UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 26, 2022

Biomea Fusion, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	001-40335	82-2520134
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

900 Middlefield Road, 4th Floor Redwood City, CA		94063
(Address of Principal Executive Offices)		(Zip Code)

Registrant's Telephone Number, Including Area Code: (650) 980-9099

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value	**BMEA**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On August 26, 2022, Biomea Fusion, Inc. (the "Company") issued a press release titled, "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." The information described in the press release was also presented in two poster presentations at the 19th International Myeloma Society (IMS) Annual Meeting, which took place August 25-27, 2022 in Los Angeles, California.

Copies of the press release and the Company's poster presentations are attached to this Current Report on Form 8-K as Exhibits 99.1 through 99.3 and incorporated herein by reference.

Forward-Looking Statements

Statements made or incorporated by reference in this Current Report on Form 8-K 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 the Company's product candidates and development programs, including BMF-219, the potential of BMF-219 as a treatment for various types of cancer and diabetes, the Company's research, development and regulatory plans, including the progress and results of the Company's ongoing COVALENT-101 trial of BMF-219, and the timing of such events, may be deemed to be forward-looking statements. The Company intends 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 is making this statement for purposes of complying with those safe harbor provisions.

Any forward-looking statements made or incorporated by reference in this Current Report on Form 8-K are based on the Company's current expectations, estimates and projections only as of the date of this Current Report on Form 8-K 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 the Company may encounter delays in patient enrollment and in the initiation, conduct and completion of its planned clinical trials and other research and development activities. These risks concerning the Company'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. The Company explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release titled, "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."
99.2	Poster presentation titled, "Anti-tumor Activity of Covalent Menin Inhibitor, BMF-219, in High Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models."
99.3	Poster presentation titled, "COVALENT-101: Phase 1 first-in-human dose escalation and dose-expansion study of BMF-219, an oral, covalent, menin inhibitor, in adult patients with acute leukemia (AL), diffuse large B-cell lymphoma (DLBCL), and multiple myeloma (MM)."
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

BIOMEA FUSION, INC.

Date: August 29, 2022

By: /s/ Thomas Butler

Thomas Butler
Principal Executive Officer

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

- 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 mM and 0.37 mM, 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 mM and 0.2 mM, respectively) and demonstrated complete growth inhibition at 1 mM exposure. In contrast, two clinical reversible menin inhibitors demonstrated much lower potency (IC50 = ~1 mM to >10 mM). 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 mM to 0.5 mM and achieved 100% inhibition at 1 mM. Notably, BMF-219 demonstrated single-agent efficacy (IC50 = 0.1 mM to 0.3 mM) 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 Data

Contact:

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Contact

Exhibit 99.2

Anti-tumor Activity of Covalent Menin Inhibitor, BMF-219, in High Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models

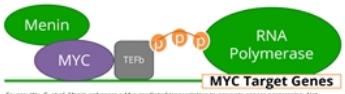
We Aim to Cure™

Daniel Lu, MS[1], Priyanka Somanath, PhD[1], Brian Law, BS[1], Lekha Kumar, MS[1], James T. Palmer, PhD[1], Taisei Kinoshita, PhD[1], Mini Balakrishnan, PhD[1] and Thomas Butler, MSc MBA[1]

[1]Biomea Fusion, Inc. Redwood City, CA

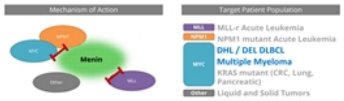
INTRODUCTION

- Menin is a scaffold protein that drives oncogenic function through its regulation of genes such as *HOXA9*, with distinct effects on transcription that are directed by various cofactors. A recent study reported that knockdown of *HOXA9* resulted in marked growth inhibition of multiple myeloma (MM) cells (Chapman et al., 2017).
- Double/Triple Hit Lymphoma (DHL/THL) and Double Expresser Lymphoma (DEL) are high-grade B-cell lymphomas (HGBL) that exhibit low responses to standard therapeutic regimens resulting in poor prognosis.
- DHL harbor translocations in MYC and BCL2 or BCL6, THL contain translocations in MYC/BCL2/BCL6, and DEL are characterized by high expression of MYC and BCL2.
- We previously reported the ability of irreversible menin inhibitor, BMF-219, to modulate MYC expression and exhibit high potency against DHL Diffuse Large B-Cell Lymphoma (DLBCL) preclinical models (Somanath et al., 2021).



