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): January 12, 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

650 Main Street
Redwood City, CA 94063
(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 7.01. Regulation FD Disclosure.

Biomea Fusion, Inc. (the "Company") from time to time presents and/or distributes to the investment community at various industry and other conferences slide presentations to provide updates and summaries of its business. On January 12, 2022, the Company will present an updated corporate presentation virtually at the 40th Annual J.P. Morgan Healthcare Conference and post the presentation in the "Investors & Media" portion of its website at *www.biomeafusion.com*. A copy of the Company's current corporate slide presentation is attached to this Current Report on Form 8-K as Exhibit 99.1. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information contained in Item 7.01 of this Form 8-K (including Exhibit 99.1 attached hereto) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly provided by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Corporate Slide Presentation of Biomea Fusion, Inc. dated January 2022
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: January 12, 2022

By: /s/ Thomas Butler

Thomas Butler
Principal Executive Officer

Exhibit 99.1

Disclaimer and Forward-Looking Statement

Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future business and financial performance of Biomea Fusion, Inc. (the "Company") and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "potential" or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including any projections of financial information or profitability, the initiation, timing and results of pending or future preclinical studies and clinical trials, the actual or potential actions of the FDA, the status and timing of ongoing research, development and corporate partnering activities, any statements about historical results that may suggest trends for the Company's business; any statements of the plans, strategies, and objectives of management for future operations; any statements of expectation or belief regarding future events, potential markets or market size, or technology developments, and other factors affecting the Company's financial condition or operations. The Company has based these forward-looking statements on its current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company's control. These and other important factors may cause actual results, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. The forward-looking statements in this presentation are made only as of the date hereof. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company's expectations. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

- Experienced and Successful Management Team
- Novel FUSION™ Platform
- BMF-219 - Clinical Stage Oncology Asset
- Multiple Oncology Programs built from FUSION™ Platform

We Aim To Cure

Biomea Fusion is a clinical-stage biopharmaceutical company focused on the discovery and development of irreversible small-molecule drugs to treat patients with genetically defined cancers. We believe that our approach may lead to significant improvement and extension of life for patients. Our team is engaged in all phases of drug discovery and development, including target selection, small molecule design, and preclinical and clinical studies to develop innovative medicines.

BMF-219 – Novel Irreversible Covalent Inhibitor of Menin

Pipeline-in-a-Pill – Single Agent for Multiple Indications

Strong Pathway Control

Large effect on target genes and proteins leading to cell death

Multiple Shots on Goal

Acute leukemias, MYC addicted and driven cancers, RAS/RAF driven solid tumors

Consistent On-Target Effect

Pathway control and cell killing seen at same predicted dose across indications

Wide Safety Margin

Strong preclinical safety profile from animal studies

Our Team – 10+ Years of Success Together

Thomas Butler
Chairman & CEO

15+ years in Life Science
Pharmacyclics
Gilead Sciences
UCLA – MBA Finance
UCSB, MS – Chemistry

Ramses Erdtmann
President & COO

15+ years in Life Science
Pharmacyclics
Oxygen Investments
Commerzbank
University of Münster, Master's in Banking & Corp Finance

Franco Valle
Chief Financial Officer

15+ years in Life Science
Eidos Therapeutics
Iovance Biotherapeutics
Pharmacyclics
CallidusCloud
PricewaterhouseCoopers
San Jose State University, BS Corporate Finance

Naomi Cretcher
Chief of People

15+ years in Life Science
Pharmacyclics
Genentech
UC Irvine, BA Comm
SF State University, Comm

Heow Tan
Chief Technical & Quality Officer

22+ years in Life Science
Pharmacyclics
Collegium Pharmaceutical
Praecis Pharmaceuticals
Ohio State University
Santa Clara University Leavey School of Business, MBA – Finance & Mgmt

Steve Morris MD
Chief Medical Officer Consultant

25+ years in Life Science
HealthChart LLC
Insight Genetics
St. Jude Children's Research Hospital
Board certified internist (Univ. of Texas SW HSC) and medical oncologist (Yale University School of Medicine)

Thorsten Kirschberg
EVP of Chemistry

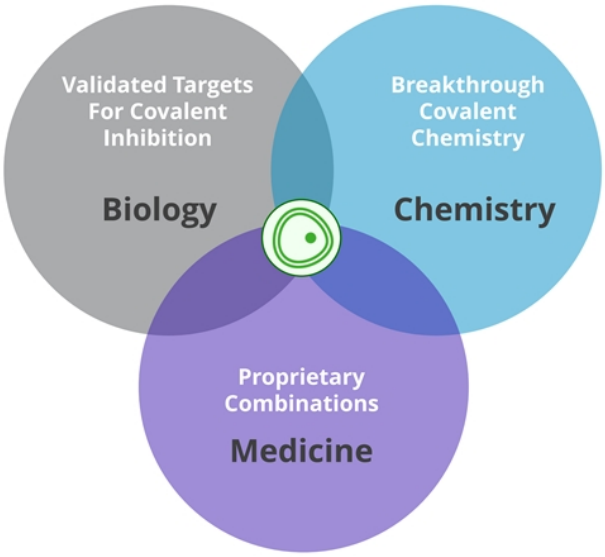
25+ years in Life Science
Terns Pharmaceuticals
Gilead Sciences
Cell Gate
Golden Gate University, MBA
University of Münster, Ph.D., Chemistry

Jim Palmer
VP of Drug Discovery

30+ years in Life Science
Biota Ltd
Cytopia Ltd.
Rigel, Inc.
Celera Genomics
Prototek Inc.
Purdue University
Ph.D. Organic Chemistry

Our Vision – We Are Patient Focused and Aim to Cure

Biomea leverages the FUSION™ Platform to create a suite of novel agents to improve and extend life for patients



Validated Disease Targets

Drugs pursuing validated targets have a ~2x higher likelihood of approval than molecules pursuing a new mechanism of action

Sources: Nelson et al. (2015) Nat Genet.; Thomas et al. (2016) BIO; In a Landscape of 'Me Too' Drug Development, What Spurs Radical Innovation? HBS Weekly Review (Jun 2018)

Irreversible Sm. Mol. Inhibitors

Irreversible covalent inhibitors provide deep target inactivation and a wider therapeutic window, allowing for longer duration on therapy

Sources: Singh et al. (2011) Nature Reviews Drug Discovery; Cheng et al. (2020) Journal of Hematology & Oncology; Strelow (2017) SLAS Discovery; Kalgutkar & Dalvie (2012) Expert Opin. Drug Discov.;

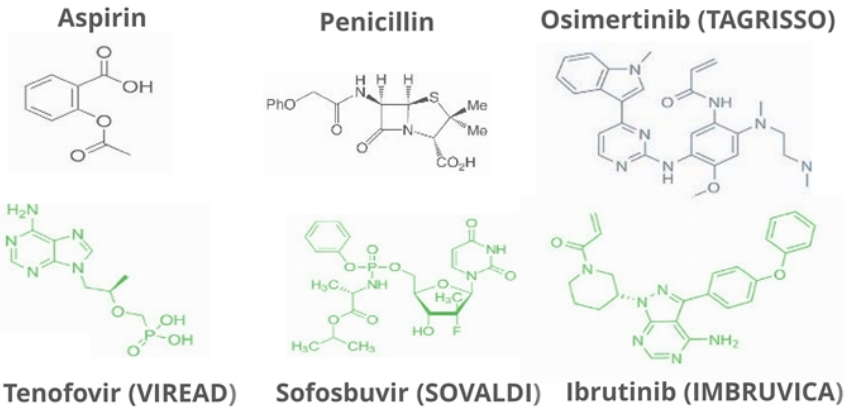
Proprietary Combinations

Combination therapy with non-overlapping resistance mechanisms results in more durable responses and better outcomes

