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 9, 2023

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 January 9, 2023, Biomea Fusion, Inc. (the "Company") issued a press release titled, "Biomea Fusion to Present at 41st Annual J.P. Morgan Healthcare Conference and Highlight 2023 Corporate Milestones." The information described in the press release was presented by the Company in an updated corporate presentation at the 41st Annual J.P. Morgan Healthcare Conference, which took place from January 9-12, 2023 in San Francisco, California.

Copies of the press release and the Company's presentation are attached to this Current Report on Form 8-K as Exhibits 99.1 and 99.2 and are 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 and BMF-500, the potential of BMF-500 as an FLT3 inhibitor, the potential of BMF-219 as a treatment for various types of cancer and diabetes, the Company's research, development and regulatory plans, the progress of the Company's ongoing clinical trials, including COVALENT-101, COVALENT-102 and the Company's Phase I/II clinical COVALENT-111 study of BMF-219 in Type 2 diabetes, the Company's plans to present clinical data from the Company's COVALENT-101 study and the first two cohorts of the Phase II portion of the Company's COVALENT-111 study, the Company's plans to dose the first patient in the Company's COVALENT-102 study, the Company's plans to submit an IND application for BMF-500 in patients with FLT3 mutations, the Company's plans to provide clinical updates on the healthy volunteer section of the Company's Phase I/II Type 2 diabetes study of BMF-219, the Company's plans to announce a third development candidate from the FUSION platform, 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 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 the Company may encounter delays in preclinical or clinical development, the preparation, filing and clearance of INDs, patient enrollment and in the initiation, conduct and completion the Company's ongoing and 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 to Present at 41st Annual J.P. Morgan Healthcare Conference and Highlight 2023 Corporate Milestones."
99.2	Corporate Slide Presentation of Biomea Fusion, Inc., titled "JP Morgan 2023 Corporate Presentation"
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, 2023

By: /s/ Thomas Butler

Thomas Butler
Principal Executive Officer

Exhibit 99.1

Biomea Fusion to Present at 41st Annual J.P. Morgan Healthcare Conference and Highlight 2023 Corporate Milestones

REDWOOD CITY, Calif., Jan. 9, 2023 (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, today announced that Thomas Butler, Biomea Fusion's Chief Executive Officer and Chairman of the Board, will present recent progress and 2023 corporate milestones at the 41st Annual J.P. Morgan Healthcare Conference on Wednesday, January 11, 2023 from 11:15 – 11:55 am ET, and that Biomea management will hold 1x1 meetings during the conference January 9 – 11.

A live webcast of the presentation will be available on the Investors & Media page of Biomea's website at: https://investors.biomeafusion.com/news-events/events.

"2022 was a year of strong execution and fundamental infrastructure build as we transitioned to a clinical-stage company and expanded our pipeline. We enter 2023 with three clinical trials studying BMF-219 across 8 cancer indications covering both blood cancers and solid tumors as well as in Type 2 diabetes, the 7th leading cause of death in the United States," stated Thomas Butler, Biomea Fusion's Chief Executive Officer and Chairman of the Board. "We anticipate advancing BMF-500 into the clinic during the first half of 2023, subsequent to FDA clearance of an IND, which will increase our clinical pipeline to 4 clinical trials covering 10 indications. COVALENT-111, our Phase I/II study in Type 2 diabetes is now due to report initial safety and efficacy from the first two cohorts of the Phase II portion by the end of Q1."

Mr. Butler further commented, "we continue to activate sites and enroll patients in our Phase I/Ib (COVALENT-101) study of BMF-219 in patients with several liquid tumor types, and plan to report initial clinical data from this study in the first half of 2023. In addition, we anticipate initiating dosing imminently in our Phase I/Ib (COVALENT-102) study of BMF-219 in patients with KRAS-mutated solid tumors. In 2023, we will continue the patient-centric urgency and disciplined execution that are now well-established hallmarks of Team Biomea."

RECENT & ANTICIPATED MILESTONES

ONCOLOGY

- COVALENT-101 (BMF-219)
  - Presented robust anti-tumor activity of covalent menin small molecule inhibitor, BMF-219, as a single agent and mechanistic evidence for novel inhibition of the menin protein in preclinical models of diffuse large B-cell lymphoma (DLBCL), multiple myeloma (MM), and chronic lymphocytic leukemia (CLL). BMF-219 displayed single agent potency, surpassing greater than 90% cell killing at clinically relevant exposures in DLBCL, MM and CLL cell lines and patient-derived samples.
  - BMF-219 is the first investigational menin inhibitor in clinical development to show potential as a therapeutic agent in hematologic malignancies outside of MLLr and NPM1 mutated acute myeloid leukemia/acute lymphoblastic leukemia (AML/ALL) patients, specifically in subsets of DLBCL, MM and CLL patients.
  - Biomea continued site activation and patient enrollment for the dosing of BMF-219 across four liquid tumor cohorts in the COVALENT-101 study, including patients with AML/ALL, DLBCL, MM and CLL.

- **Next Anticipated Milestone:**

  On track to present initial clinical data of AML/ALL patients (including those with MLL rearrangement and NPM1 mutation) dosed in the COVALENT-101 study in the first half of 2023.

- COVALENT-102 (BMF-219)
  - Presented strong and highly specific pan-KRAS anti-cancer activity of BMF-219 as a single agent across KRAS G12C, G12D, G12V and G13D mutant cell lines including in non-small cell lung cancer (NSCLC), colorectal cancer (CRC) and the most prevalent type of pancreatic cancer, PDAC.
  - BMF-219 is the first investigational menin inhibitor in development to enter clinical trials for the treatment of solid tumors. A targeted pan-KRAS inhibitor could have the potential to treat 25-35% of NSCLC, 35-45% of CRC, and approximately 90% of PDAC patients.
  - Biomea received FDA clearance of its IND in the fourth quarter of 2022 and has since initiated a Phase I/Ib clinical trial of BMF-219 as a monotherapy in patients who have unresectable, locally advanced, or metastatic NSCLC, CRC or PDAC with an activating KRAS mutation.
  - **Next Anticipated Milestone:**

    On track to dose first patient in COVALENT-102 study in January 2023.

