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

FORM 8-K

Biomea Fusion, Inc.
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 11, 2021

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.)**

650 Main Street **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 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 November 11, 2021, the Company posted an updated corporate slide presentation in the "Investors & Media" portion of its website at *www.biomeafusion.com*. A copy of its 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 November 2021
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: November 15, 2021

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 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 clinical trials, the actions or potential action of the FDA, the status and timing of ongoing research, 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.

OUR MISSION is to...

revolutionize current medicine by creating and developing novel single agent and combination therapies that maximizes patient benefit

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. Our discovery team is engaged in all phases of development, including target selection, small molecule design, and preclinical and clinical studies to develop innovative medicines

Our Team

Experienced and successful team designed, discovered, and developed breakthrough therapies

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

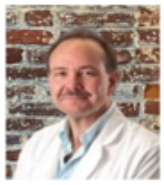
15 years in Life Science
Eidos Therapeutics
Iovance Biotherapeutics
Pharmacyclics
CallidusCloud
PricewaterhouseCoopers
San Jose State University, BS
Corporate Finance

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 Scientific Advisory Board

Bruce Lipshutz PhD
Professor of Chemistry
UCSB

40+ year academic career
Ph.D.: Yale University

- Developing new technologies to assist with the transition of organic chemistry to a sustainable discipline, focusing on both chemo- and bio-catalysis, all done in water.

Urte Gayko, PhD
SVP, Drug Dev. & Reg. Affairs Nektar Therapeutics

20+ years industry experience at Amgen, Nodality, Pharmacyclics, AbbVie, Nektar
Ph.D.: Harvard University

- Currently SVP at Nektar. Prior roles at AbbVie (Global Head of Regulatory Affairs), Pharmacyclics (SVP, Regulatory Affairs), Nodality, (VP of Regulatory and Clinical Affairs), Amgen (Director Global Regulatory Leader and Program Manager).

Dave Ball PhD
Professor of Chemistry
CSUC

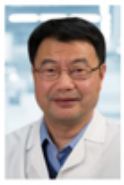
40+ year academic career
Ph.D.: UCSB

- Research has focused on novel synthesis of organic compounds including activators of PKC, and analogs of indolactam V.

Rohit N. Kulkarni, M.D., Ph.D.
Professor of Medicine
Harvard Medical School
Joslin Diabetes Center &
Broad Institute

20+ year academic and clinical career
M.D. and Ph.D.: St. John's Medical College and the Royal Postgraduate Medical School in London

- Dr.Kulkarni's academic work explores growth factor signaling mechanisms in the regulation of human islet biology, and pathways that allow regeneration of beta cells in type 1 diabetes.
- Translational work includes creating genetic and knockout models to examine the roles of various drivers of diabetes and insulin homeostasis.



Xianxin Hua, M.D., Ph.D.
Professor of Cancer Biology
University of Pennsylvania

20+ years academic and clinical career

- Dr. Hua has over 100 publications with more than 50 in the field of menin biology.
- Dr. Hua's lab has investigated the critical role and mechanism for the Menin pathway in a wide variety of biological and physiological functions, including epigenetic regulation of gene transcription, beta cell signaling and proliferation, neuro-endocrine tumors , colorectal cancer (CRC), and AML.
- He has also investigated how inhibition of menin by small molecules inhibitors influences beta cell proliferation and dysregulation of metabolism in colorectal cancer (CRC) cells.

David Smith, Ph.D.
Biostatistician; Former BOD Pharmacyclics

20+ years in academics, NIH/FDA, Industry

- David Smith, Ph.D. was a board member of Pharmacyclics. Prior to Pharmacyclics, he was a senior biostatistician at City of Hope and served as a Biostatistical Reviewer for the Division of Oncology Drug Products, U.S. Food and Drug Administration ("FDA") for 3 years. During his tenure at FDA, he reviewed more than 40 chemotherapy INDs and NDAs.

Jeffery Rubnitz, M.D., Ph.D.
Director, Leukemia / Lymphoma Division
St. Jude Children's Research Hospital

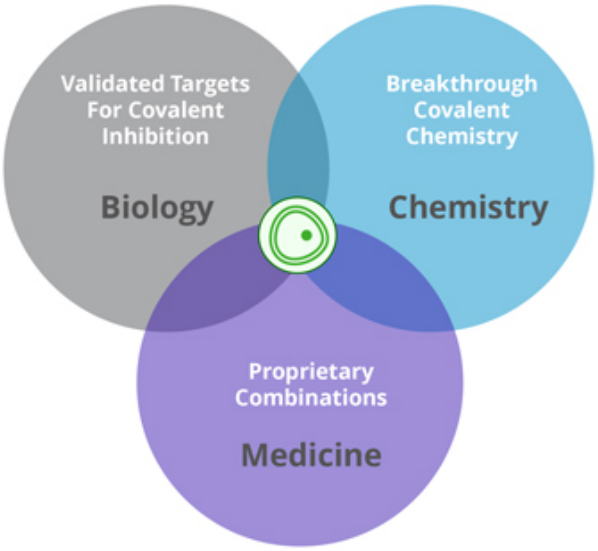
20+ years as academic and clinician
M.D. and Ph.D.: UCSD School of Medicine

- Dr. Rubnitz's academic work at St Jude explores the potential for developing new strategies for the treatment of acute myeloid leukemia (AML). Prior to St. Jude, Dr. Rubnitz completed his pediatrics residency and heme/onc fellowship at Stanford Children's Hospital.

biomea FUSION

Our Vision – We Aim to Cure

Biomea leverages the FUSION™ Platform to create a suite of novel agents to maximize the depth and durability of response



Validated Disease Targets

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

Source: 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 inhibitors provide deep target inactivation and a large therapeutic window, allowing for longer duration on therapy

Source: Singh et al. (2011) Nature Reviews Drug Discovery; Cheng et al. (2020) Journal of Hematology & Oncology;

Proprietary Combinations

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

Source: Strelow (2017) SLAS Discovery; Kalgutkor & Dalvie (2012) Expert Opin. Drug Discov.; Palmer et al. (2019) eLife; Mokhtari et al. (2017) Oncotarget