Sources: Palmer et al. (2019) eLife; Mokhtari et al. (2017) Oncotarget

Irreversible Inhibitors Have a History of Medical Success

Notable Irreversible Inhibitors



- **Aspirin** was the first commercialized irreversible drug
- Notable precision oncology and infectious disease programs leverage irreversible mechanisms
  - Precision Oncology**: Osimertinib** and **Ibrutinib** both target kinases and are used in subpopulations with specific genetic biomarkers
  - Antivirals**: Sofosbuvir** and **Tenofovir** both target reverse transcriptases and are leveraged to treat HCV and HIV

Important Attributes of Irreversible Small Molecule Inhibition

High Selectivity

Irreversible inhibitors

- two-step inhibition: 1) requires initial reversible binding followed by 2) covalent interaction, which increases target selectivity
- Greater ligand efficiency provides high selectivity and potency without jeopardizing pharmaceutical properties

Deep Target Inactivation

Irreversible inhibitors

- can cause permanent inactivation of bound protein
- can drive target elimination through normal cellular degradation processes
- can trigger rapid apoptosis or differentiation into normal, mature cells

Greater Therapeutic Window

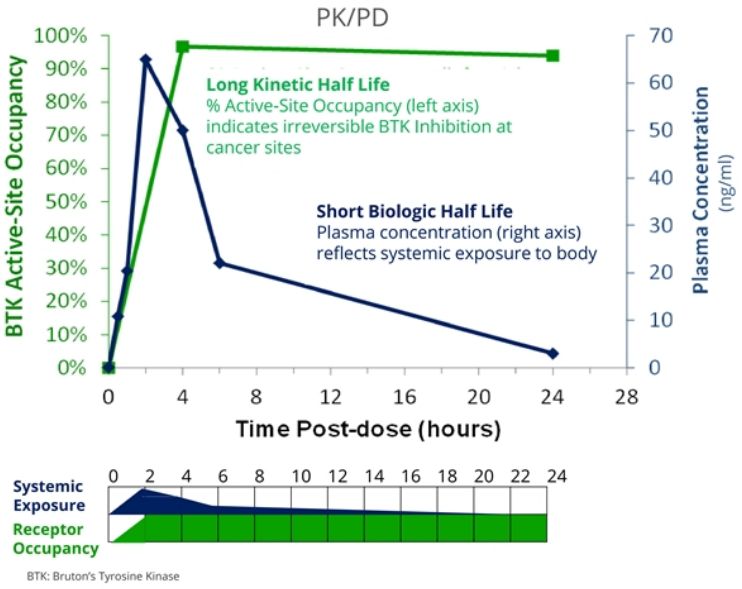
Irreversible inhibitors

- are designed to maintain an effect without sustained systemic exposure, unlike conventional reversible drugs, which typically need to be present to provide benefit
- Uncoupling of drug effects from drug exposure can potentially enable lower drug dosing or less frequent dosing regimens vs. reversible approaches

Benefits of Covalent Irreversible Inhibition

Irreversible inhibitors facilitate prolonged target occupancy effect, without prolonged systemic exposure

Example: Ibrutinib, an Irreversible Inhibitor with Long Kinetic Half Life and Short Biologic Half Life



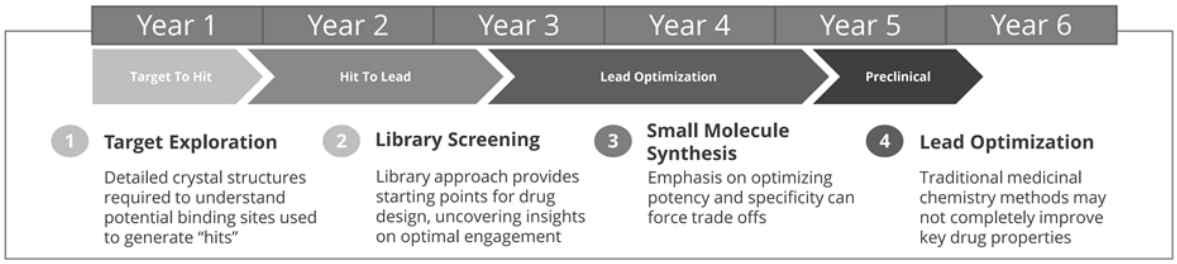
BTK: Bruton's Tyrosine Kinase

- Ibrutinib has a short biologic half life of ~4-6 hrs but **prolonged receptor occupancy**
- Ibrutinib rapidly achieved **high receptor occupancy**, sustained for over 24 hours, **without constant systemic exposure**
- Reversible inhibitors often require constant systemic exposure to maintain occupancy and reach IC_{90}, thereby potentially limiting tolerability

biomea FUSION

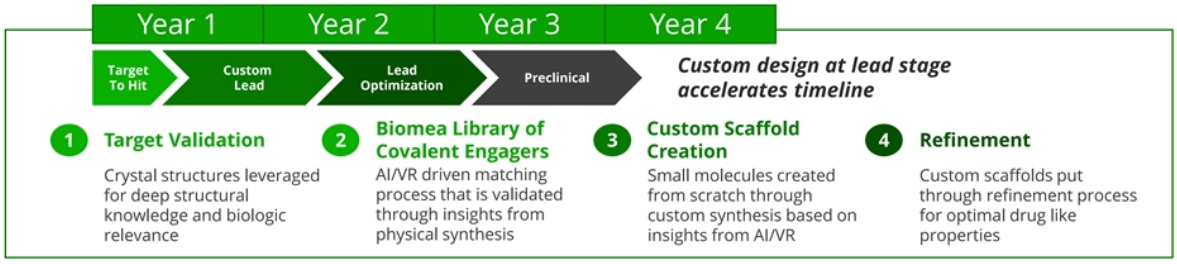
Our Technology Platform – Irreversible Inhibitors

Traditional Small Molecule Design
(Library Screening and Synthesis)



Modified after Insilico Medicine & Paul, S. M.et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Reviews Drug Discovery, 9(3), 203–214.

biomea FUSION
FUSION™ Platform
(AI/VR Matching + Custom Synthesis)

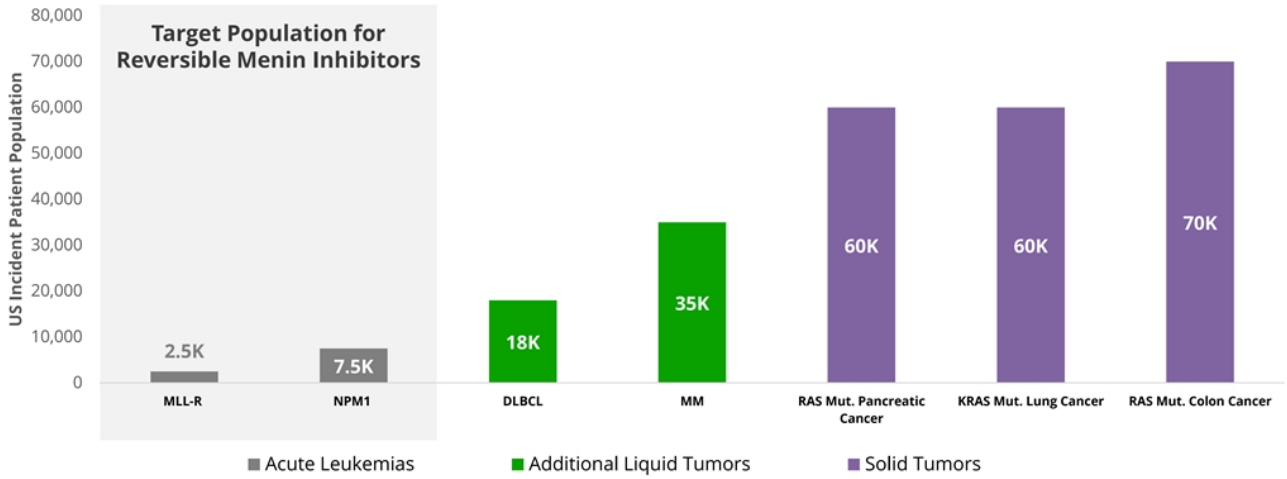


Biomea Pipeline – Pursuing Up to 7 Tumor Types and Diabetes in the Clinic in 2022