- COVALENT-103 (BMF-500)
  - Presented data showing multi-fold higher potency and increased cytotoxicity of Biomea's covalent FLT3 small-molecule inhibitor BMF-500 compared to the commercially available reversible, non-covalent FLT3 inhibitor gilteritinib, and complete, sustained tumor regression in mouse models of FLT3-ITD AML with maintenance of effect after cessation of therapy.
  - **Next Anticipated Milestone:**

    On track to file IND for BMF-500 in the first half of 2023 to initiate COVALENT-103 study of the covalent FLT3 inhibitor in patients with acute leukemia.

DIABETES

- COVALENT-111 (BMF-219)
  - Presented preclinical data highlighting the ability of BMF-219 in a Type 2 diabetes rat model to restore normal HOMA-B, a measure of pancreatic beta cell function, following only 4-weeks of treatment and to significantly lower HbA1c compared to active control, liraglutide, -3.5% vs -1.7%, respectively.
  - BMF-219 is the first investigational menin inhibitor in development to enter clinical trials for the improvement of glycemic control and insulin sensitivity in Type 2 diabetes patients.
  - Biomea completed the healthy volunteer portion of the Phase I/II COVALENT-111 study of BMF-219 in Canada. BMF-219 was well tolerated with an encouraging pharmacokinetic and pharmacodynamic profile in healthy volunteers and with no safety signals detected.
  - Biomea received FDA clearance in December 2022 to expand the Phase II portion of COVALENT-111 to sites in the U.S. and in January 2023 announced dosing of the first U.S. patient with Type 2 diabetes. The company continues to enroll Type 2 diabetes patients in the Phase II portion of the study in Canada as well.
  - **Next Anticipated Milestones:**

    On track to present initial clinical data from the first two cohorts of the Phase II portion of the study by the end of Q1 2023, and to present details of the healthy volunteer (Phase I) portion of the study at a scientific medical meeting in 2023.

FUSION™ SYSTEM DISCOVERY PLATFORM

- Developed two covalently binding small molecules (BMF-219 and BMF-500), each within 18 months from target identification to IND candidate, leveraging the proprietary FUSION™ System Discovery Platform and showing excellent preclinical profiles.
- **Next Anticipated Milestone:**

  On track to announce a third development candidate from the FUSION platform in the first half of 2023.

About Biomea Fusion

Biomea Fusion is a 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 the clinical and therapeutic potential of our product candidates and development programs, including BMF-219 and BMF-500, the potential of BMF-500 as an FLT3 inhibitor, the potential of BMF-219 as a treatment for various types of cancer and diabetes, our research, development and regulatory plans, the progress of our ongoing clinical trials, including COVALENT-101, COVALENT-102 and our Phase I/II clinical COVALENT-111 study of BMF-219 in Type 2 diabetes, our plans to present clinical data from our COVALENT-101 study and the first two cohorts of the Phase II portion of our COVALENT-111 study, our plans to dose the first patient in our COVALENT-102 study, our plans to submit an IND application for BMF-500 in patients with FLT3 mutations, our plans to provide clinical updates on the healthy volunteer section of our Phase I/II Type 2 diabetes study of BMF-219, our plans to announce a third development candidate from the FUSION platform, 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.

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Contact:

Sasha Blaug
Senior Vice President, Corporate Development
SB@biomeafusion.com
(650) 460-7759

Exhibit 99.2

biomea FUSION™

JP Morgan 2023 Corporate Presentation

Disclaimer

Legal Disclaimer & Forward-Looking Statements

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.

Excellent Science - Combining Validated Targets with Breakthrough Chemistry

We aim to cure

- Experienced Management Team
- Novel FUSION™ System
- BMF-219 - Clinical Stage Lead Asset
- BMF-500 and additional Programs

biomea FUSION™ We Aim to Cure™

Biomea Fusion is a clinical-stage biopharmaceutical company focused on the discovery and development of **oral covalent small-molecule drugs** to treat patients with genetically defined cancers and metabolic diseases. 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.

Developing some of the most impactful medicines of our time

A long history of developing successful drugs together

Thomas Butler
Chairman & CEO

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

Veklury® remdesivir 100 MG/20 mL INJECTION

Co-inventor of
Remdesivir at Gilead

Ramses Erdtmann
President & COO

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

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)

Franco Valle
Chief Financial Officer

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

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

HARVONI® ledipasvir / sofosbuvir

Co-lead of Ledipasvir at Gilead

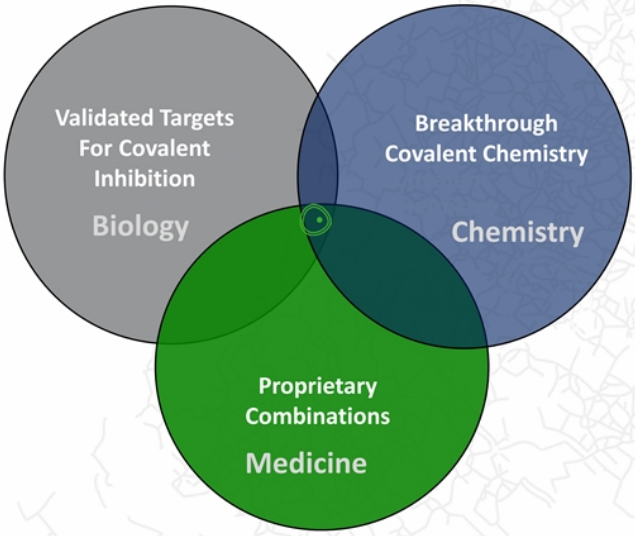
Jim Palmer
VP of Drug Discovery

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

imbruvica® (ibrutinib)
560, 420, 280, 140 mg tablets | 140, 70 mg capsules

Co-inventor of
ibrutinib at Celera

Biomea's Development Principles



Validated Targets

Drugs pursuing **Validated Disease 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)

Covalent Inhibitors

Covalent Small Molecule 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

Biomea created the Fusion™ System specifically to address unique targets and rapidly create highly potent and safe covalent inhibitors for them.