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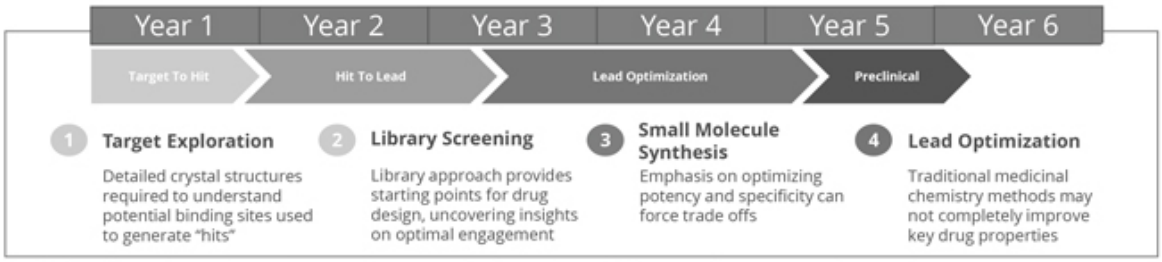
Our Technology Platform

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.

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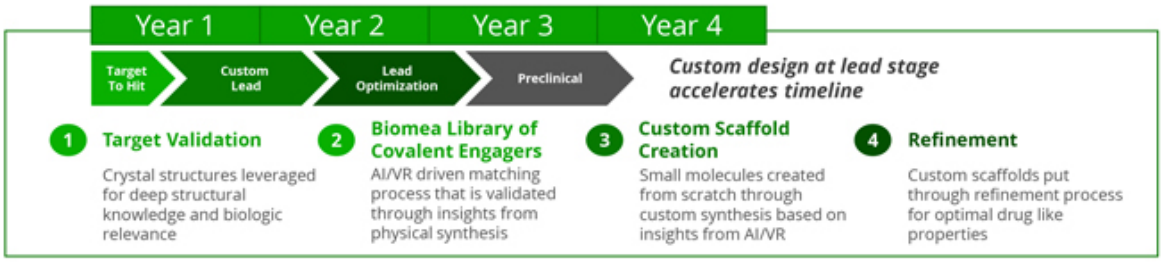
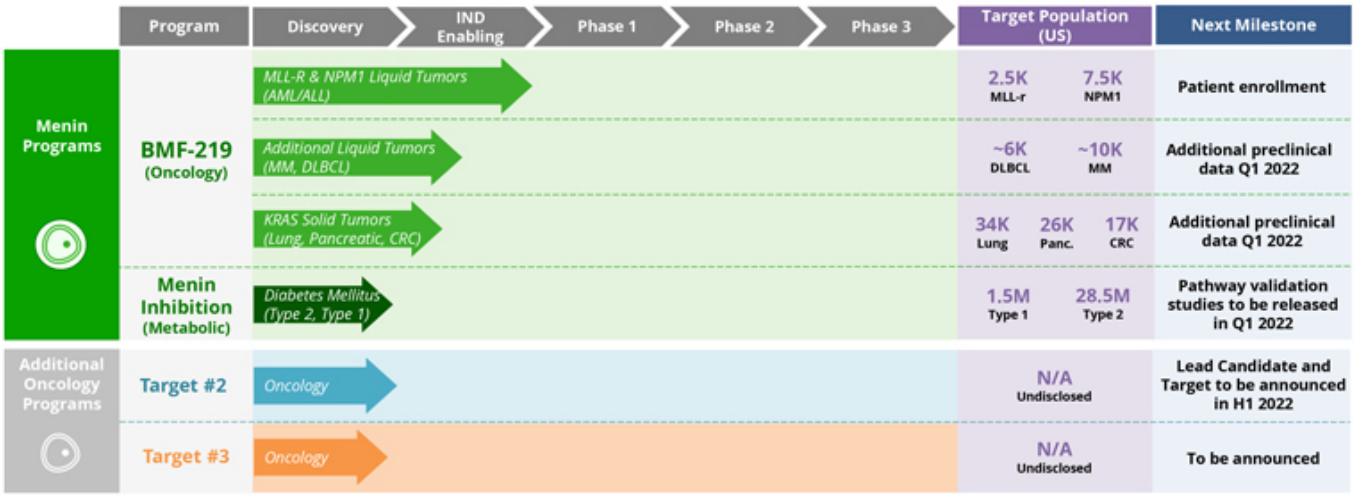
FUSION™ Platform
(AI/VR Matching + Custom Synthesis)



Biomea Pipeline

A suite of novel agents in multiple cancer indications and metabolic disease



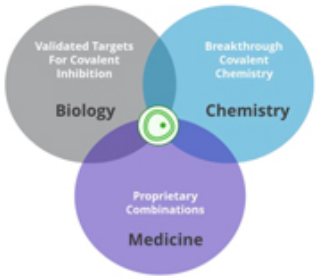
Biomea's Value Proposition

Team	Vision	Platform	Pipeline

pharmacyclics
An AbbVie Company

GILEAD

IOVANCE
BIOTHERAPEUTICS



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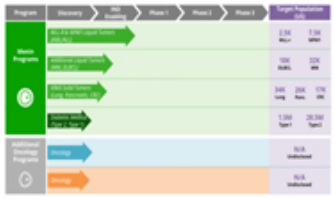
FUSION™ Platform
(AI/VR Matching + Custom Synthesis)

Target To Hit → Custom Lead → Lead Optimization



Execution
Experience designing and developing leading small molecule drugs

Strategy
Combining validated biology and proven chemistry to optimize therapeutic value

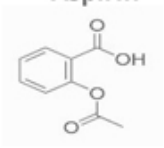
Process
Leveraging our platform with non-traditional drug design for continuous discovery of novel agents

Value Creation
Developing best-in-class covalent inhibitors for underserved indications

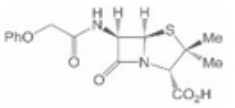
Irreversible Inhibitors Have a History of Medical Success

Notable Irreversible Inhibitors

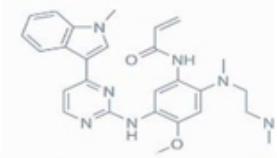
Aspirin

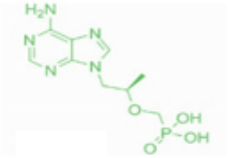


Penicillin

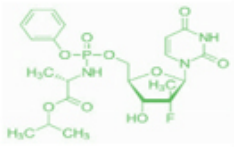


Osimertinib (TAGRISSO)