	Program	Discovery → IND Enabling → Phase 1 → Phase 2 → Phase 3	Target Population (US Incidence)	Key Milestone
Menin Programs	BMF-219 (Oncology)	*MLL-R & NPM1 Liquid Tumors (AML, ALL)*	2.5K MLL-r; 7.5K NPM1	Patient enrollment
		Additional Liquid Tumors (MM, DLBCL)	~18K DLBCL; ~35K MM	Patient enrollment
		KRAS Solid Tumors (Lung, Pancreatic, CRC)	~60K Lung (KRAS); ~60K Panc. (RAS); ~70K CRC (RAS)	IND filing
	Menin Inhibition (Metabolic)	*Diabetes Mellitus (Type 2, Type 1)*	1.6M Type 1; 25.3M Type 2	Preclinical data presentation at an upcoming meeting
Additional Oncology Programs	Target #2	*Oncology*	N/A Undisclosed	Lead candidate and target announcement
	Target #3	*Oncology*	N/A Undisclosed	Update on progress in 2022

BMF-219 to Pursue Multiple Tumor Types in 2022

Target Patient Population for BMF-219



*Sources: Jovanović, K. K., Roche-Lestienne, C., Ghobrial, I. M., Facon, T., Quesnel, B., & Manier, S. (2018). Targeting MYC in multiple myeloma. Leukemia, 32(6), 1295–1306. https://doi.org/10.1038/s41375-018-0036-x ; Riedell, P. A., & Smith, S. M. (2018). Double hit and double expressors in lymphoma: Definition and treatment. Cancer, 124(24), 4622–4632. https://doi.org/10.1002/cncr.31646; Kempf, E., Rousseau, B., Besse, B., & Paz-Ares, L. (2016). KRAS oncogene in lung cancer: focus on molecularly driven clinical trials. European respiratory review : an official journal of the European Respiratory Society, 25(139), 71–76. https://doi.org/10.1183/16000617.0071-2015; Lanfredini, S., Thapa, A., & O'Neill, E. (2019). RAS in pancreatic cancer. Biochemical Society transactions, 47(4), 961–972. https://doi.org/10.1042/BST20170521; Serna-Blasco, R., Sanz-Álvarez, M., Aguilera, Ó., & García-Foncillas, J. (2019). Targeting the RAS-dependent chemoresistance: The Warburg connection. Seminars in cancer biology, 54, 80–90. https://doi.org/10.1016/j.semcancer.2018.01.016; Park, W., Chawla, A., & O'Reilly, E. M. (2021). Pancreatic Cancer: A Review. JAMA, 326(9), 851–862. https://doi.org/10.1001/jama.2021.13027; NCI SEER Estimated 2021 Incidence <seer.cancer.gov>

BMF-219 – Novel Irreversible Covalent Inhibitor of Menin

Pipeline-in-a-Pill – Single Agent for Multiple Indications

Strong Pathway Control

Large effect on target genes and proteins leading to cell death

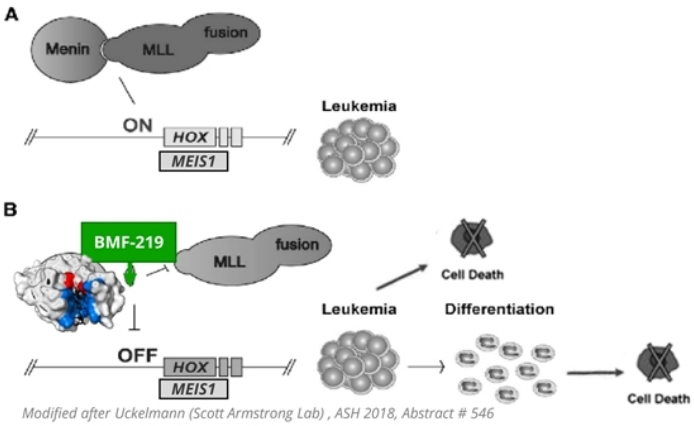
Multiple Shots on Goal

Consistent On-Target Effect

Wide Safety Margin

BMF-219 Shown to Inhibit A Complex Interaction Independent of the MLL Fusion Partner

Role of Menin-MLL Complex



Modified after Uckelmann (Scott Armstrong Lab) , ASH 2018, Abstract # 546

BMF-219: an irreversible covalent inhibitor at the Menin-MLL interface

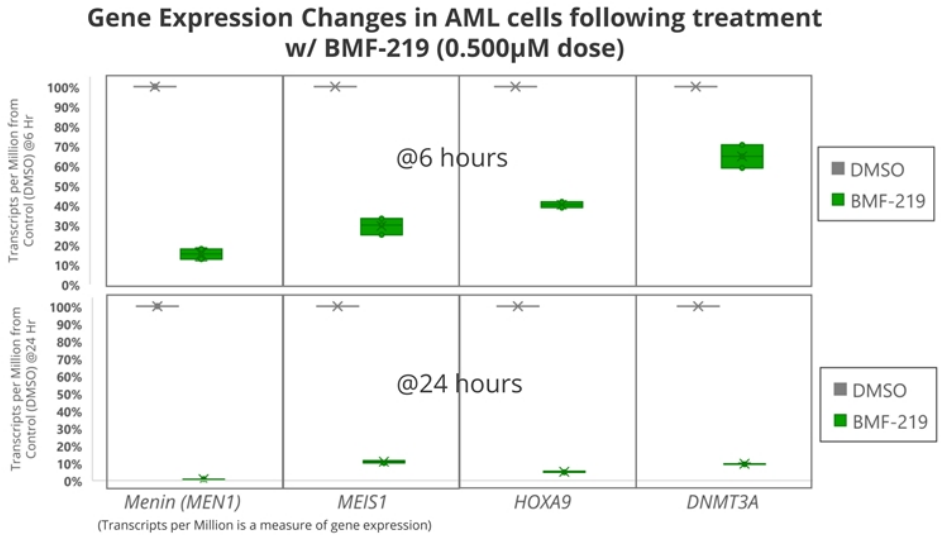
Menin-MLL Fusions

Different fusions result in different binding affinities between MLL fusion proteins and Menin

MLL Fusions (AML/ALL)	Prevalence (%)
AF4	**36%**
AF9	**19%**
ENL	**13%**
AF10	**8%**
ELL	**4%**
PTD	**4%**
...80+ additional fusions	**16%**

Source: Meyer, C. et al. (2017). The MLL recombinome of acute leukemias in 2017. Leukemia, 32(2), 273–284.

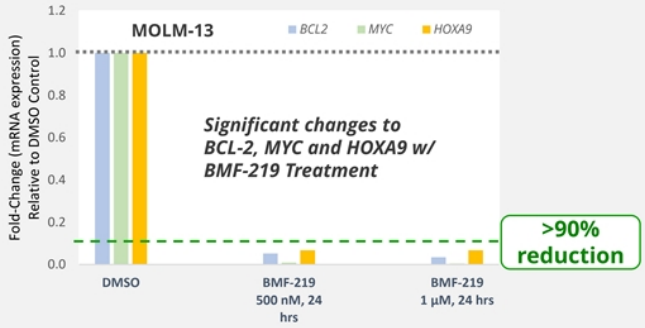
BMF-219 Demonstrated Rapid and Near Complete Reduction of Expression of Oncogenes



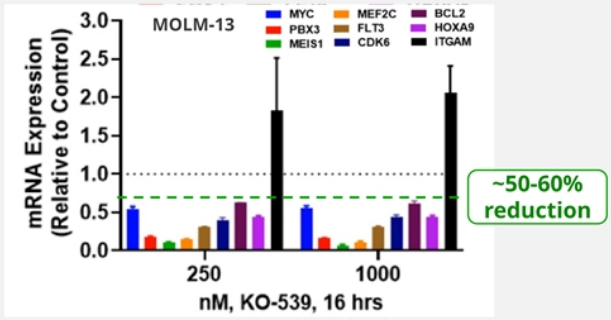
- Irreversible inhibitor, BMF-219, downregulates expression of Menin (via the target *MEN1* gene) and critical leukemogenic genes (e.g. *MEIS1* and *HOXA9*)
  - *MEIS1* is a gene that can be an accelerator of leukemic transformation (along with *HOXA9*)
  - *HOXA9* is a gene involved in myeloid differentiation and can be leukemogenic
  - *DNMT3A* is a gene that codes for a methyltransferase, which can be leukemogenic when mutated
- BMF-219 demonstrated up to 80% reduction in readout genes by 6 hours and approximately 90%+ reduction at 24 hours

BMF-219 Displayed Superior Impact on Key Gene Signatures in MLL-rearranged AML Cell Line

Relative Gene Expression – BMF-219



Relative Gene Expression – Clinical Reversible Inh. (KO-539)



Blood (2021) 138 (Supplement 1): 3357.