- Protein-protein interactions
- Difficult to target kinases, including avoiding high homology family members
- Transcriptional factors
- Low expressing targets
- Scaffold proteins
- Small GTPases
- Shallow, limited, or dynamic binding sites
- High affinity competitive ligands
- Systemic tolerability issues at efficacious dose
- Targeting optimal confirmation
- Identify small molecules for new targets

Most proteins are considered undruggable because it's impossible to get high enough drug exposure to effectively silence the target without significant side effects… Our Optimized Covalent Inhibitors Uniquely Solve That Problem.

Our Technology Platform – The FUSION™ SYSTEM – provided 3 Program leads over the past 4 years!

Target identification to IND candidate in 18 months

Target to Hit

Target validation
Visual integration of crystal structures of target and reactive cysteine

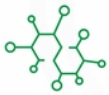
Utility:
Differentiated insights from X-ray crystal structures, identifying target cysteines

Custom Lead

Library of custom engagers
Proprietary AI platform with VR validation matches novel DRUG LIKE PROBES to cysteines; we do not screen via library probes.

Utility:
Library of covalent scaffolds provide for ~1,000 de novo scaffolds for AI/VR scoring

Lead Optimization



Custom scaffold creation
Custom built Synthesis to create candidates with desired

Utility:
AI/VR program platform yields over 300 scaffolds, which are synthesized for in vitro testing

IND

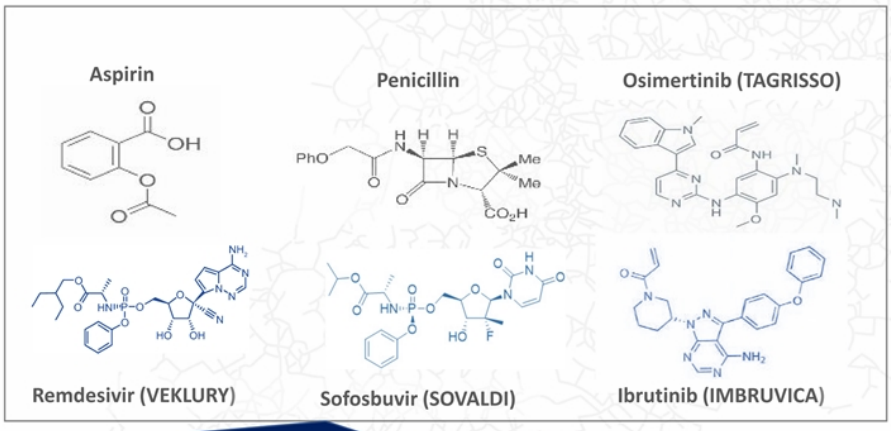
Refinement
Building in drug-like properties, optimizing PK/PD profile, and maintaining specificity

Utility:
Scaffolds are further refined with Mass spec, animal, and cell-based assays to two IND candidates

Covalent Chemistry creates very powerful results

Covalent Inhibitors - a History of Medical & Commercial Success

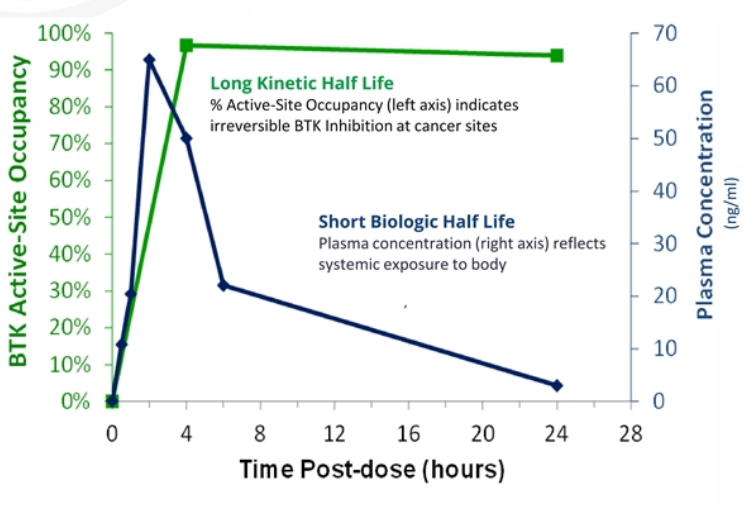
Notable Covalent Inhibitors



Compounds in blue were invented or developed by Biomea Fusion senior leadership

- **Aspirin** was the first commercialized covalent drug
- Notable precision oncology and infectious disease programs leverage covalent mechanisms
  - Precision Oncology**:** **Osimertinib** and **Ibrutinib** both target kinases and are used in subpopulations with specific genetic biomarkers
  - Antivirals**:** **Remdesivir** and **Tenofovir** both target reverse transcriptases and are leveraged to treat HCV and other viruses including HIV and COVID-19

Imbruvica – a Covalent Inhibitor with Long Kinetic but very Short Biological Half Life



High Selectivity

Two-step inhibition: 1) Initial reversible binding followed by 2) covalent interaction, increasing target selectivity

Deep Target Inactivation

Permanent inactivation of bound protein drives target elimination through normal cellular degradation processes

Greater Therapeutic Window

Designed to maintain an effect without sustained systemic exposure, unlike conventional non-covalent inhibitors

JPM 2022 Announcement BMF-219 Goals for the year 2022

Initiation of "Clinical Trials in 7 tumor types and in Diabetes" – and WE DID IT!