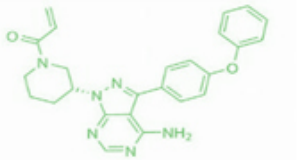




Tenofovir (VIREAD)



Sofosbuvir (SOVALDI)



Ibrutinib (IMBRUVICA)

- **Aspirin** was the first commercialized irreversible drug
  - Discovered in 1899, Aspirin is the most utilized drug in the world
- 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 Benefits of Irreversible Small Molecule Inhibition

Biomea only develops optimized irreversible small molecule inhibitors due to their favorable properties

High Selectivity

- Irreversible drugs have non-covalent and covalent interactions, which increase target selectivity
- Unlike reversible inhibitors, irreversible drugs can achieve high selectivity and potency without jeopardizing pharmaceutical properties
- High selectivity reduces non-specific, off-target interactions that often lead to safety and tolerability challenges

Deep Target Inactivation

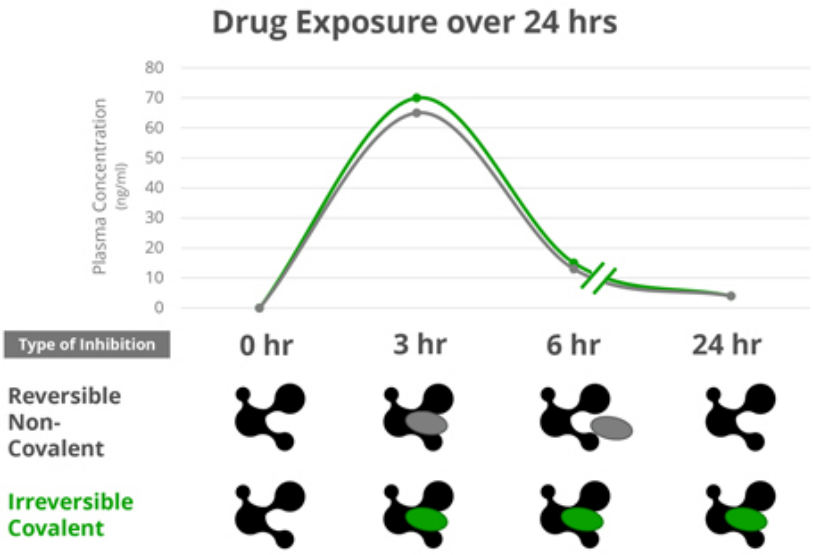
- Irreversible inhibitors can cause permanent inactivation of bound protein
- Irreversible binding may result in the target elimination through normal cellular degradation processes
- Target inactivation can trigger rapid apoptosis or differentiation into a normal, mature cell

Greater Therapeutic Window

- Irreversible drugs are designed to maintain their effect in the absence of sustained systemic drug 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 and less frequent dosing regimens versus reversible approaches

Irreversible Inhibition Enables Large Therapeutic Window

Irreversible small molecule inhibitors have uncoupled drug effect from drug exposure, resulting in more optimal PD/PK profile that maximizes target engagement



Irreversible drugs:

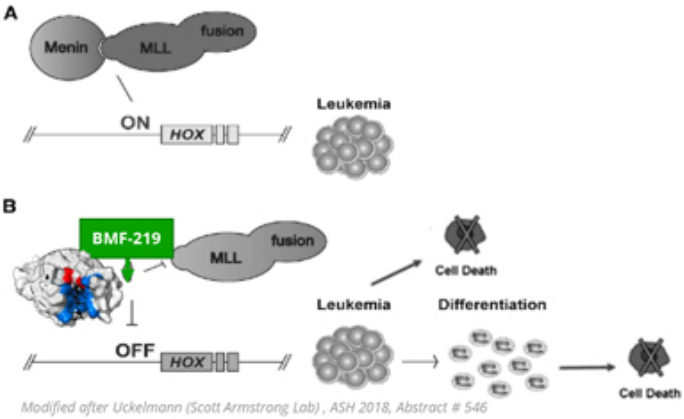
- Can quickly achieve nearly **complete and sustained occupancy** (long kinetic half-life)
- Drive high specificity via engaging a **single amino acid** within the target
- Designed with a short biologic half-life to **minimize systemic off target toxicity**

Thus, **IC_{90}** may be **reached and maintained with relatively low exposure**

Sources: Cheng, S.-S. et al, (2020). The design and development of covalent protein-protein interaction inhibitors for cancer treatment. Journal of Hematology & Oncology, 13(1).; Strelow, J. M. (2016). A Perspective on the Kinetics of Covalent and Irreversible Inhibition. SLAS DISCOVERY: Advancing Life Sciences R&D, 22(1), 3–20.

Menin-MLL: A Complex Interaction

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

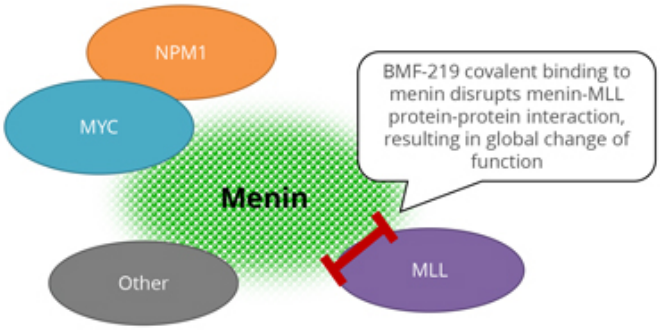
Different fusions result in different binding affinities between MLL fusion proteins and Menin

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 Impacts More than MLL Driven Tumors