- **BCL2 expression was reduced *~20 to 30-fold* at 24 hrs** post-treatment with BMF-219 and remained largely unaltered at 6 hrs post-treatment with BMF-219
- ***HOXA9* expression was reduced *~15-fold* at 24 hrs** post treatment with BMF-219
- ***MYC* expression was reduced *~100-200 fold* at 6 hrs and 24 hrs** post-treatment with BMF-219

BMF-219 – Novel Irreversible Covalent Inhibitor of Menin

Pipeline-in-a-Pill – Single Agent for Multiple Indications

Strong Pathway Control

Multiple Shots on Goal

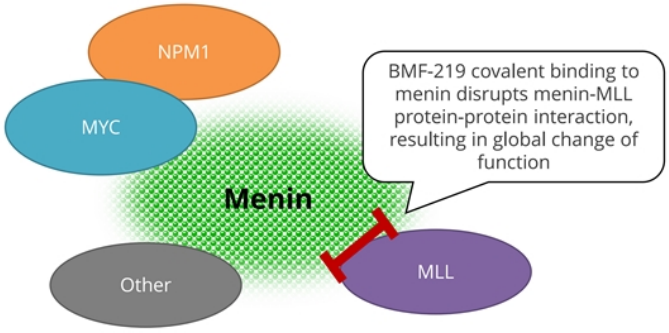
Acute leukemias, MYC addicted and driven cancers, RAS/RAF driven solid tumors

Consistent On-Target Effect

Wide Safety Margin

BMF-219 Has the Potential to Impact Important Binding Partners Involved in Multiple Tumors

Mechanism of Action



Resulting change of function of menin impacts important binding partners involved in oncogenesis

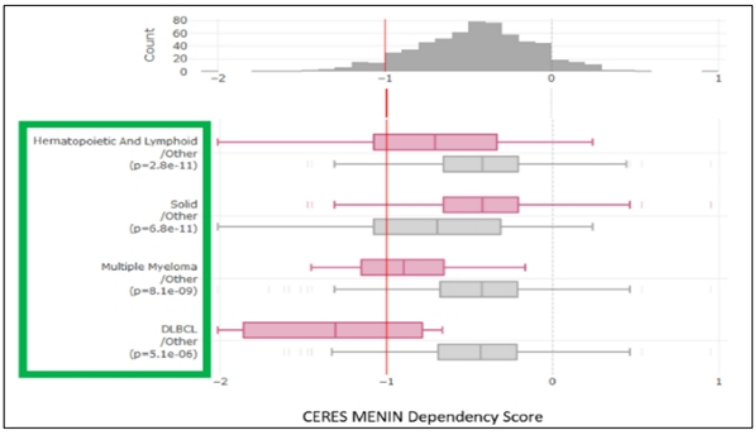
Target Patient Population

MLL-r Acute Leukemia
NPM1 mutant Acute Leukemia
DHT / DEL DLBCL
Multiple Myeloma
KRAS mutant (CRC, Lung, Pancreatic)
Liquid and Solid Tumors

BMF-219 has the potential to address additional patient populations that are dependent on menin or some of its binding partners

Acute Leukemia, DLBCL, MM, & Other Tumor Types Have High Menin Dependency Based on Broad Institute DEPMAP Dataset

BROAD Institute Cancer Dependency Map (DEPMAP) for Menin (*MEN1*)

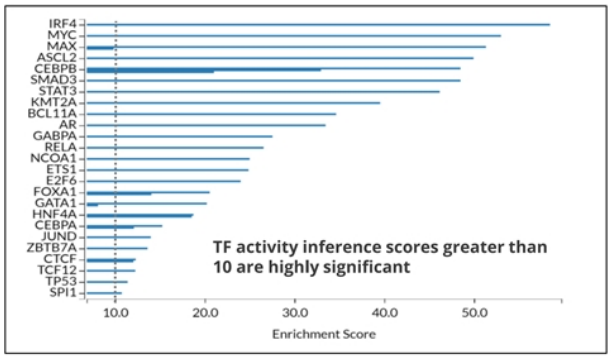


Note: CERES MENIN Dependency scores less than -1 in various tumor types imply that menin is considered essential for cell survival in those tumor types

- Cell viability scores have shown that **menin plays a key role in survival of multiple tumors**
- **High menin dependency in liquid and solid tumors,** beyond acute leukemias, provides rationale for further analysis in dependent tumor types
- Biomea is exploring the potential for **irreversible inhibition of menin in a variety of liquid and solid tumor types**

BMF-219 Shown to Disrupt MYC Genomic Function via Broad Impact on the Complexes Surrounding Menin

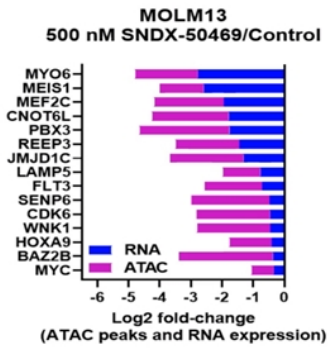
Irreversible Covalent Menin Inhibitor – BMF-219



TF activity inference using ChIP-seq of differentially expressed genes in MOLM-13 cells incubated with 500 nM BMF-219 at 24 hours. Each bar represents a study in the GEO repository using the specified TF antibody.

- **In MOLM-13 cells treated with BMF-219, the top transcription factors regulating gene expression are MYC and MAX**
- IRF4, MYC, and MAX are known drivers for some forms of DLBCL, (addicted) multiple myeloma, and multiple additional tumors

Reversible Menin Inhibitor – SNDX-50469



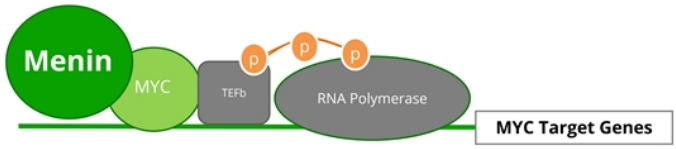
***Blood* (2021) 138 (Supplement 1): 3340.**

- **Significantly less impact on *MYC* expression** (2x fold) and genomic function by clinical reversible menin inhibitor
- In contrast, **BMF-219 treatment led to a ~100-200x reduction in *MYC*** expression at 24 hours

Menin is a Key Node for MYC and KRAS Addicted Tumors

MYC is constitutively and aberrantly expressed in over 70% of human cancers

MYC transcriptional complex facilitates expression of oncogenesis via MYC target genes



Source: *Madden et al., Molecular Cancer volume 20, Article number: 3 (2021); Martínez-Martín et al. Cancer Drug Resist 2021;4:842-65; Xia Y. et al., Acta Haematol 2020;143:520–528; Zhu L., et al. (2017).. Nat. Commun. 8, 15278.; Musti et al., Oncogene . 2002 Sep 19;21(42):6434-45.*

KRAS Mutant Solid Tumors

- **Menin regulates downstream pathways associated with KRAS signaling, including MYC,** MAPK/ERK, and JunD
- ~30% of newly diagnosed NSCLC have a KRAS mutation
- ~97% of pancreatic cancer patients have a RAS mutation
- ~45% of CRC patients have a RAS mutation

Multiple Myeloma (MM)