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	H1 2022 ✓
BMF-219 Ph. I DLBCL/MM Trial Initiation Plus CLL	H1 2022 ✓

BMF-219 – Solid Tumors

Additional Preclinical Data in KRAS Tumors	H1 2022 ✓
IND Filing	H2 2022 ✓
BMF-219 Ph. I KRAS Mut. Trial Initiation	Q4 2022 ✓

Menin Inh. – Diabetes

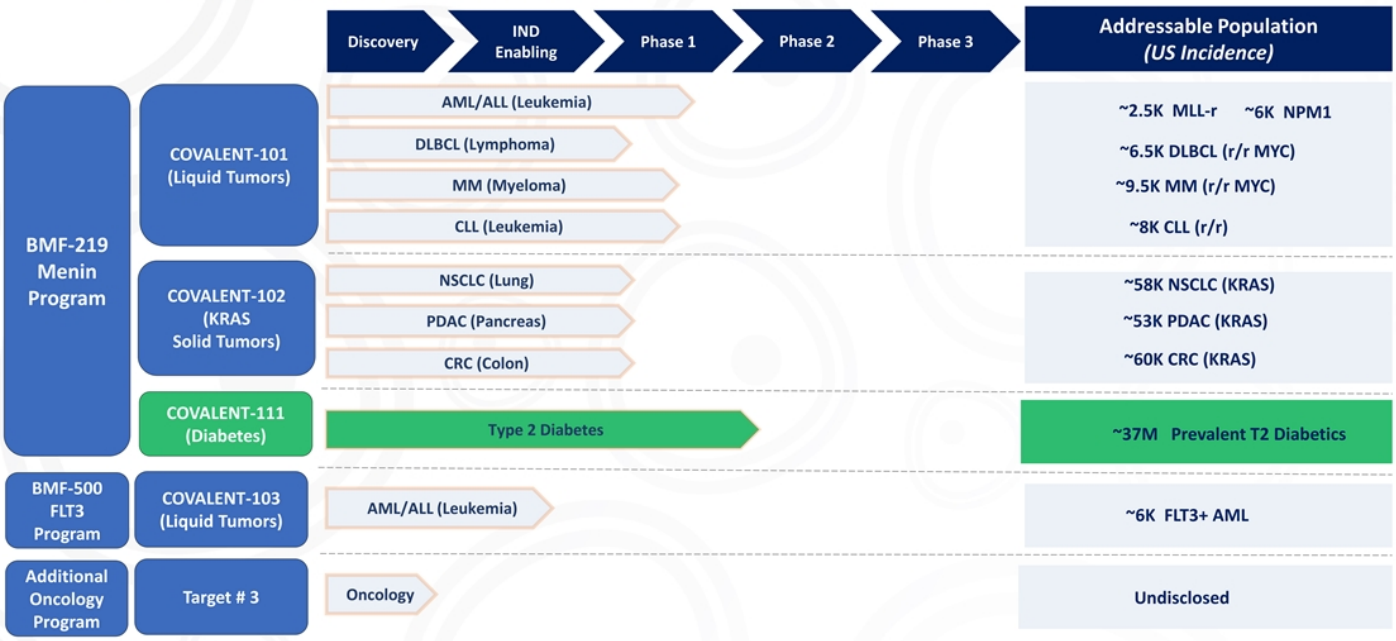
Diabetes Menin Pathway Validation	H1 2022 ✓
IND Filing	H2 2022 ✓
Ph. I Diabetes Trial Initiation	H2 2022 ✓
Completion of Healthy Volunteer Portion of Study	Completed ✓
Enrollment of First Diabetes Patient	Completed ✓

Additional Programs

2nd Pipeline Candidate Announced	H1 2022 ✓
3rd Pipeline Candidate Announced	To be announced

In 2022 Biomea Expanded into Eight Different Solid and Liquid Tumors as well as Type 2 Diabetes

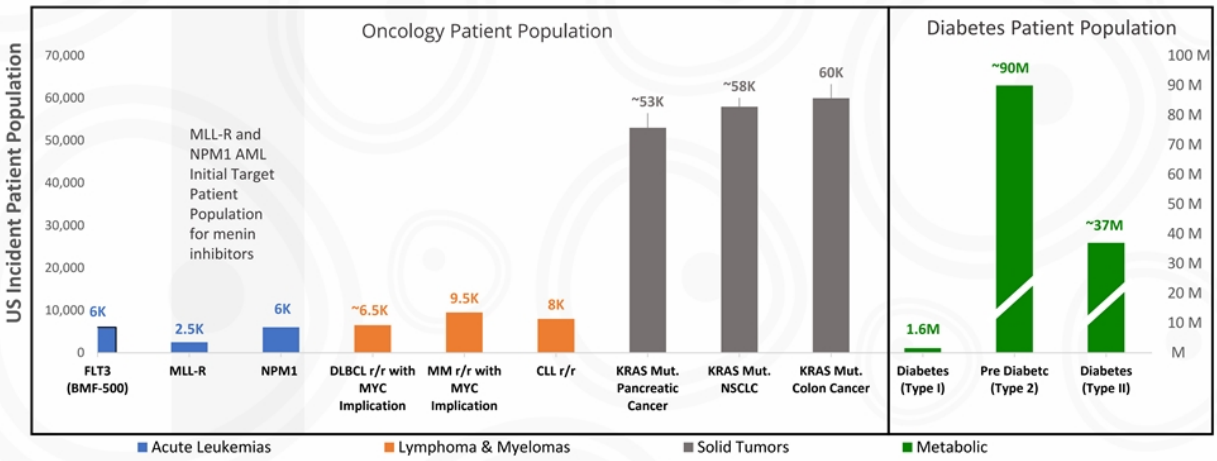
Biomea's Pipeline as of January 2023



BMF-219 and BMF-500 Patient Populations in the US

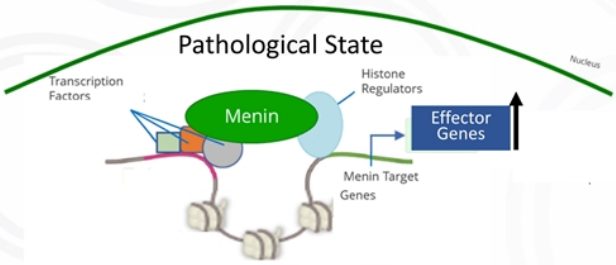
Cancer Indications: >200K and Diabetes: >125M