Mechanism of Action



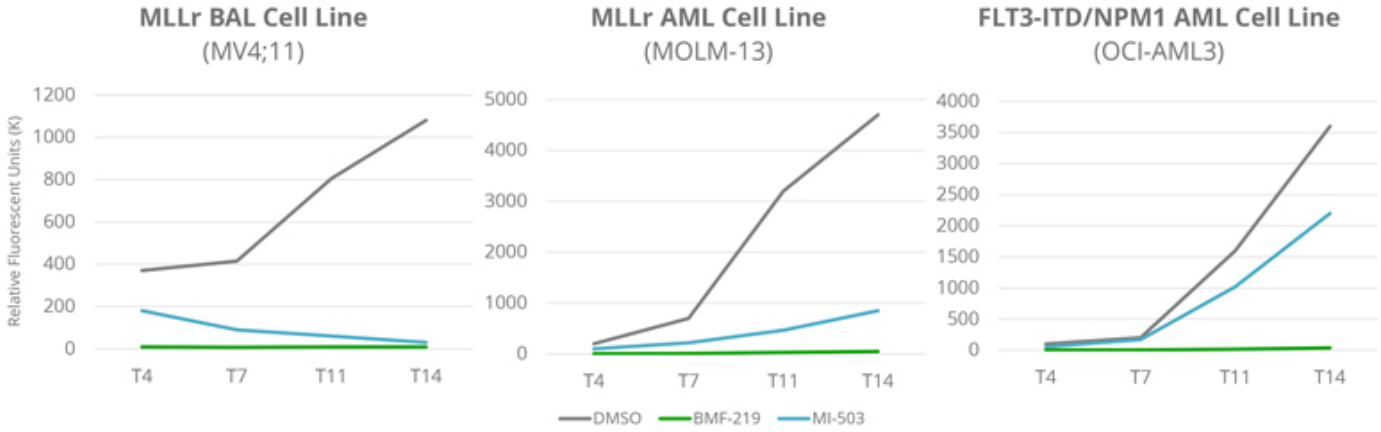
Resulting change of function of menin impacts important binding partners involved in oncogenesis

Target Patient Population

- MLL — **MLL-r Acute Leukemia**
- NPM1 — **NPM1 mutant Acute Leukemia**
- MYC — **DHT / DEL DLBCL**
- MYC — **Multiple Myeloma**
- MYC — **KRAS mutant (CRC, Lung, Pancreatic)**
- Other — **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

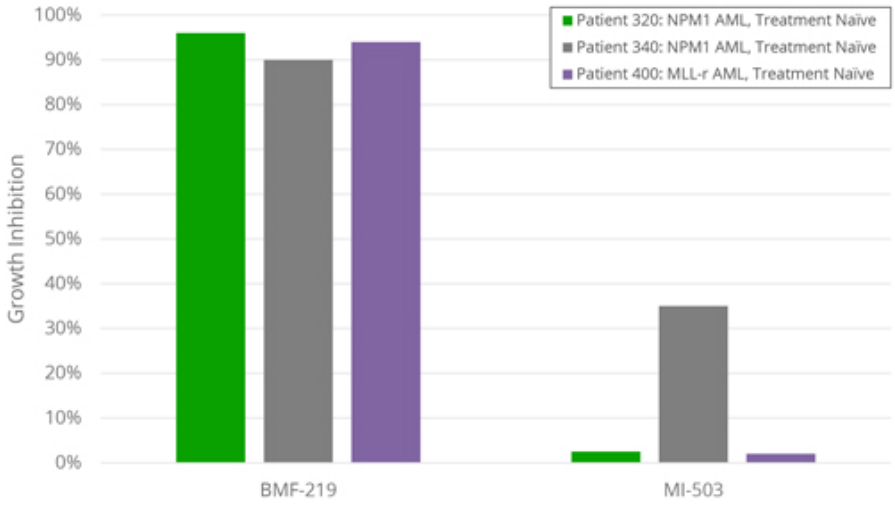
BMF-219 Shows Strong Cell-Growth Inhibition Across Menin Dependent Cell Lines



- 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 Produces Near Complete Inhibition of Growth in AML ex-vivo Samples

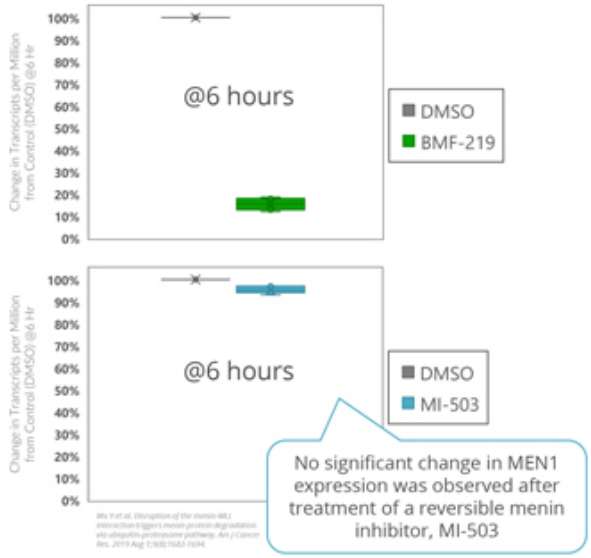
Growth Inhibition of Ex-Vivo AML Cells from Patients (1µM Exposure)



- 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 Shuts Down Target Gene – MEN1

MEN1 Gene Expression Decreases w/ BMF-219 Treatment



No significant change in MEN1 expression was observed after treatment of a reversible menin inhibitor, MI-503

Menin Half Life Varies By Compartment

Half Life in Cytoplasm: <1hr

Half Life in Nucleus: 6-8 hrs

Menin's half-life in nucleus is most relevant for pharmacological intervention

- BMF-219 produces **robust decrease in expression of target protein** (Menin)
- **Effect continues beyond established nuclear half-life** of menin, indicating robust effect that is not impacted by protein turnover