- **MYC addiction increases with stage and line of therapy**
- ~20-50% MYC dysregulation or translocations in newly diagnosed MM patients
- ~50-70% of advanced r/r MM patients have MYC dysregulation

Diffuse Large B-Cell Lymphoma (DLBCL)

- Double and Triple Hit and Double expressors (BCL2 and MYC overexpression) DLBCL represents ~40% of patients
- **>50% of relapsed/refractory DLBCL are double expressors**

Sources: Jovanović, K. K., Roche-Lestienne, C., Ghobrial, I. M., Facon, T., Quesnel, B., & Manier, S. (2018). Targeting MYC in multiple myeloma. Leukemia, 32(6), 1295–1306. https://doi.org/10.1038/s41375-018-0036-x ; Riedell, P. A., & Smith, S. M. (2018). Double hit and double expressors in lymphoma: Definition and treatment. Cancer, 124(24), 4622–4632. https://doi.org/10.1002/cncr.31646; Kempf, E., Rousseau, B., Besse, B., & Paz-Ares, L. (2016). KRAS oncogene in lung cancer: focus on molecularly driven clinical trials. European respiratory review : an official journal of the European Respiratory Society, 25(139), 71–76. https://doi.org/10.1183/16000617.0071-2015; Lanfredini, S., Thapa, A., & O'Neill, E. (2019). RAS in pancreatic cancer. Biochemical Society transactions, 47(4), 961–972. https://doi.org/10.1042/BST20170521; Serna-Blasco, R., Sanz-Álvarez, M., Aguilera, Ó., & García-Foncillas, J. (2019). Targeting the RAS-dependent chemoresistance: The Warburg connection. Seminars in cancer biology, 54, 80–90. https://doi.org/10.1016/j.semcancer.2018.01.016

biomea FUSION

BMF-219 – Novel Irreversible Covalent Inhibitor of Menin

Pipeline-in-a-Pill – Single Agent for Multiple Indications

Strong Pathway Control

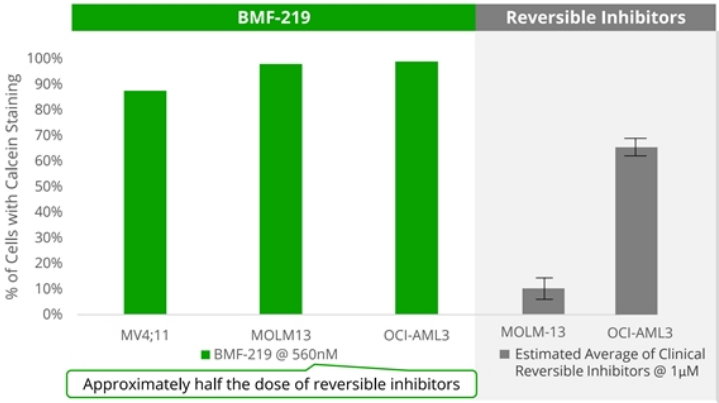
Multiple Shots on Goal

Consistent On-Target Effect

Pathway control and cell killing seen at same predicted dose across indications

Wide Safety Margin

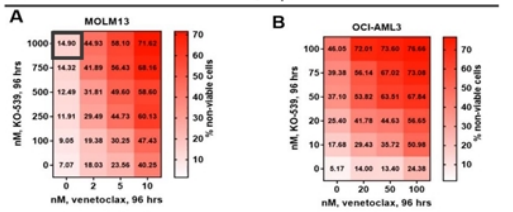
BMF-219 Exerted Superior Cell Killing of AML Cell Lines at Half the Dose



- **BMF-219 killed >90% of AML cells in MLL-rearranged and NPM1 mutant cell lines at 4 days post-treatment**
- **Reversible menin inhibitors generally report significantly less cell killing of AML cell lines as a single agent**

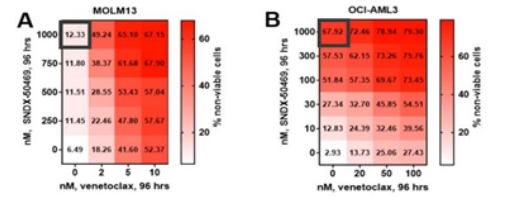
Source Data from ASH 2021 Publications

KO-539 is 15% effective @ 1µM in MOLM-13 cells



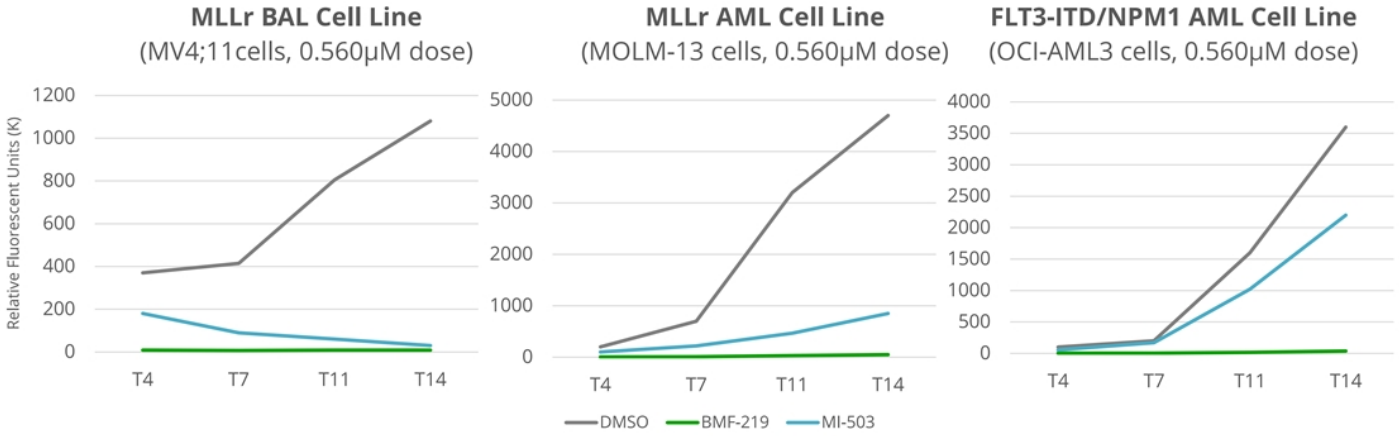
Blood (2021) 138 (Supplement 1): 3357. ASH, 2021.

SNDX-50469 is 12% effective @ 1µM in MOLM-13 cells



Blood (2021) 138 (Supplement 1): 3340., ASH 2021.

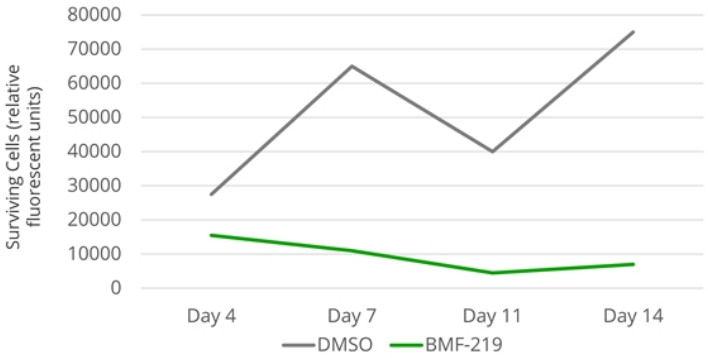
BMF-219 Produced Near Complete Inhibition of Growth at 0.560µM Across Acute Leukemia Cell Lines



- BMF-219 demonstrated rapid shut down of metabolic activity, sustained over the 14-day study duration
- BMF-219 responses were superior to a tested reversible menin inhibitor (MI-503) with respect to both onset and durability of metabolic suppression