Addressable Annual US 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>

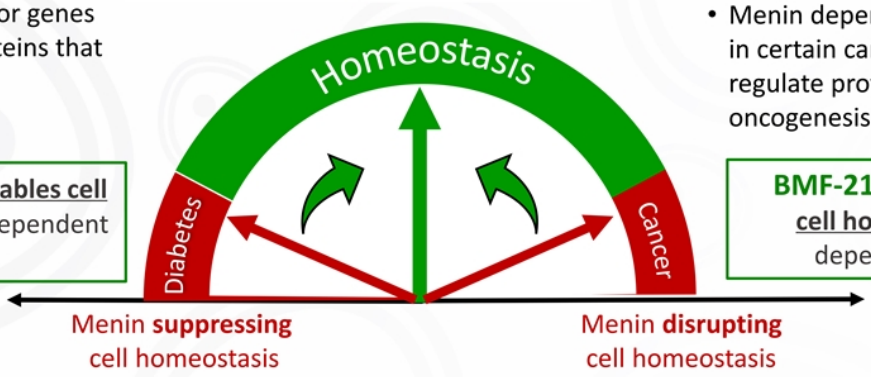
Restoring Balance in Menin Dependents Diseases is Context Specific



Treating Diabetes

- Menin dependent effector genes in beta-cells express proteins that repress beta-cell growth

BMF-219 selectively **enables cell homeostasis** of menin dependent beta cells



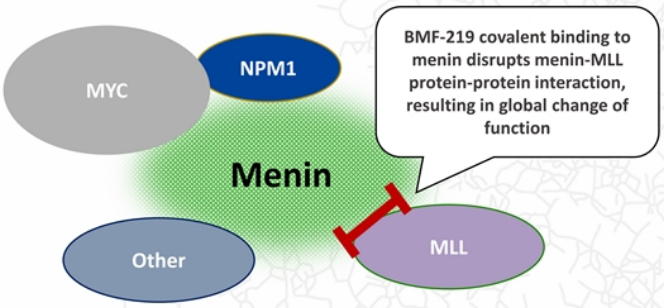
Treating Cancer

- Menin dependent effector genes in certain cancers express or regulate proteins that drive oncogenesis

BMF-219 selectively **enables cell homeostasis** of menin dependent cancer cells

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

Mechanism of Action



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

Target Patient Population

- Acute Leukemia: MLL-r
- Acute Leukemia: NPM1 mutant
- Acute Leukemia: Ras mutant
- DLBCL: DHT / DEL
- Multiple Myeloma: MYC addicted
- KRAS mutant Solid Tumors:
  Colorectal
  Lung
  Pancreatic
- CLL: r/r population
- Liquid and Solid Tumors

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

Novel Covalent Inhibitor of Menin

BMF-219

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

MLL Fusion & NPM1 Driven Tumors

Initial clinical validation in r/r acute leukemias with MLL fusions in addition to NPM1 mutations

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Pathway and clinical validation of covalent menin inhibition

First Development Success with BMF-219 in MLL Fusion and NPM1 Driven Tumors

In Acute Leukemia

Development Stage:
Phase I Clinical Trial (COVALENT-101) enrolling patients with relapsed/refractory acute leukemia

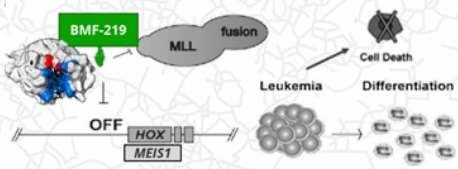
Key Facts

Estimated Addressable Population

Acute Leukemia (Mutation)	Estimated US Patient Population (Annual Incidence)
MLL-r	~2,500
NPM1 mutant	~6,000
Ras Driven	~6,000

MOA

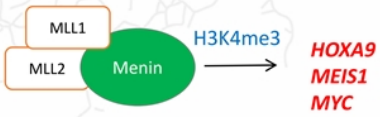
BMF-219 covalently blocks menin / MLL interaction



- BMF-219 directly inhibits MLL-menin interaction and was optimized to cause cell killing, rather than cell differentiation.
- In preclinical studies, BMF-219 shows robust cell killing and reduction of expression of key genes (including MYC, MEIS1, HOXA9, and BCL2)

Relevant Pathway

Menin / MLL interaction can modify chromatin, activating key leukemic genes



Menin / MLL complex forms and modifies chromatin at histone H3, activating *HOXA9* and *MEIS1*

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

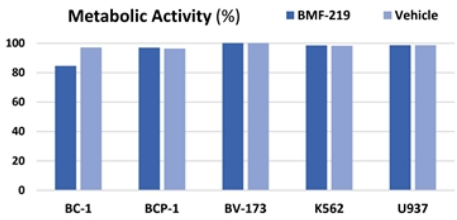
No Histopathology Findings Were Observed with BMF-219 in GLP and non-GLP IND-Enabling Toxicology Studies