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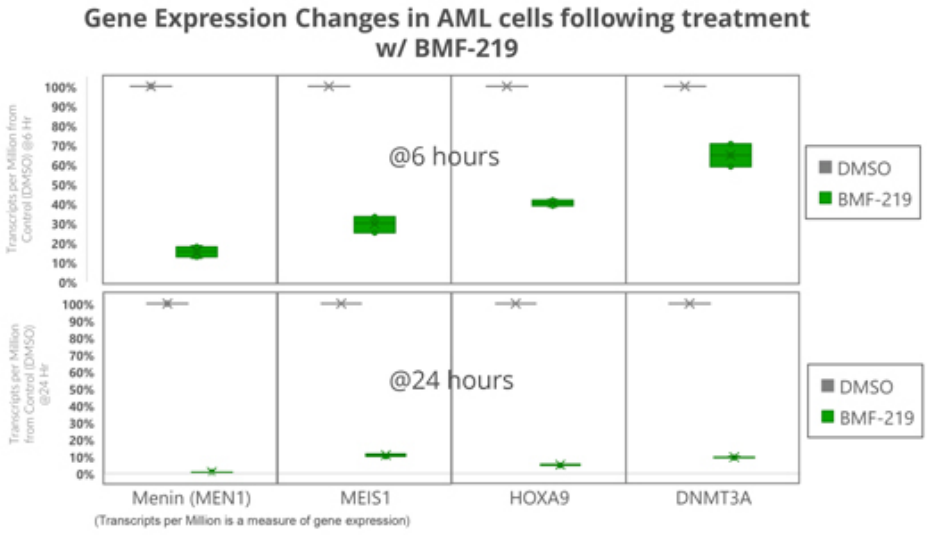
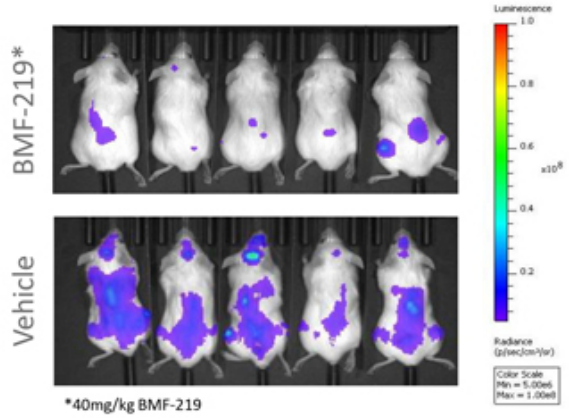
BMF-219 Shuts Down Gene Expression of Oncogenes

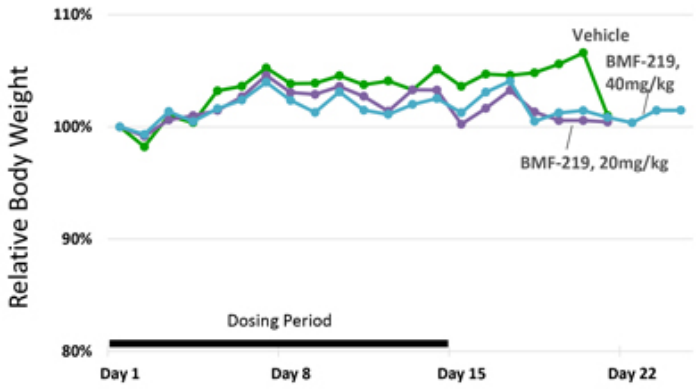


- Irreversible inhibitor, BMF-219, downregulates expression of Menin (via the target MEN1 gene) and critical leukemogenic genes (e.g. MEIS1 and HOXA9)
  - MEIS1 is a gene that can be an accelerator of leukemic transformation (along with HOXA9)
  - HOXA9 is a gene involved in myeloid differentiation and 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 Showed Significant Survival Benefit in a Disseminated Leukemia Xenograft Model vs. Standard of Care

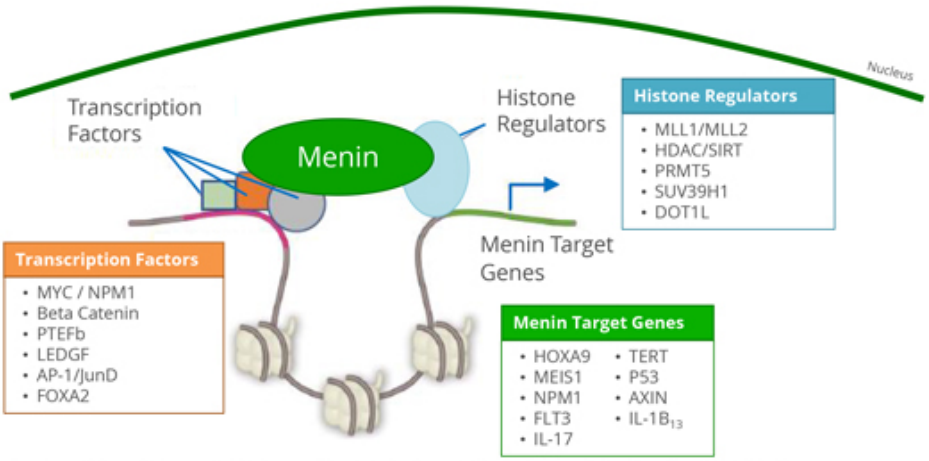


*40mg/kg BMF-219



- 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

Menin Can Play a Key Role in the Regulation of Oncogenesis



Modified after Issa, G. C., et al. (2021). Therapeutic implications of menin inhibition in acute leukemias. Leukemia, 35(9), 2482–2495.

AML/ ALL Implications
- MLLr
- NPM1
- FLT3
- MYC

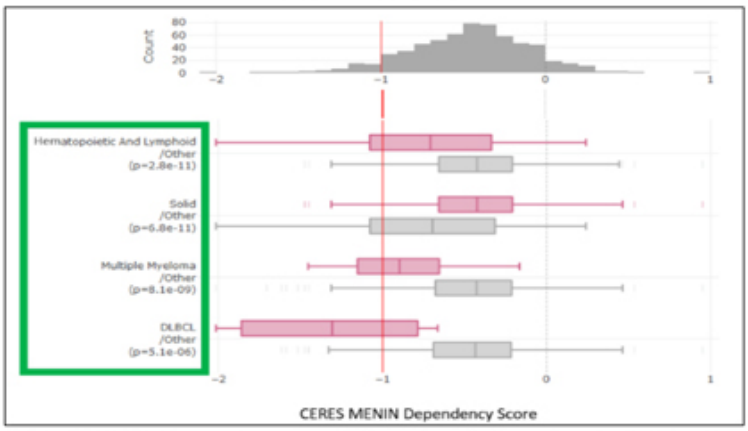
DLBCL MM Implications
- MYC
- BCL2
- CREB
- PI3K/MTOR