Source: Wu, G. et al. Menin enhances c-Myc-mediated transcription to promote cancer progression. Nat. Commun. 8, 15278 (2017).

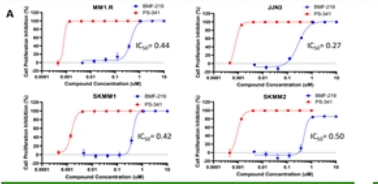
- Here, we demonstrate the anti-tumor activity of BMF-219 in MM and HGBL preclinical models harboring various mutational backgrounds.

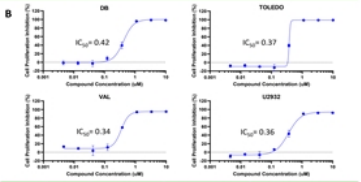


METHODS

- MM and DLBCL cell lines were cultured in the presence of BMF-219 or bortezomib (PS-341) for 4 days and cell proliferation was measured by Cell Titer Glo.
- Patient-derived MM patient derived BMMCs and DLBCL PDX models were cultured *ex vivo* in the presence of BMF-219 or PS-341 for 6 days and cell proliferation was measured by Cell Titer Glo.
- MM and DLBCL cell lines were cultured in the presence of BMF-219 or clinical reversible menin inhibitors for 14 hours. Menin protein expression was measured by the Wes system and analyzed using the Compass software (automated western blotting, Protein Simple). Signal was normalized to GAPDH and referenced to DMSO control.

BMF-219 exerts >99% lethality against MM and DLBCL cell lines





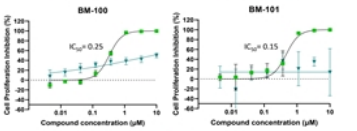
MM Cell Line	Translocation	Mutation	Average % Max Inhibition by BMF-219	Average IC_{50} ± Standard Deviation (μM)
MM1.S	t(14;16)	KRAS G12A	99.5	0.47 ± 0.17
MM1.R	t(14;16)	KRAS G12A	99.6	0.46 ± 0.17
SKMM1	t(14;20)	NRAS G12A	99.2	0.47 ± 0.05
SKMM2	t(11;14)	TP53	80.2	0.65 ± 0.15
JJN3	t(14;16)	NRAS Q61K	99.2	0.29 ± 0.02
OPM2	t(4;14)	TP53	98.4	0.55

DLBCL Cell Line	Category	Translocation	Average % Max Inhibition by BMF-219	Average IC_{50} ± Standard Deviation (μM)
DB	DHL	MYC/BCL2	98.5	0.41 ± 0.07
Toledo	DHL	MYC/BCL2	98.8	0.31 ± 0.07
DOHH2	DHL	MYC/BCL2	99.7	0.32 ± 0.03
VAL	THL	MYC/BCL2/BCL6	97.1	0.27 ± 0.07
U2932	DEL-ABC	MYC/BCL2 Overexpression	92.4	0.37 ± 0.01
SUDHL8	GCB	-	99.6	0.60 ± 0.21
Pfeiffer	GCB	-	99.6	0.17 ± 0.04
OCI-LY7	GCB	-	99.6	0.65 ± 0.26

Potent killing activity of BMF-219 at clinically relevant concentrations in representative MM and DLBCL cell lines. (A). MM1.R, JJN3, SKMM1, SKMM2 and OPM2 cell lines and (B). DHL (DB, Toledo, DOHH2), THL (VAL), DEL (U2932), and GCB (SUDHL8) subtypes were cultured in the presence of BMF-219 (blue) or PS-341 (red) for 4 days. Average IC_{50} values of at least two experiments, maximal percentage cell killing, and cytogenetic background cell lines are summarized in the table.