✓ Kinase Screening

169 kinases screened; only **two** showed >50% inhibition with BMF-219

✓ Oncopanel Screen

Minimal impact of BMF-219 on cell metabolism in leukemia and lymphoma cell lines that have **wild type MLL1**



✓ Safety Screen

SafetyScreen44 panel (CEREP/Eurofins Discovery)* showed **no meaningful impact** (>50% activation or inhibition)

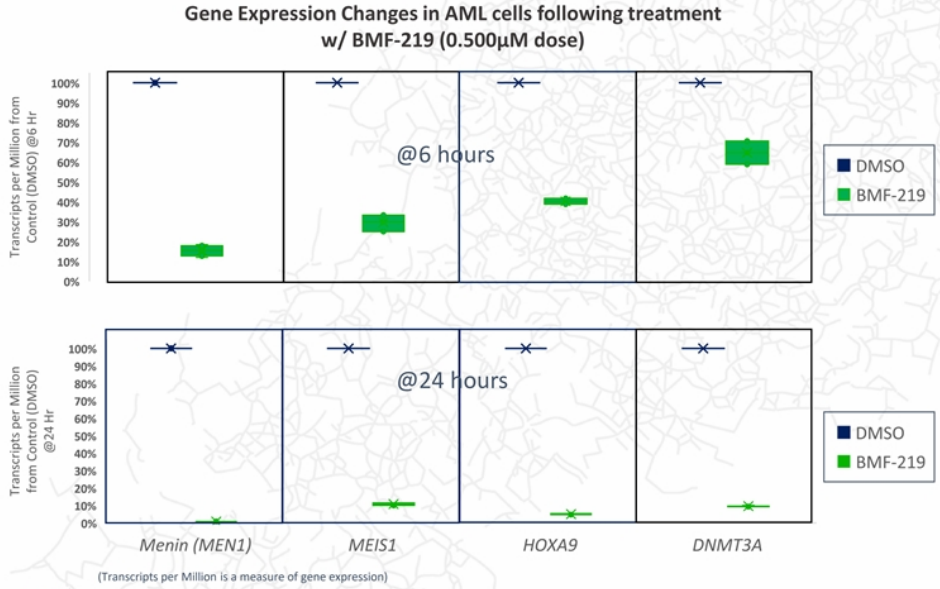
*SafetyScreen44 *in-vitro* panel of 44 common selected targets to identify significant off-target interactions

✓ Glutathione Reactivity

BMF-219 had **less reactivity than the approved covalent drugs omeprazole and neratinib**

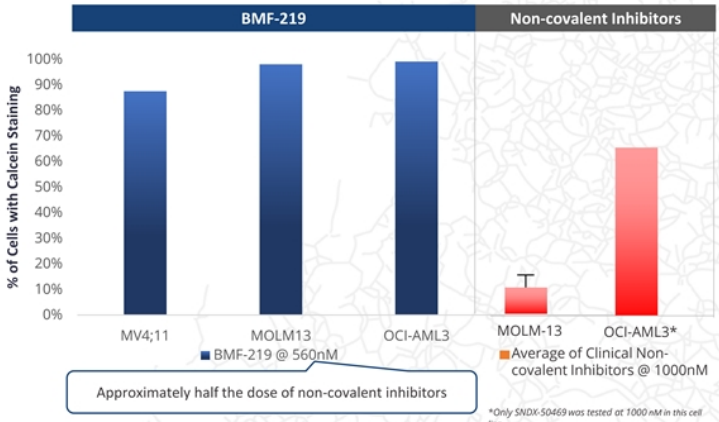
Drug	Mean half-life (min)
Omeprazole	123.3
Neratinib	197.7
Ibrutinib	>360
BMF-213	322.3
BMF-214	>360
BMF-219	>360

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

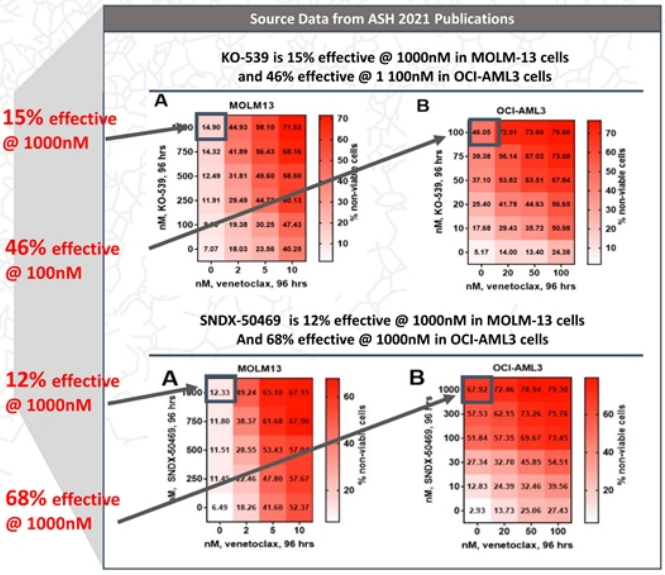


- Covalent inhibitor, BMF-219, downregulates expression of Menin (via the target *MEN1* gene) and critical leukemogenic genes (e.g., *MEIS1* and *HOXA9*)
  - *MEIS1* is a gene that can be an accelerator of leukemic transformation (along with *HOXA9*)
  - *HOXA9* is a gene involved in myeloid differentiation 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 Superior Cell killing of the Target AML Cell Lines at Half the Dose vs Reversible Competitive Menin Inhibitors



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



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

Novel Covalent Inhibitor of Menin

BMF-219

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

MLL Fusion & NPM1 Driven Tumors

Initial clinical validation in r/r acute leukemias with MLL fusions in addition to NPM1 mutations