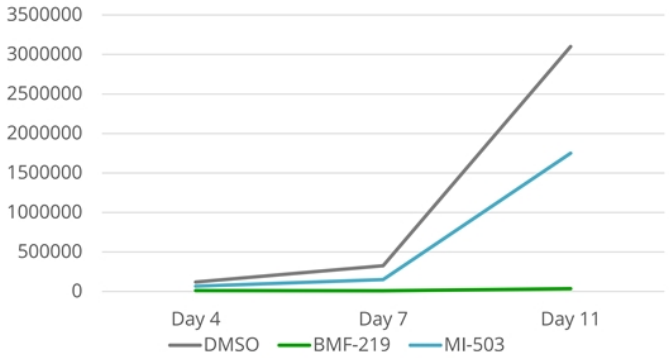
BMF-219 Produced Near Complete Inhibition of Growth at 0.560µM in Multiple Myeloma and KRAS Solid Tumor Cell Lines

Multiple Myeloma Cell Viability
(KMS-20 cells, 0.560µM dose)



Impairment of survival in multiple myeloma model (KMS-20 cell line, 0.56µM doses) by irreversible menin inhibitor BMF-219

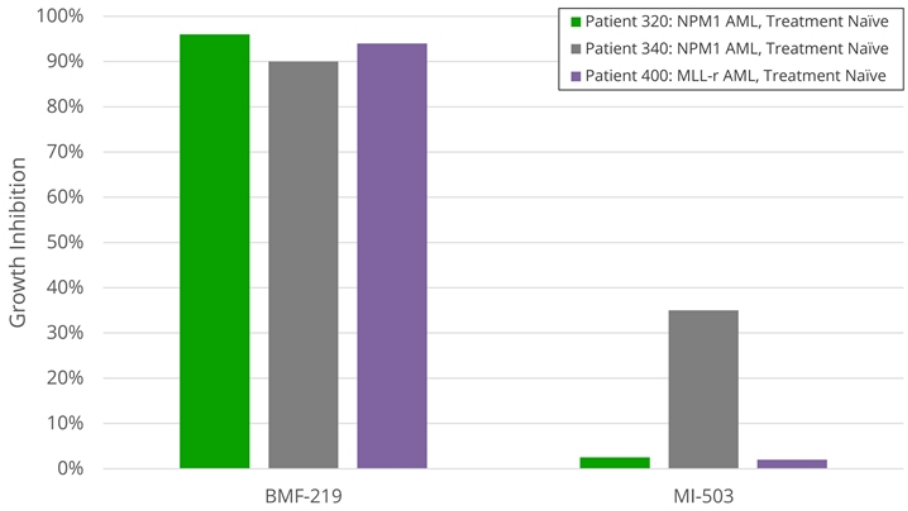
KRAS Pancreatic Cancer Viability
(MIA-PaCa--2 cells, 0.560µM)



Impairment of survival in G12C KRAS mutation driven pancreatic cancer model (MIA-PaCa-2, 0.56µM doses) by irreversible menin inhibitor BMF-219 versus a reversible menin inhibitor (MI-503)

BMF-219 Produced Near Complete Inhibition of Growth at 1µM in AML ex-vivo Samples

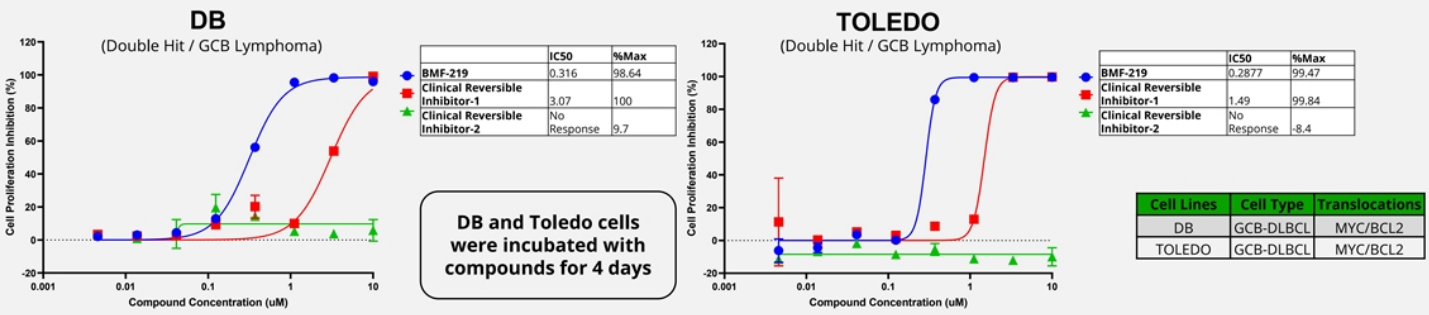
Growth Inhibition of ex-vivo AML Cells from Patients (1µM Exposure)



- 1µM exposure of BMF-219 produces robust growth inhibition in both NPM1 and MLL-R ex-vivo cell lines
- BMF-219 responses were superior to a tested reversible menin inhibitor, MI-503, with respect to cell growth inhibition

BMF-219 Produced Near Complete Inhibition of Growth at 1µM in DLBCL Cell Lines

BMF-219 Growth Inhibition in DLBCL Cell Lines, ASH 2021



	IC50	%Max
BMF-219	0.316	98.64
Clinical Reversible Inhibitor-1	3.07	100
Clinical Reversible Inhibitor-2	No Response	9.7

	IC50	%Max
BMF-219	0.2877	99.47
Clinical Reversible Inhibitor-1	1.49	99.84
Clinical Reversible Inhibitor-2	No Response	-8.4

DB and Toledo cells were incubated with compounds for 4 days

Cell Lines	Cell Type	Translocations
DB	GCB-DLBCL	MYC/BCL2
TOLEDO	GCB-DLBCL	MYC/BCL2

Source: *Blood* (2021) 138 (Supplement 1): 4318. ASH, 2021.

- Irreversible menin inhibition by BMF-219 led to marked growth inhibition in multiple DLBCL cell lines
- We believe this is due to disruption of Menin-MYC
- One of the clinical stage reversible menin inhibitors tested displayed activity, but at 5-10x higher concentration
- The other clinical reversible inhibitor did not achieve IC50 in the tested cell lines at any concentration tested

BMF-219 – Novel Irreversible Covalent Inhibitor of Menin

Pipeline-in-a-Pill – Single Agent for Multiple Indications

Strong Pathway Control

Multiple Shots on Goal

Consistent On-Target Effect

Wide Safety Margin

Strong preclinical safety profile from animal studies

BMF-219 Was Highly Selective in Key Screening and Safety Panels

No Histopathology Findings Were Observed with BMF-219 in GLP and non-GLP Toxicology Studies

Kinase screening

- **169 kinases screened**; only **two** wild type kinases showed greater than 50% inhibition upon treatment with BMF-219
- In-house analysis of menin revealed no relevant structural similarity between targeted binding pocket and tyrosine kinases with known involvement in hematological cancers

Glutathione reactivity

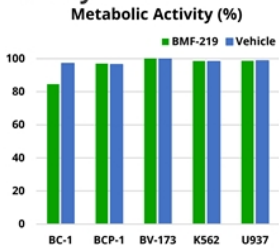
Drug	Mean half-life (min)
Omeprazole	123.3
Neratinib	197.7
Ibrutinib	>360
BMF-213	322.3
BMF-214	>360
BMF-219	>360

- Drugs with limited non-specific interactions have long half-lives
- BMF-219 had **less reactivity than the approved irreversible drugs omeprazole and neratinib** based on the results from the study

Oncopanel screening

- **Minimal impact** of BMF-219 treatment on cell metabolism in leukemia and lymphoma cell lines that have **wild type MLL**, but no menin-linked mechanism for disease
- Findings are consistent with external studies, showing that **menin-MLL interaction is not generally cell-essential and only critical to survival in those cells that contain aberrant biology**