BMF-219 exerts pronounced lethality in DLBCL PDX models *ex vivo*

THL- Responded, then progressed on R-EPOCH | **MYC Amplified- Responded, then progressed on R-CHOP**



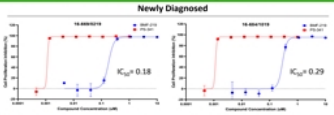
BMF-219 Clinical Reversible Menin

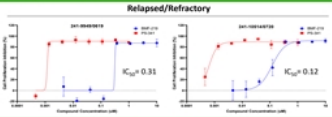
Treatment	Growth Inhibition IC_{50} (μM)	% Max Inhibition	Growth Inhibition IC_{50} (μM)	% Max Inhibition
	BM100		BM101	
BMF-219	0.250	100	0.151	100
Clinical Reversible	6.31	50	> 10	30

Growth inhibition of patient-derived DLBCL Triple Hit Lymphoma (THL) and MYC-amplified PDX samples treated with BMF-219 or clinical reversible menin inhibitor after 6 days of treatment. IC_{50} values and maximal percentage cell killing are summarized in the table.

BMF-219 dramatically reduces growth of both newly diagnosed and R/R MM patient specimens

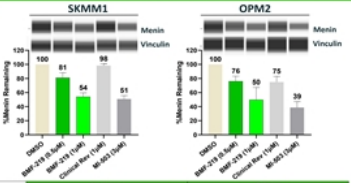
Multiple Myeloma Specimen ID	Stage at Diagnosis	Treatment Status	Prior Therapy and Response	Translocation
16-669/0219	IIIA	Newly Diagnosed	None	No data
16-684/1019	IIIA	Newly Diagnosed	None	No data
241-9949/06-19	IIIA	Refractory	VCD N4 (resistant)	p53 deletion
241-10514/0720	IIIA	Refractory	VCD N 4 (responded)	p53 deletion-negative
			High dose CPH (SC-mobilization) (responded)	
			Consolidation (AutoSCT, double transplant)	
			Bortezomib- maintenance (resistant)	
			RVD #4 (resistant)	
			PRD #4 (resistant)	

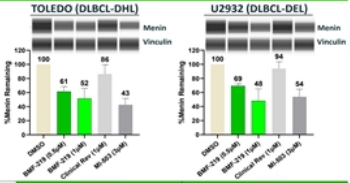




Growth inhibition of newly diagnosed (A-B) and R/R (C-D) MM patient-derived bone marrow mononuclear cells (BMMCs) after 6 days of treatment with BMF-219 (blue) or PS-341 (red). Clinical profiles of MM patient-derived BMMC specimens are summarized in the table.

BMF-219 exerts pronounced decrease in menin protein expression in MM and DLBCL cell lines





% Cell Death	SKMM1 BMF-219 (0.4μM)	SKMM1 BMF-219 (0.5μM)	SKMM1 BMF-219 (1μM)	SKMM1 Clin Rev (1μM)	SKMM1 MI-503 (3μM)	OPM2 BMF-219 (0.5μM)	OPM2 BMF-219 (0.5μM)	OPM2 BMF-219 (1μM)	OPM2 Clin Rev (1μM)	OPM2 MI-503 (3μM)
72 hr	27	-	86	4	33	22	-	80	3	21
14 hr	-	15	25	0	13	-	8	57	0	14

% Cell Death	TOLEDO BMF-219 (0.4μM)	TOLEDO BMF-219 (0.5μM)	TOLEDO BMF-219 (1μM)	TOLEDO Clin Rev (1μM)	TOLEDO MI-503 (3μM)	U2932 BMF-219 (0.4μM)	U2932 BMF-219 (0.5μM)	U2932 BMF-219 (1μM)	U2932 Clin Rev (1μM)	U2932 MI-503 (3μM)
72 hr	32	-	97	0	35	29	-	86	3	34
14 hr	-	18	12	0	11	-	19	36	0	7

BMF-219 reduces menin protein in MM and DLBCL cells. Quantitation of menin protein expression in SKMM1, OPM2, Toledo and U2932 cell line treated with BMF-219, clinical reversible menin inhibitor or preclinical reversible menin inhibitor, MI-503, for 14 hours. Average menin protein expression are of 3 independent experiments. WES blot is a representative from 1 single experiment. Cells were cultured in the presence of menin inhibitors for 72hr or 14hr. Average % cell killing treated at 72hr and 14hr are from 2 independent experiment.

