) application, plans to initiate clinical trials evaluating BMF-500 as a single agent and in novel combinations.

"We believe the preclinical data we will present at ASH has the potential to establish BMF-500 as the most potent and selective FLT3 inhibitor reported to date. BMF-500's unique profile and robust preclinical data demonstrate our growing expertise in developing next-generation covalently binding small molecules through our FUSIONTM System," said Dr. Steve Morris, Biomea's CMO. "Given the picomolar activity against key isoforms of FLT3, high specificity to FLT3, and the potential to combine with other agents, including our own novel menin inhibitor, BMF-219, we believe BMF-500 has the potential to produce deep and durable remissions in patients with FLT3 mutant AML."

Presentation Details

Session Name: 616. Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster II
Session Date: Sunday, December 11, 2022
Presentation Time: 6:00 PM - 8:00 PM (CST)
Publication Number: 2756
Title: BMF-500: An Orally Bioavailable Covalent Inhibitor of FLT3 with High Selectivity and Potent Antileukemic Activity in FLT3-Mutated AML

Full Text of Abstract:
Activating mutations of the FMS-like tyrosine kinase 3 (FLT3) are the most frequent genetic alteration in AML and are associated with poor prognosis. Though several FLT3 inhibitors have entered clinical trials and reached commercialization, adverse events and dose-limiting toxicities often restrict the therapeutic window and limit their long-term use. Such limitations impact the ability to achieve long-lasting response in patients and ultimately result in therapy-induced resistance. Exquisite potency combined with high selectivity and improved safety profile is expected to help improve tolerance and overall treatment outcomes of FLT3-targeted therapy.

BMF-500 was designed as a highly potent and selective, covalent, small molecule inhibitor of FLT3, that binds irreversibly to a reactive cysteine in the kinase active site. BMF-500 is a picomolar inhibitor with markedly improved potency over gilteritinib, a reversible inhibitor of FLT3. BMF-500 selectively killed AML cells harboring FLT3 activating mutations, including MV4-11 and MOLM-13, and engineered cells expressing FLT3 internal tandem duplications (FLT3-ITD) and/or FLT3 tyrosine kinase domain (TKD) mutations. In ex vivo cultures, BMF-500 as a single agent induced potent growth inhibition of patient-derived AML cells harboring either FLT3-ITD or FLT3 non-ITD mutations.

The potent covalent inhibition of FLT3 by BMF-500 manifested in effective and durable cellular response that was improved over gilteritinib. For example, a 3-hour exposure followed by wash-out of BMF-500 outperformed 4 days of continuous exposure to gilteritinib, at all concentrations tested. In cells harboring FLT3 activating mutations, BMF-500 induced dose-dependent inhibition of FLT3 phosphorylation and downstream signaling, including phospho-STAT5 and phospho-ERK. A 1-hour pulse treatment with BMF-500 was sufficient to achieve deep and durable target inhibition for greater than 24 hours, an effect not observed with gilteritinib under similar conditions. Profiling BMF-500 across a broad panel of kinases and key cell-surface receptors revealed high selectivity for FLT3 mutants and selectivity against cKit.

Potent FLT3 inhibition and high selectivity of BMF-500 translated to sustained tumor regression and improved survival in both subcutaneous and disseminated xenograft models of mutant FLT3-driven AML. Orally administered BMF-500 was well tolerated over 4 weeks of dosing. Study results including efficacy and PD response will be presented.

Collectively these data demonstrate BMF-500 to be a novel FLT3 inhibitor with best-in-class potential, given its efficacy, durability, and selectivity in comparison to existing FLT3 inhibitors.

About FLT3 (fms-like tyrosine kinase 3)

FLT3 is a tyrosine kinase receptor that plays a central role in the survival, proliferation, and differentiation of immature blood cells. Notably, FLT3 gene mutations are common in patients with AML and are associated with a poor prognosis. Nearly 30% of AML patients have a FLT3 mutation, representing more than 6,000 incident patients in the United States each year. 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 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 and BMF-500, the potential of BMF-500 as a treatment for various types of cancer, our research, development and regulatory plans, including our plans to submit an IND for BMF-500 and to initiate clinical trials of BMF-500 as a single agent and in novel combinations, 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 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.

Contact: Sasha Blaug SVP Corporate Development sb@biomeafusion.com (650) 460-7759