Solid Tumors Implications
- MAPK/KRAS
- MYC
- CDK

DLBCL, MM, & Other Tumors Have High Menin Dependency

Double knock-out of MEN1 via Broad Institute's DEPMAP dataset shows that menin is essential for a wide variety of tumor types, including DLBCL, MM, leukemias and lymphomas

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



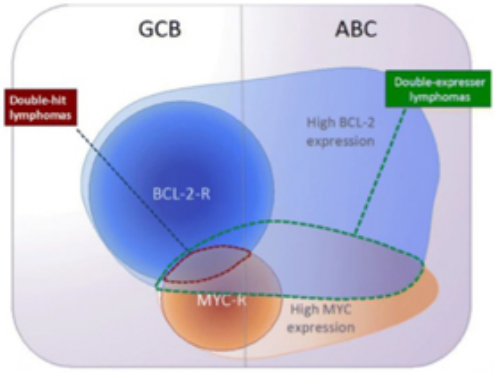
Note: CERES MENIN Dependency scores less than -1 in various tumor types imply that menin is considered essential for cell survival in those tumor types

- 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**

Menin is Critical for MYC-dependent Aggressive DLBCL

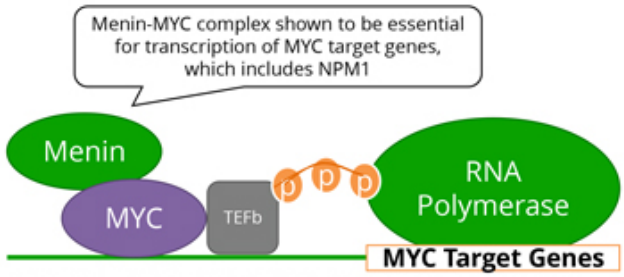
MYC is a transcription factor implicated in oncogenesis. MYC regulates genes associated with cellular proliferation, differentiation, and apoptosis

MYC Overexpression Is a Critical Factor For Highly Aggressive DLBCL Subtypes



Source: Cabanillas, F., & Shah, B. (2017). Advances in Diagnosis and Management of Diffuse Large B-cell Lymphoma. Clinical Lymphoma Myeloma and Leukemia, 17(12), 783–796.

Menin is Critical for Expression of MYC Target Genes



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

BMF-219 Elicits Broad Impact on the Complexes Surrounding Menin. Resulting in Strong Modulation of MYC Driven Expression

BMF-219 Transcription Activity Inference Data

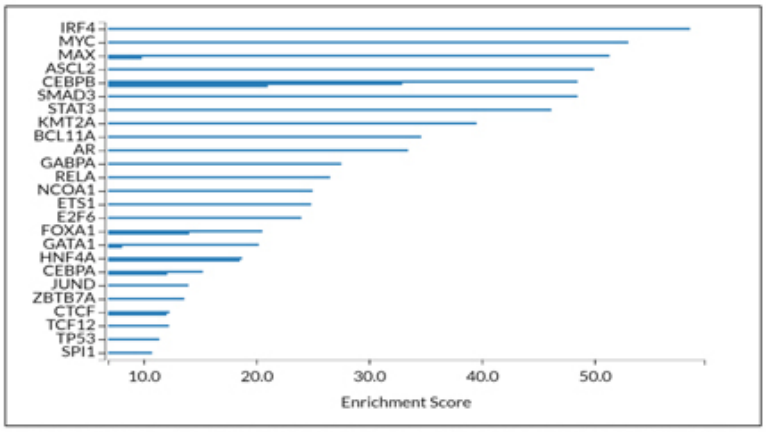
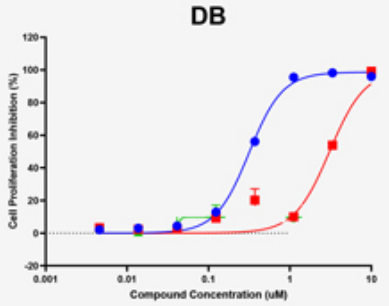


Figure: Transcription factor (TF) activity inference using ChIP-seq of differentially expressed genes in MOLM-13 cells incubated with 500 nM BMF-219 at 24 hours. Each bar represents a study in the GEO repository using the specified TF antibody. TFs with more than one bar represent multiple study sets in GEO that overlap with BMF-219 mediated differentially expressed genes. MYC and MAX are top TFs regulating this subset of differentially expressed genes ($p=10^{-49.3}$). Established menin co-factors (KMT2A, JUND) also emerged as top candidates in this dataset.

- **MYC and co-factor MAX emerged** as top candidates based on the analysis
- **KMT2A and JUND**, which are known menin co-factors, also **emerged as top candidates** in the analysis
- These results strongly point toward **altered MYC-activity mediated by BMF-219 in leukemia cells** and provided **rationale for pursuing MYC-dependent lymphoid malignancies**

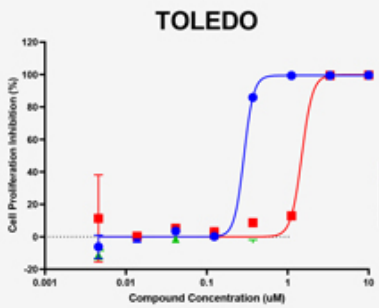
BMF-219 Inhibits Growth in Double Hit DLBCL Cell Lines. Providing Initial Validation of Anti-Cancer Activity Beyond AML