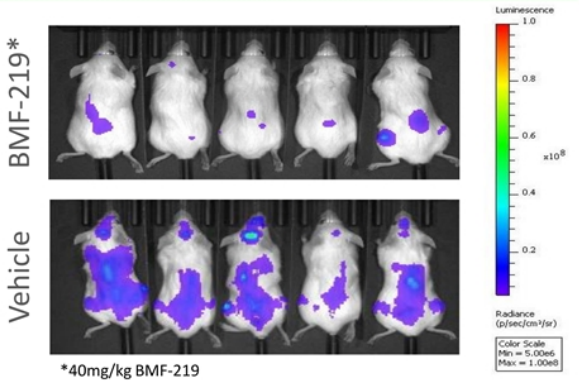
Safety screen



- BMF-219 was also profiled on the **SafetyScreen44** panel (CEREP/Eurofins Discovery), an *in-vitro* panel of 44 common selected targets to identify significant off-target interactions
- Findings showed **no meaningful impact** (greater than 50% activation or inhibition) of BMF-219 across these key safety assays

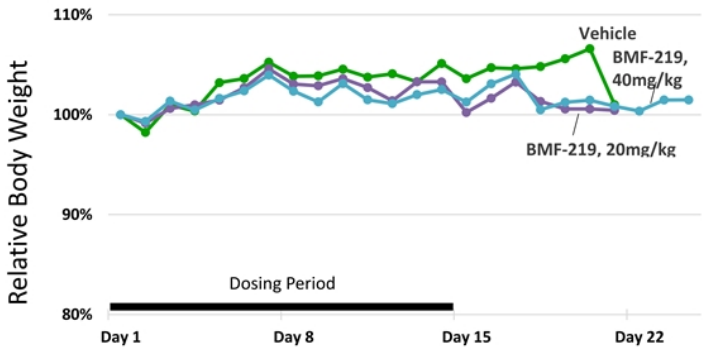
BMF-219 Achieved Significant Survival Benefit in A Disseminated Leukemia Xenograft Model

Anti-Tumor Effect



*40mg/kg BMF-219

Body Weight



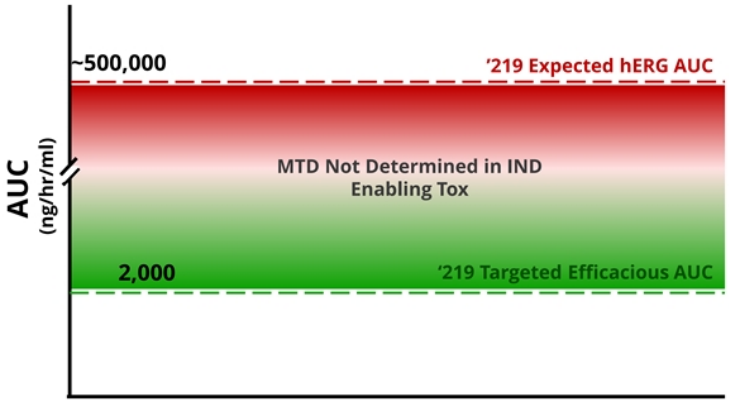
- Mice were inoculated with xenograft cancer cells at high levels ($1x10^7$ MV4;11-luc) with greater than 90% viability
- BMF-219 treatment showed notable reduction in tumor burden and **survival benefit over vehicle control (72% at 20mg/kg and 94% at 40mg/kg)**
- Daily dosing for 14 days was well-tolerated and caused **minimal body weight changes**

BMF-219: Next Generation Irreversible Covalent Menin Inhibitor

BMF-219: A Molecule That Really Grabs You and Won't Let Go

BMF-219 Properties	
Molecular Weight Approximately 500 kD	✓
Nanomolar Potency in Key Targeted Cell Lines:	
MLL-r	✓
NPM1 FLT3-ITD	✓
DLBCL MYC Driven Tumors	✓
MM	✓
KRAS Mutants (pan mutation)	✓
hERG inhibition ~5% at 10 µM	✓
Significant Downregulation of *HOXA9, MEN1, and MYC*	✓
No Histopath Findings in IND Enabling Tox Studies	✓

Predicted Efficacious Human AUC for BMF-219



BMF-219 → Next Generation Menin Inhibitor

Attacks the target by forming a covalent bond (irreversible inhibitor)

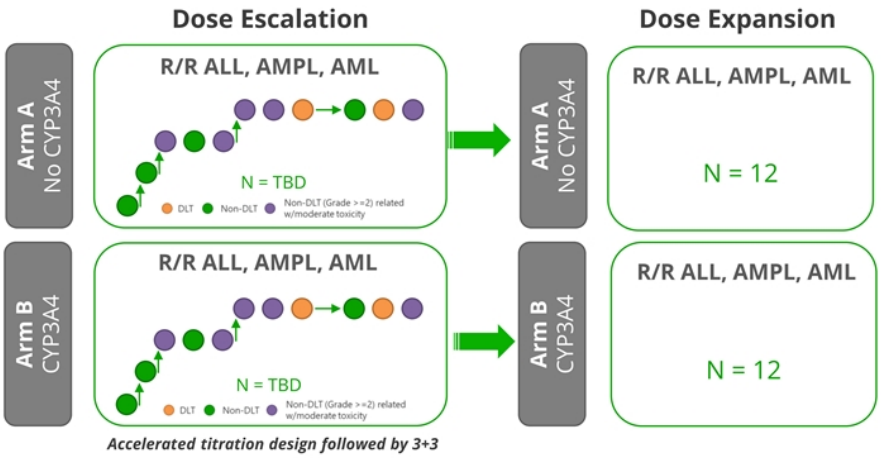
Challenges of 1st Gen Menin Inhibitors	Solutions Offered by BMF-219
Poor PK/PD Properties (Inefficient Pharmacology)	Efficient Pharmacology (Target AUC/Daily Exposure) Leading to Wider Therapeutic Window
Limited impact on Key Gene Signaling (*MEN1, HOXA9, MYC*) at Clinically Achievable Dose Levels	Significant Impact on *MEN1, HOXA9, and MYC*
Focused on Menin-MLL Disruption For AML/ALL	Broad Tumor Type Impact via MYC Inhibition (ALL, AML, DLBCL, MM, RAS activated Solid Tumors)
Poor impact on Cell Viability in Key Leukemia Sub-Types	Deep Tumor Impact Across Multiple Tumor Types (ALL, AML, DLBCL, MM, RAS activated Solid Tumors)
Dose Limiting Cardiac Toxicity	Minimum Impact on hERG at 10uM (at ≥10x the Targeted Clinical Dose Level)
Single Agent CR Rate @ 6-month ~10%	**TBD - Currently Enrolling Patients**

Complete Remission (CR) is defined as: Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC ≥1.0 X 10^9/L (1,000/μL); platelet count ≥100 X 10^9/L (100,000/ μL)

BMF-219 Phase I Study in r/r Acute Leukemia Patients

Phase I first-in-human dose-escalation and dose-expansion study of BMF-219 enrolling adult patients with acute leukemia, including those with an MLL/KMT2A gene rearrangement or NPM1 mutation

Phase I Study Design



Accelerated titration design followed by 3+3

Eligibility:

- All patients:
  - R/R ALL, AMPL, AML agnostic of mutation
  - > 18 years

Endpoints:

