Biomea Fusion Presents Additional Preclinical Data Demonstrating Anti-Tumor Activity and Mechanistic Evidence for BMF-219 in Diffuse Large B-Cell Lymphoma and Multiple Myeloma Models at International Myeloma Society Annual Meeting

August 26, 2022

- Data demonstrated robust anti-tumor activity of BMF-219 and mechanistic evidence for novel inhibition of menin protein in preclinical models of Diffuse Large B-cell Lymphoma (DLBCL) and multiple myeloma (MM).
- BMF-219 displayed single agent potency, surpassing greater than 90% inhibition at clinically relevant exposures in both DLBCL and MM cell lines and patient-derived samples.
- A Trial In Progress (TIP) poster was also presented, detailing the design of Biomea's ongoing Phase I clinical trial (COVALENT-101), which is currently enrolling patients with relapsed / refractory acute leukemias, DLBCL, and MM.

REDWOOD CITY, Calif., Aug. 26, 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 today the presentation of two posters at the 19th International Myeloma Society (IMS) Annual Meeting, which took place August 25-27, 2022 in Los Angeles, California. Both poster presentations can be viewed on Biomea's website at https://biomeafusion.com/publications.

"Our team has continued to accumulate novel scientific evidence demonstrating compelling preclinical activity of BMF-219 as a potential first-in-class and best-in-class menin inhibitor across a spectrum of tumor types where menin is known to play a critical role. To that end, we are pleased to present additional preclinical data at the IMS Annual Meeting that support the expansion of our ongoing COVALENT-101 clinical trial to enroll patients with DLBCL and MM. We look forward to seeing how BMF-219's preclinical effect translates to patient benefit in the clinical setting," said Thomas Butler, CEO, Chairman of the Board and Co-Founder of Biomea.

Poster Presentation Details:

Poster P-107: Anti-tumor activity of covalent menin inhibitor, BMF-219, in High-Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models

Abstract Text:
Introduction

Menin is a scaffold protein that interacts with various transcriptional regulators and partner proteins to promote tumorigenesis in a context-dependent manner. Menin drives oncogenic signaling by regulating expression of genes such as HOXA9 and MEIS1 and is also known to play a key role in MYC-mediated transcriptional activities. BMF-219 is a highly selective, potent, orally bioavailable, small molecule covalent inhibitor of menin. We previously reported the ability of BMF-219 to modulate MYC expression and exhibit high potency against Double HIT Lymphoma (DHL) DLBCL (Diffuse Large B Cell Lymphoma) preclinical models.

Methods
In the current study we demonstrate the anti-tumor activity of BMF-219 in multiple myeloma (MM), and Double/Triple Hit Lymphoma (DHL/THL) and Double Expressor Lymphoma (DEL) high-grade B-cell lymphomas (HGBCL) preclinical models harboring various mutational backgrounds. Additionally, we provide mechanistic evidence for direct inhibition of menin protein, in cell line models representing MM, DHL and DEL.

Results

BMF-219 exhibited high potency in THL and DEL cell lines (IC50 = 0.27 μM and 0.37 μM, respectively), achieving >90% growth inhibition as single agent. BMF-219 was multi-fold more potent and exerted dramatically greater growth inhibition compared to clinical reversible menin inhibitors in all DLBCL cell lines tested, including an expanded panel of DHL cell lines. In ex vivo studies, an R-CHOP refractory THL patient sample and an R-EPOCH refractory MYC-amplified DLBCL patient sample were highly sensitive to BMF-219 treatment (IC50 = 0.15 μM and 0.2 μM, respectively) and demonstrated complete growth inhibition at 1 μM exposure. In contrast, two clinical reversible menin inhibitors demonstrated much lower potency (IC50 = ~1 μM to >10 μM). MM cell lines harboring mutations in TP53, KRAS and NRAS were all sensitive to BMF-219 with growth inhibition IC50 values in the range of 0.25 μM to 0.5 μM and achieved 100% inhibition at 1 μM. Notably, BMF-219 demonstrated single-agent efficacy (IC50 = 0.1 μM to 0.3 μM) against a panel of newly diagnosed and R/R ex vivo MM samples, including a p53-deleted clinical profile. Mechanistically, BMF-219 induced a reduction in menin protein levels, the direct target of this covalent inhibitor. The dose-dependent reduction in menin protein across the collection of MM and DLBCL cell lines with varying cytogenetic and mutational backgrounds will be discussed. Analysis of additional proteins modulated by BMF-219 in these cell line models will also be addressed.

