Biomea Fusion Announces IND Candidate Selection: BMF-500, a Potential Best-in-Class Oral Covalent Inhibitor of FLT3

May 19, 2022

- BMF-500, an investigational third-generation covalent inhibitor of FLT3, demonstrated picomolar IC_{50} values across key FLT3 isoforms, potentially making it the most potent inhibitor of its class
- Highly selective for FLT3, BMF-500 was observed to avoid other type III receptor tyrosine kinase (RTK) family members, including cKIT, which drives myelosuppression and limits utility of some first and second-generation FLT3 inhibitors
- Initial *in vivo* studies demonstrated that BMF-500 elicited complete tumor regression of FLT3-ITD in mouse tumor models and maintained its effect without continued exposure
- BMF-500 is potentially synergistic with BMF-219, Biomea's investigational covalent menin inhibitor currently in a Phase I clinical trial, COVALENT-101, for acute myeloid leukemia (AML)
- Together, BMF-500 and BMF-219 could potentially treat the majority of AML patients as single agents or in combination
- BMF-500 was designed and developed in-house, from target to IND candidate, utilizing Biomea's proprietary FUSION™ System

REDWOOD CITY, Calif., May 19, 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, announced the nomination of its second product candidate, BMF-500, a highly selective and potent covalent investigational third-generation FLT3 inhibitor.

Approximately 30% of AML patients present with a FLT3 mutation and remain poorly controlled with currently available therapies. First and second-generation FLT3 inhibitors frequently have a narrow therapeutic window and patients often acquire rapid resistance to treatment, limiting the clinical efficacy of these agents. As a third-generation FLT3 inhibitor, BMF-500 is designed to overcome some of the characteristics that are believed to limit the duration of response and utility of these earlier generation FLT3 inhibitors.

BMF-500 was discovered and developed in-house at Biomea using the company's proprietary FUSION™ System. BMF-500, like BMF-219, was designed to be clinically effective at relatively low drug concentrations in order to deliver an optimal therapeutic profile. Specifically, BMF-500 was observed in preclinical studies to be a highly active inhibitor of FLT3 with picomolar affinity for key isoforms of FLT3 while avoiding other key kinases tested, including structurally related KIT.

Because patients often acquire rapid resistance to treatment with first and second-generation FLT3 inhibitors, BMF-500 is designed to strongly inhibit FLT3 variants that are key drivers of resistance. Additionally, BMF-500 is designed to potentially have a therapeutic profile that may allow for combination with standard of care and/or targeted agents like BMF-219. Many patients with AML are older and unfit candidates for intensive chemotherapy but could benefit from BMF-500 and BMF-219 either as monotherapy or in combination.

AML is often described as the result of two broad complementary classes of mutations: Type I - those that confer a proliferative/survival advantage to hematopoietic progenitors including activating FLT3 mutations or their downstream effectors such as RAS, and Type II - those that impair hematopoietic differentiation and drive cell cycle progression, including NPM1, MLL-r, RUNX1, and DNMT3A mutations. With BMF-500 and BMF-219, Biomea plans to interrogate multiple molecular mechanisms that drive AML in the pursuit of establishing long-term disease management or a potential cure for these patients.

"FLT3 has been a challenge for companies to effectively target with either non-covalent or covalent approaches due to the homology of various kinases and other receptors, leading to off-target toxicities at potentially clinically relevant drug concentrations. Leveraging our FUSION™ System, we have quickly developed BMF-500, which we believe is among the most promising investigational FLT3 inhibitors to date," said Thomas Butler, Biomea's Chief Executive Officer and Chairman of the Board. "With picomolar activity against key isoforms of FLT3, high specificity to FLT3 observed in preclinical studies, and the potential benefits of covalent engagement, we believe that BMF-500 is poised to become a leading targeted therapy for AML patients with FLT3 mutations, if approved. We look forward to leveraging the existing clinical infrastructure and know-how that we have developed through the planning and execution of our ongoing trial with BMF-219, COVALENT-101, and plan to explore the potential synergy between BMF-500 and BMF-219."

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 FDA approved 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-500 and BMF-219, the potential of BMF-500 as an FLT3 inhibitor, the potential of BMF-219 as a treatment for various types of cancer and diabetes, our research, development and regulatory plans, the progress of our COVALENT-101 Phase 1 clinical trial, including ongoing enrollment in the trial, our plans to continue IND-enabling studies for BMF-500 and file an IND, 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 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