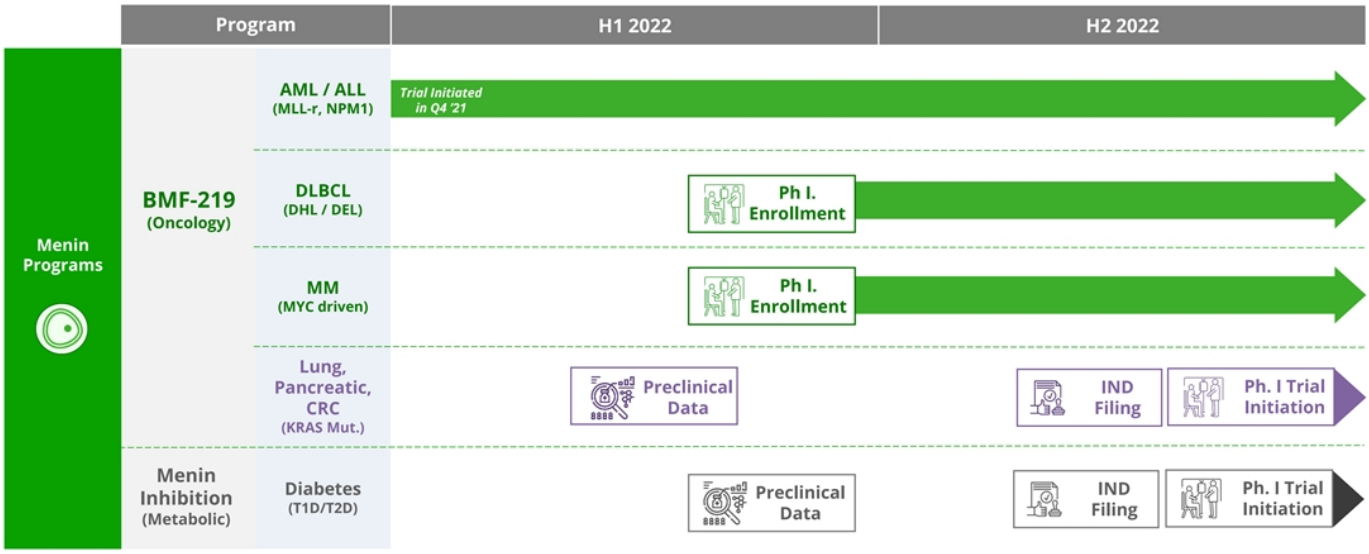
- Phase I: Safety, PK, determine the Optimal Biological Dose and the Recommended Phase II Dose

Treatment:

- BMF-219 will be administered orally daily

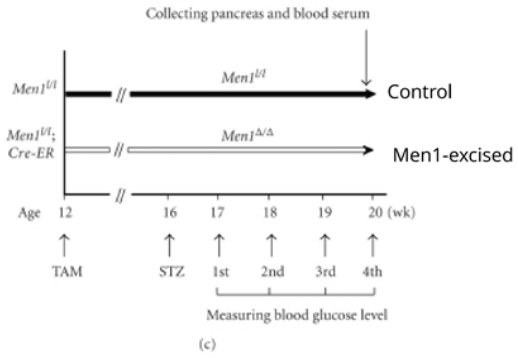
Abbreviations: **ALL** Acute Lymphoblastic Leukemia **AML** Acute Myeloid Leukemia **AMPL** Acute Mixed Phenotype Leukemia **CRR** Complete Response Rate **CYP3A4** Cytochrome 450 3A4 **DLT** Dose Limiting Toxicity **FIH** First-in-human **KMT2A** Lysine Methyltransferase 2A **MLL** Mixed Lineage Leukemia **MLLr** Mixed Lineage Leukemia-rearranged **NPM1** Nucleophosmin 1 **PO** Administered by Mouth **PK** Pharmacokinetic **R/R** Relapsed/Refractory **RP2D** Recommended Phase 2 Dose **TEAE** Treatment Emergent Adverse Event

Clinical Study Plan – Enrolling up to 7 Tumor Types and Diabetic Patients in 2022

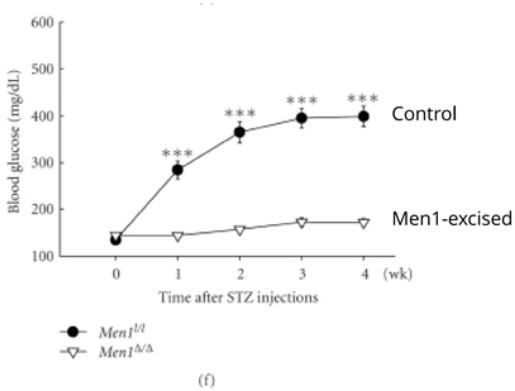


Potential for Menin Inhibition Demonstrated by Beta Cell Ablation Diabetes Model in MEN1 Excised Mice

MEN1 Excision Prevents Development of Streptozotocin (STZ)-induced Hyperglycemia



Multiple low-dose streptozotocin (MLD-STZ) administered to the control and *Men1*-excised mice to induce beta cell damage and a diabetes-like environment



***Men1*-excised mice did not develop hyperglycemia in STZ model, which was observed in the control group**

Sources: Yang et al. (2010) Deletion of the Men1Gene Prevents Streptozotocin-Induced Hyperglycemia in Mice. Experimental Diabetes Research, 2010, 1–11. doi:10.1155/2010/876701

BMF-219 Ameliorated Diabetes in Animal Models

Results

BMF-219 was able to normalize glucose levels in the majority of animals after just two weeks of treatment. The majority of the effect was maintained despite complete washout of BMF-219

Preclinical data support BMF-219 as an oral, long-acting treatment for diabetes

Experiments

Zucker Diabetic Fatty (ZFD) Rat

- **Model works to decrease beta cell counts and induce insulin resistance in male rats**
  - While males develop diabetes, Female rats do not develop diabetes

STZ-Induced Rat

- **Model inhibits production of insulin by beta cells in addition to inducing beta cell death**
  - High dose models lead to rapid ablation of beta cells and hyperglycemia while low dose models lead to less pronounced reduction in beta cells and insulin secretion

Next Steps

Engage with the FDA in Q1 2022 and File IND by H2 2022

Conduct Additional Translational Work

Submit Data for 2022 Conference Publication

Sources: King, A. J. (2012). The use of animal models in diabetes research. British Journal of Pharmacology, 166(3), 877–894; Willcox, A., Richardson, S. J., Bone, A. J., Foulis, A. K., & Morgan, N. G. (2010). Evidence of increased islet cell proliferation in patients with recent-onset type 1 diabetes. Diabetologia, 53(9), 2020–2028.

Biomea Fusion – *WE AIM TO CURE*

- **Established FUSION platform technology for discovery of irreversible covalent inhibitors**
- **Lead molecule (BMF-219) with best-in-class potential and favorable safety profile**
- **Initiate studies with BMF-219 in up to 7 tumor types (liquid and solid) in 2022**
- **Significant addressable market and scarcity of effective treatment options for clinically targeted tumor types**
- **IND enabling work in progress for diabetic patients**
- **Capitalized into 2024**

Near Term Milestones – Biomea Fusion (NASDAQ: BMEA)

BMF-219 – Liquid Tumors

IND Clearance	Completed
DLBCL Preclinical ASH 2021 Abstract	Completed
Enrolling Phase I Study in AML/ALL	In Progress
Additional Preclinical Data in DLBCL/MM	H1 2022
BMF-219 Phase I DLBCL/MM Trial Initiation	H1 2022

BMF-219 – Solid Tumors

Additional Preclinical Data in KRAS Mutant Tumors	H1 2022
IND Filing	H2 2022
BMF-219 Phase I KRAS Mutant Trial Initiation (Pancreatic, Lung, Colorectal)	Q4 2022

Menin Inh. – Diabetes

Diabetes Menin Pathway Validation	H1 2022
IND Filing	H2 2022
Phase I Diabetes Trial Initiation	H2 2022

Additional Programs

2nd Pipeline Candidate Announced	H1 2022
3rd Pipeline Candidate Announced	To Be Announced

Company Financials

Detailed Financials (unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Operating expenses:				
R&D	$ 7,886	$ 789	$ 16,908	$ 1,339
G&A	$ 4,752	$ 346	$ 10,022	$ 489
Total Operating Expenses	$ 12,638	$ 1,135	$ 26,930	$ 1,828
Loss from operations	$ (12,638)	$ (1,135)	$ (26,930)	$ (1,828)
Interest and other income, net	$ 32	—	$ 73	$ 2
Net loss	$ (12,606)	$ (1,135)	$ (26,857)	$ (1,826)
Other comprehensive loss:				
Changes in unrealized gain on short term investments, net	—	—	$ 2	—
Comprehensive loss	$ (12,606)	$ (1,135)	$ (26,855)	$ (1,826)
Net loss per common share, basic and diluted	$ (0.43)	$ (0.10)	$ (1.21)	$ (0.18)
Weighted-averaged number of common shares used to compute basic and diluted net loss per common share	29,001,213	11,724,100	22,105,321	10,082,667

$192M

Cash, cash equivalents, and investments as of the end of Q3 2021


Thank You
biomea
FUSION