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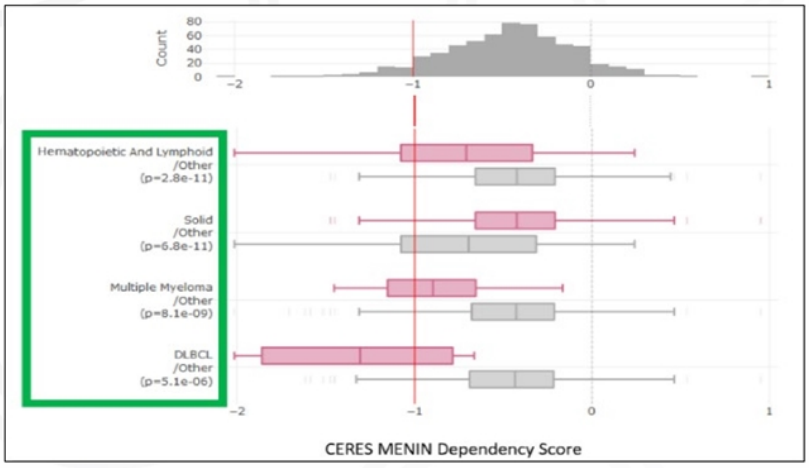
Pathway and clinical validation of covalent menin inhibition

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*)



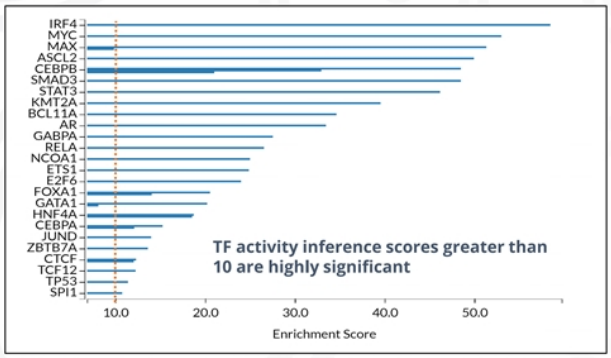
Note: CERES MENIN Dependency scores less than -1 in various tumor types imply that menin is considered essential for cell survival in those tumor types

- 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 clinically exploring the potential for **covalent inhibition of menin in a variety of liquid and solid tumor types**

BMF-219 Covalent Binding of Menin has Broad Impact

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

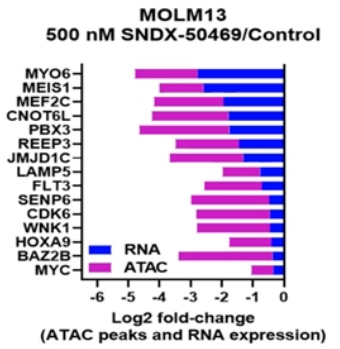
Covalent Menin Inhibitor – BMF-219



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

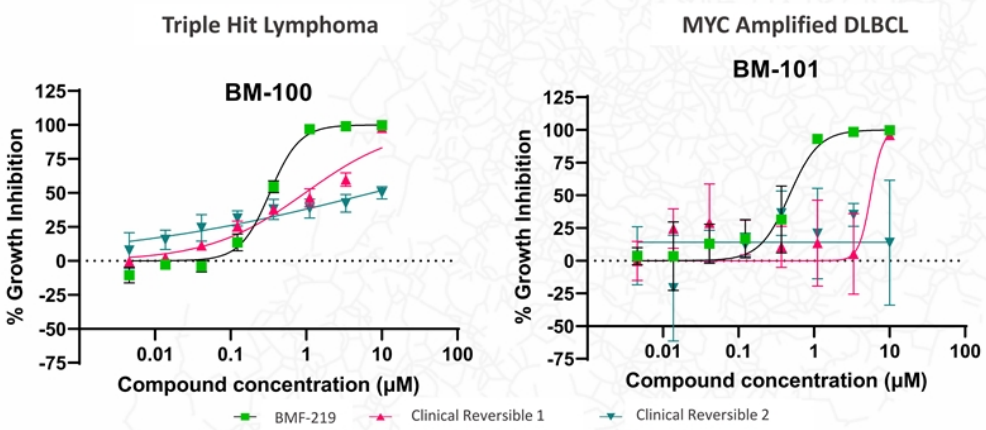
Non-Covalent Menin Inhibitor – SNDX-50469



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

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

BMF-219 Led to near Complete Inhibition of Growth at 1µM in DLBCL in ex-vivo Samples



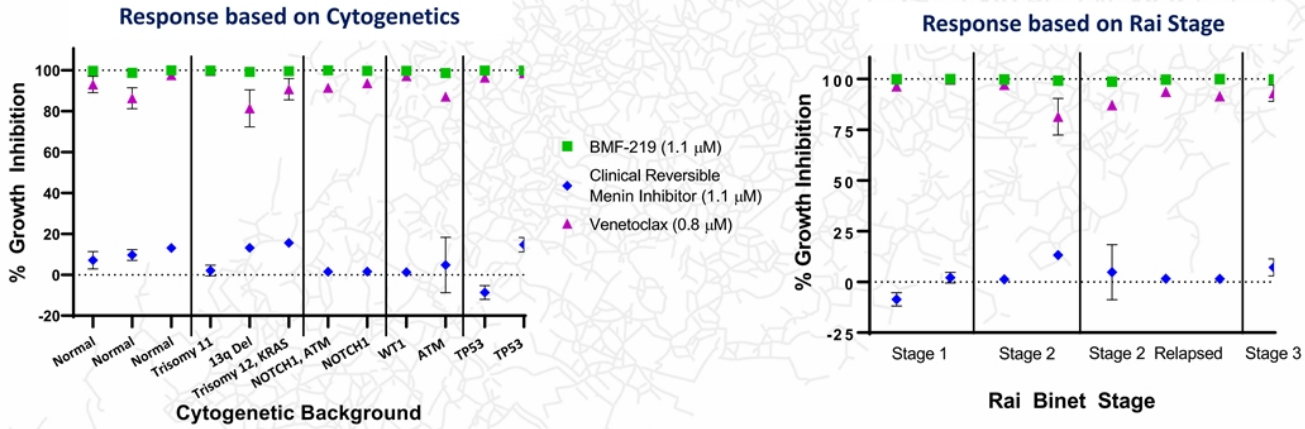
Treatment	Growth Inhibition IC_{50} (mM)	
	BM100	BM101
BMF-219	0.250	0.151
Clinical Reversible-1	0.969	5.63
Clinical Reversible-2	6.31	Max killing <30%