Conclusions:

Collectively, our data demonstrate the novel and robust anti-tumor activity of BMF-219 in HGBCL and MM preclinical models that represent categories of high unmet need. BMF-219 exhibits multi-fold higher potency and complete growth inhibition in these preclinical models compared to clinical reversible menin inhibitors, demonstrating its unique anti-tumor potential in these cancers.

Poster P-269: COVALENT-101: A Phase 1 study of BMF-219, a novel oral covalent menin inhibitor, in patients with relapsed/refractory (R/R) acute leukemia, diffuse large B-cell lymphoma, and multiple myeloma

Abstract Text:
Introduction

Trial in Progress
Background: Menin, a protein involved in transcriptional regulation, impacting cell cycle control, apoptosis, and DNA damage repair, plays a direct role in oncogenic signaling in multiple cancers. Inhibition of menin is a novel approach to cancer treatment. Preclinical data of BMF-219, a highly selective, orally bioavailable, small-molecule covalent inhibitor of menin, show sustained potent abrogation of menin-dependent oncogenic signaling in vitro and in vivo. BMF-219 exhibited a strong anti-proliferative effect on various menin-dependent acute myeloid leukemia (AML) cell lines, diffuse large B-cell lymphoma (DLBCL) lines representing Double/Triple Hit Lymphoma (DHL/THL) & Double Expressor Lymphoma (DEL), and MM cell lines with diverse mutational backgrounds. BMF-219 also showed high potency ex vivo in patient samples from MLL-rearranged and NPM1-mutant AML, THL and MYC-amplified DLBCL, and bone marrow mononuclear cells from treatment-naive and R/R MM.

Methods
COVALENT-101 (BF-MNN-101; NCT05153330) is a prospective, open-label, multi-cohort, non-randomized, multicenter Phase I study evaluating the safety, tolerability, and clinical activity of escalating doses of once daily oral BMF-219 in patients with R/R acute leukemia (AL), DLBCL, and MM who have received or are ineligible for standard therapy. Utilizing an accelerated titration design, doses of BMF-219 will be escalated in single-subject cohorts independently for each indication until 1 subject experiences either a ≥ Grade 2 related adverse event or dose limiting toxicity (DLT). At that point, the cohort will switch to a classical “3 + 3” design. Treatment will continue in 28-day cycles until progression or intolerability. Expansion cohorts for each indication will enroll patients to obtain further safety and efficacy data.

Patients with R/R AL who have failed or are ineligible for any standard therapies, R/R DLBCL following ≥ 2 but ≤ 5 prior therapies, and R/R MM who have received ≥ 3 therapies are eligible. Patients must have ECOG PS ≤ 2, and adequate organ function. Key exclusion criteria include known CNS disease involvement, prior menin inhibitor therapy, and clinically significant cardiovascular disease.

Results
The primary objective is to determine independently for each cohort/indication the optimal biological dose (OBD)/ recommended Phase 2 dose (RP2D) of BMF-219 oral monotherapy. Key secondary objectives include further evaluation of safety and tolerability, characterization of the pharmacodynamics and pharmacokinetics of BMF-219, and assessment of its antitumor activity based on best overall response rate (ORR), duration of response (DOR), progression-free survival (PFS), and time to progression (TTP) per disease specific response criteria as assessed by the investigator. Food-effect studies will be performed in DLBCL and MM patients at certain dose levels.

Conclusions
Enrollment in COVALENT-101 commenced in January 2022.

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, the potential of BMF-219 as a treatment for various types of cancer and diabetes, our research, development and regulatory plans, including the progress and results of our ongoing COVALENT-101 trial of BMF-219, 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 or unforeseen results in preclinical development, IND-filing and acceptance, patient enrollment and in the initiation, conduct and completion of our ongoing and 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: Sasha Blaug SVP Corporate Development sb@biomeafusion.com (650) 460-7759