BMF-219 Growth Inhibition in DLBCL Cell Lines



	IC50	%Max
BMF-219	0.316	98.64
Clinical Reversible Inhibitor-1	3.07	100

DB and Toledo cells were incubated with compounds for 4 days

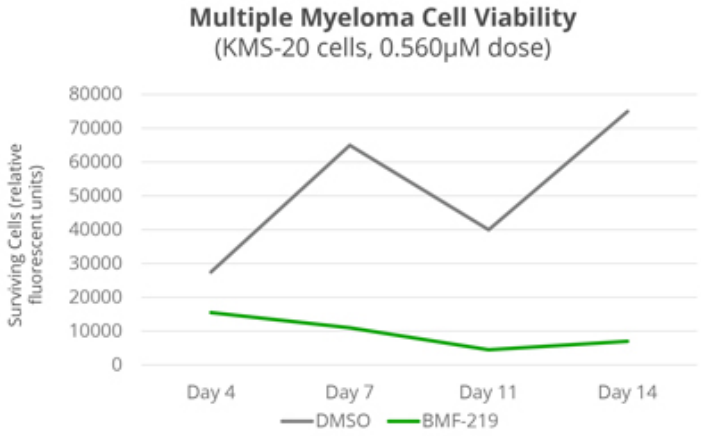


	IC50	%Max
BMF-219	0.2877	99.47
Clinical Reversible Inhibitor-1	1.49	99.84

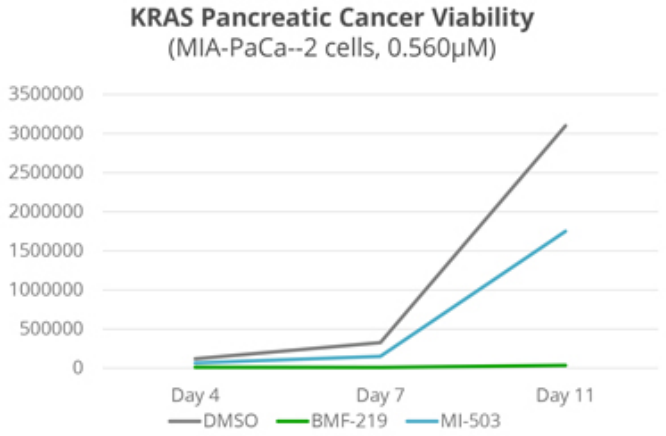
Cell Lines	Cell Type	Translocations
DB	GCB-DLBCL	MYC/BCL2
TOLEDO	GCB-DLBCL	MYC/BCL2

- Irreversible menin inhibition by BMF-219 leads 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 displays activity, but at 5-10x higher concentration

BMF-219 Impairs Growth in Multiple Myeloma and KRAS Solid Tumor Cell Lines



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



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 is Highly Selective In Key Screening and Safety Panels

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

Oncopanel screening

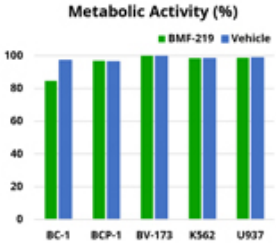
- Minimal impact of BMF-219 treatment on cell metabolism in leukemia and lymphoma cell lines that have wild type MLL, but no menin-linked mechanism for disease
- Findings are consistent with external studies, showing that menin-MLL interaction is not generally cell-essential and only critical to survival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

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 less reactivity than the approved irreversible drugs omeprazole and neratinib