CONCLUSIONS

- BMF-219 achieved >99% cell lethality in MM cell lines with RAS mutations with IC_{50} values between 0.3 μM and 0.5 μM.
- BMF-219 demonstrated single-agent efficacy (IC_{50} values between 0.1 μM and 0.3 μM) against a panel of newly diagnosed and R/R *ex vivo* MM samples, including a p53-deleted clinical profile.
- BMF-219 exhibited high potency as a single agent against DHL, THL and DEL DLBCL cell lines, with IC_{50} values of 0.3 μM and 0.4 μM, respectively.
- In *ex vivo* studies, BMF-219 was highly effective against R-CHOP and R-EPOCH refractory patient samples with THL and MYC-amplified genetic backgrounds.
- BMF-219 was multi-fold more potent and exerted dramatically greater growth inhibition compared to clinical reversible menin inhibitors in DLBCL patient-derived *ex vivo* samples.
- BMF-219 induces reduction of menin protein levels across MM and DLBCL cell lines. This reduction however appears to be transient. An incubation time of 14 hours may not be a good predictor of cellular growth inhibition.

REFERENCES

- Chapman, M., Lawrence, M., Keats, J. et al. Initial genome sequencing and analysis of multiple myeloma. *Nature* **471,** 467–472 (2011).
- Somanath, P., Lu, D., Law, B. et al. Novel Irreversible Menin Inhibitor, BMF-219, Shows Potent Single Agent Activity in Clinically Relevant DLBCL Cells. *Blood* 2021; 138 (Supplement 1): 4318.
- Wu, G., Yuan, W., Shen, S. et al. Menin enhances c-Myc-mediated transcription to promote cancer progression. *Nat Commun* **8,** 15278 (2017).
- Borkin, D. et al. Pharmacologic inhibition of the Menin-MLL interaction blocks progression of MLL leukemia in vivo. *Cancer Cell.* 2015 Apr 13;27(4):589-602.

Acknowledgements- We acknowledge Champions Oncology for generation of ex vivo studies.

biomea FUSION

Exhibit 99.3
We Aim to Cure™

COVALENT-101 (NCT05153330)

Phase 1 first-in-human dose-escalation and dose-expansion study of BMF-219, an oral, covalent, menin inhibitor, in adult patients with acute leukemia (AL), diffuse large B-cell lymphoma (DLBCL), and multiple myeloma (MM)

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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.[1]

BMF-219

- BMF-219, is an orally bioavailable, potent and selective covalent inhibitor of menin, an important transcriptional regulator.
- Preclinical data of BMF-219 showed sustained potent abrogation of menin-dependent oncogenic signaling in vitro and in vivo.
- BMF-219 demonstrates a strong anti-proliferative effect on various menin-dependent acute myeloid leukemia (AML) cell lines, DLBCL cell lines representing Double/Triple Hit Lymphoma (DHL/THL), Double Expressor Lymphoma (DEL), and MM cell lines harboring diverse mutational backgrounds.[2]
- BMF-219 also exhibits potent cell killing activity on ex vivo cultured MLL-rearranged and NPM1-mutant AML patient samples, THL and MYC-amplified DLBCL, bone marrow mononuclear cells from treatment-naive and R/R MM[2].
- For current clinical trials, BMF-219 is supplied as 25 and 100 mg strength capsules for once daily oral administration.

COVALENT-101 (BF-MNN-101) STUDY OVERVIEW

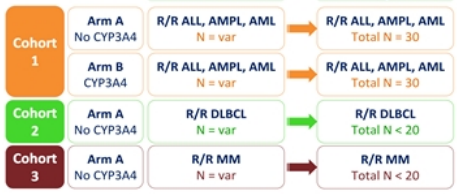
- COVALENT-101 is a prospective, open-label, multi-cohort, non-randomized, multicenter, first-in-human Phase I study evaluating the safety, tolerability, and clinical activity of escalating doses of oral BMF-219 administered either once or twice daily in patients with R/R ALL, AML, DLBCL & MM who have received standard therapy.
- Approximately 20 clinical sites in the United States.