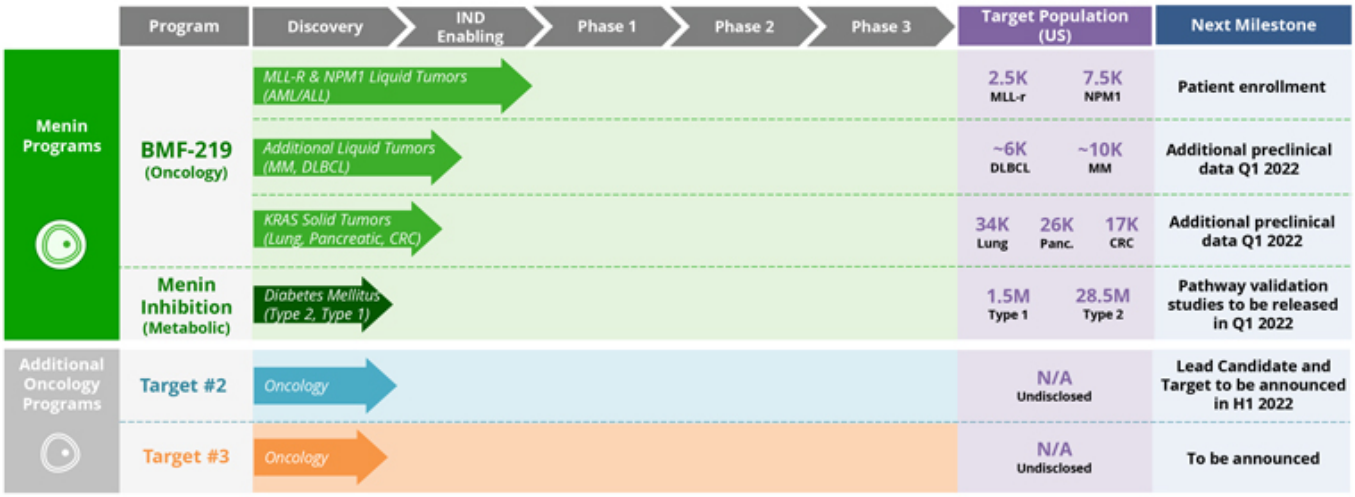
Safety screen



- 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

Biomea Pipeline

A suite of novel agents in multiple cancer indications and metabolic disease

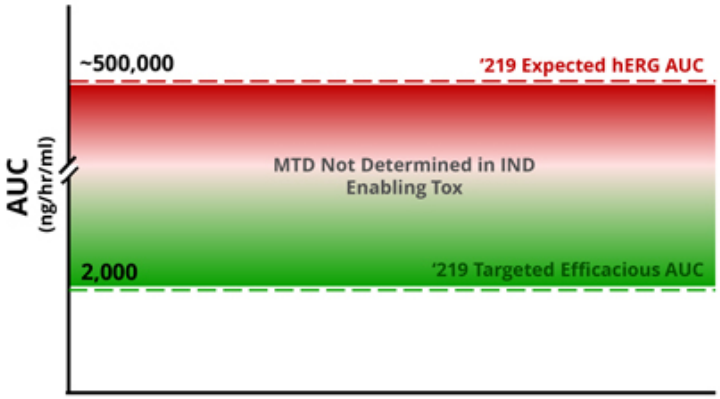


BMF-219: Biomea's Covalent Menin Inhibitor

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	✓

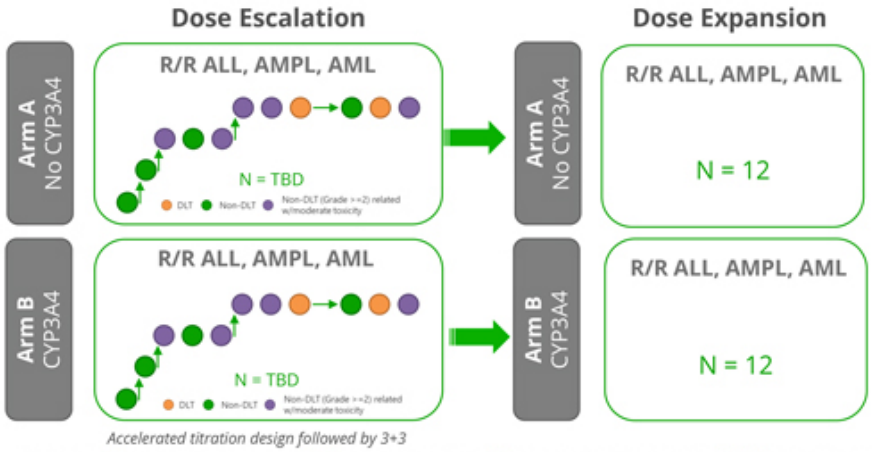
Predicted Efficacious Human AUC for BMF-219



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

Phase I first-in-human dose-escalation and dose-expansion study of BMF-219 will enroll 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

Additional Study Details

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:

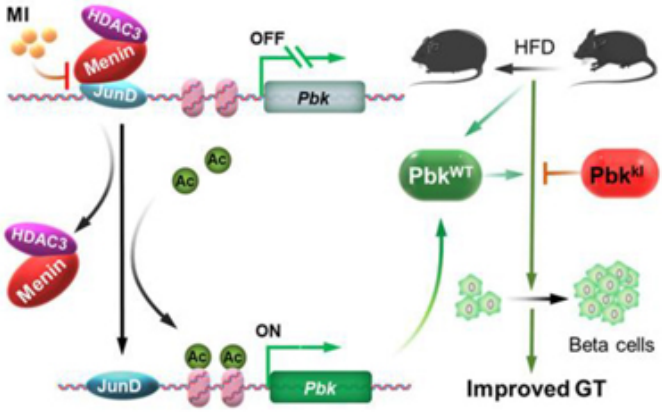
- BMF-219 will be administered PO daily

Abbreviations: **ALL** Acute Lymphoblastic Leukemia **AML** Acute Myeloid Leukemia **AMPL** Acute Mixed-Phenotype Leukemia **CEBP/A** CCAAT Enhancer Binding Protein Alpha **CRR** Complete Response Rate **CYP3A4** Cytochrome 450 3A4 **FIH** first-in-human **FLT3** FMS-like Tyrosine Kinase **KMT2A** Lysine Methyltransferase 2A **MLL** Mixed Lineage Leukemia **MLLr** Mixed Lineage Leukemia-rearranged **MN1** Meningioma 1 gene **NPM1** Nucleophosmin 1 **OBD** Optimal biologic dose **PICALM-AF10** Phosphatidylinositol Binding Clathrin Assembly Protein AF10 **PK** Pharmacokinetic **R/R** Relapsed/Refractory **RP2D** Recommended Phase 2 Dose **TEAE** Treatment Emergent Adverse Event

Role of Menin in Diabetes: Beta Cell Regeneration

Menin is implicated in the proliferation of beta islet cells, providing rationale for a menin inhibitor as an agent for beta cell regeneration and turnover

Pancreatic beta cells proliferation regulated via the menin/JunD/Pbk axis



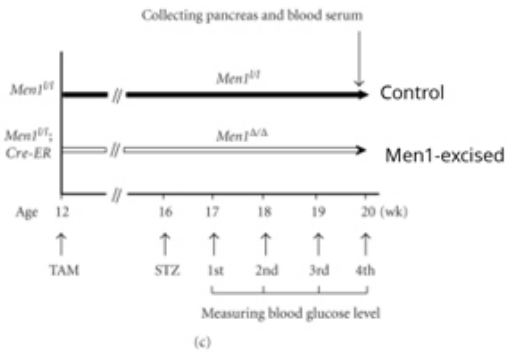
- Pbk is crucial for regulating compensatory pancreatic beta cell proliferation of high fat diet (HFD) fed mice
- Menin and HDAC3 complex are recruited by JunD to epigenetically repress Pbk expression
- Menin-JunD interaction was interrupted by small molecule menin inhibitors (MIs), leading to upregulating of Pbk gene expression, beta cell proliferation, and improved glucose tolerance in diet-induced obese and diabetic mice
- Pbk is required for MI-induced beta cell proliferation and improved glucose tolerance in HFD-induced diabetic mice

Sources: Ma et al. (2021) Menin-regulated Pbk controls high fat diet-induced compensatory beta cell proliferation May 7;13(5):e13524.

Role of Menin in Diabetes: Glucose Tolerance

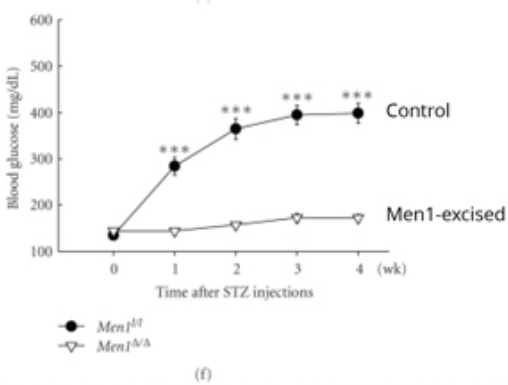
Potential for menin inhibition demonstrated by beta cell ablation diabetes model in MEN1 excised mice

MEN1 Excision Prevents Development of STZ-induced Hyperglycemia



(c)

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



(f)

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

Sources: Yang et al. (2010) Deletion of theMen1Gene Prevents Streptozotocin-Induced Hyperglycemia in Mice. Experimental Diabetes Research, 2010, 1–11. doi:10.1155/2010/876701

Near Term Milestones

BMF-219 – Liquid Tumors

IND Clearance	Completed
DLBCL Preclinical ASH 2021 Abstract	Completed
BMF-219 Ph. I AML Trial Initiation	In Progress
Additional Preclinical Data in DLBCL/MM	Q1 2022

BMF-219 – Solid Tumors

Additional Preclinical Data in KRAS Tumors	Q1 2022

Menin Inh. – Diabetes

T2D Menin Pathway Validation	Q1 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