OBJECTIVES & ENDPOINTS

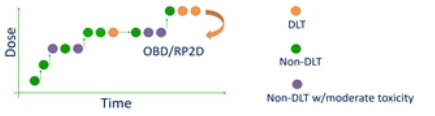
Primary	Determine OBD & RP2D of BMF-219 for each Cohort (1, 2 & 3) and Arm (A & B)	•OBD/RP2D will be determined based on PK/PD/Safety/Efficacy
Secondary	Further evaluate Safety and tolerability of BMF-219	•TEAE / SAE incidence •C_{max}, T_{max}, and $AUC_{0-\infty}$ of BMF-219
	PK/ PD evaluation of BMF-219 Additional Evidence of Efficacy of antitumor activity	•Cohort 1: CRR* •Cohort 2: ORR[↗] •Cohort 3: ORR[Q] } & other efficacy parameters per investigator assessment
Exploratory	To characterize the PD effects of BMF-219 for each cohort independently	•Changes in gene expression •Explore predictive and pharmacodynamic markers

* Based on European LeukemiaNet (ELN) 2017 recommendation for diagnosis and management of AML or the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines, ALL (Version 2. 2021)
↗ Revised criteria for response assessment of lymphoma (Cheson, 2014)
Q International Myeloma Working Group (IMWG) response criteria (Kumar, 2016)

STUDY DESIGN

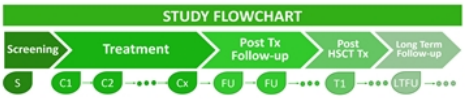


Accelerated titration design followed by 3+3



- Doses of BMF-219 will be escalated in single-subject cohorts independently for each indication until 1 subject experiences either any ≥ Grade 2 related-TEAE which does not meet DLT criteria, or a DLT in the first cycle.
- At that point, the dose level for the specific cohort will follow a classical "3 + 3" dose escalation design.

STUDY FLOWCHART



Screening	• Up to 28 days from consent
Treatment	• Daily treatment with BMF-219 in 28-day cycles
Post Tx Follow-Up	• Regular post-tx efficacy assessment visits
Post HSCT Treatment	• Post adequate response to BMF-219 patient may proceed with HSCT and then resume BMF-219
Long Term Follow-Up	• Survival follow-up calls

KEY ELIGIBILITY CRITERIA

Inclusion Criteria

- ≥ 18 years with ECOG performance status of 0-2 and an estimated life expectancy of > 3 months
- Adequate liver function: Bilirubin ≤ 1.5 ULN; ALT/AST ≤ 2.0 ULN
- Adequate renal function: estimated creatinine clearance (eCrCl) ≥ 60 mL/min (Cohort 1) or eCrCl ≥ 30 mL/min (Cohorts 2 & 3) using the Cockcroft-Gault equation
- Prior treatment-related toxicities resolved to ≤ Grade 2 prior to enrollment
- Adequate washout from prior therapies (e.g., ≥ 60 days from RT; ≥ 60 days from stem cell infusion; ≥ 7 days from biologics or steroids; ≥ 21 days from prior immunotherapy; ≥ 14 days from completion of last chemotherapy)

Indication & Prior Regimen Criteria

Cohort	Arm	Indication	Prior treatment regimens	*CYP3A4 inhibitors
1	A	R/R ALL, AMPL, AML agnostic of mutation	No limit, includes prior HSCT	No
1	B	R/R ALL, AMPL, AML agnostic of mutation	No limit, includes prior HSCT	Yes
2	A	R/R DLBCL / DLBCL transformed from previously indolent lymphoma (e.g., follicular lymphoma)	≥ 2 with at least 1 course of anthracycline-based chemotherapy & at least 1 course of anti-CD20 immunotherapy	No
3	A	R/R MM	≥ 3 including proteosome inhibitor & immunomodulatory	No

* Subjects are receiving concomitant medications considered to be strong or moderate inhibitors of CYP3A4

Exclusion Criteria

- Known CNS disease involvement
- Prior menin inhibitor therapy
- WBC count > 50,000/ µL (uncontrollable with cytoreductive therapy)
- Clinically significant cardiovascular disease; LVEF < 45%
- Mean QTcF or QTcB of > 470 millisecond (ms)
- Acute or chronic GVHD except disease limited to skin with adequate control using topical steroids
- Concurrent malignancy in the previous 2 years

REFERENCES

1. Issa, G. C., et al. (2021). Therapeutic implications of menin inhibition in acute leukemias. Leukemia, 35(9), 2482–2495.
2. Anti-tumor activity of irreversible menin inhibitor, BMF-219, in High Grade B-Cell Lymphoma and Multiple Myeloma Preclinical Models. Cancer Res (2022) 82 (12_Supplement): 2654.