- At ~1µM exposure, BMF-219 produces robust growth inhibition in both THL (triple hit lymphoma) and MYC amplified DLBCL ex-vivo cell lines
- BMF-219 responses were superior to clinical reversible (non-covalent) inhibitors with respect to cell growth inhibition at the concentrations tested

Somanath et al., AACR 2022 Abstract 2654

BMF-219 Achieves >98% Cell Lethality Against Diverse CLL ex vivo models

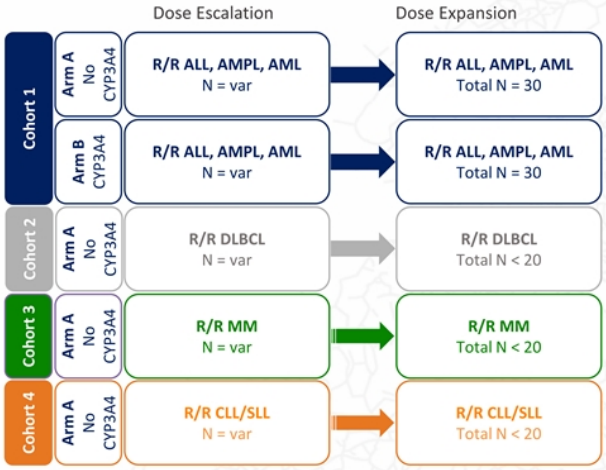
Growth inhibition of BMF-219 in CLL *ex vivo* models grouped by genetic background and Rai stage



Somanath et al., ASCO 2022 Abstract 7541

COVALENT-101 (ENROLLING 4 COHORTS)

Phase I first-in-human dose-escalation and dose-expansion study of BMF-219 enrolling adult patients with r/r acute leukemia, r/r diffuse large B cell lymphoma, r/r multiple myeloma, and r/r chronic lymphocytic leukemia (CLL) (NCT05153330)



Accelerated titration design followed by classical 3+3

Cohort 1 for R/R AML/AMPL/AML patients
Cohort 2 for R/R DLBCL with ≥ 2L of prior therapy
Cohort 3 for R/R MM with ≥ 3L of prior therapy
Cohort 4 for R/R CLL/SLL with ≥ 2L of prior therapy

Study Treatment: BMF-219

- A covalent small molecule menin inhibitor, administered orally daily in 28-day cycles

Objectives

- Primary: Determine OBD & RP2D of BMF-219 monotherapy independently for each Cohort and Arm
- Secondary: Evaluate safety and tolerability of BMF-219
  Determine PK/ PD parameters of BMF-219
  Explore additional evidence of efficacy and antitumor activity

BMF-219 is being studied in seven different blood cancers. The design of COVALENT-101 is the following: Dose escalation of each cohort is done in parallel followed by independent dose selection and dose expansion phase.

Abbreviations: ALL Acute Lymphoblastic Leukemia AML Acute Myeloid Leukemia AMPL Acute Mixed-Phenotype Leukemia CYP3A4 Cytochrome 450 OBD Optimal biologic dose DLBCL diffuse large B-cell lymphoma MM multiple myeloma R/R Relapsed/Refractory

Novel Covalent Inhibitor of Menin

BMF-219

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Further expansion into KRAS and RAS mutant colorectal, lung, and pancreatic cancer

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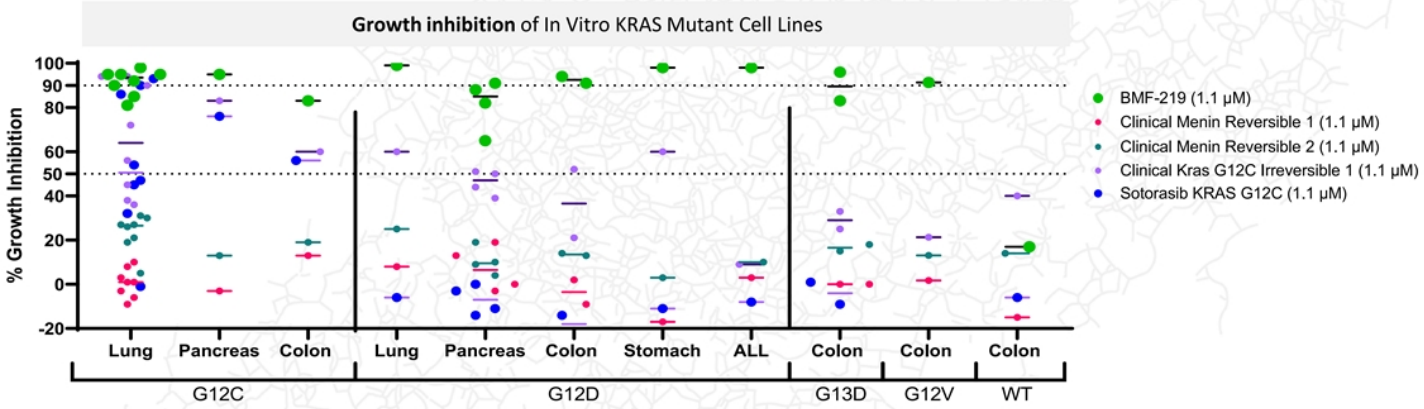
Pathway and clinical validation of covalent menin inhibition

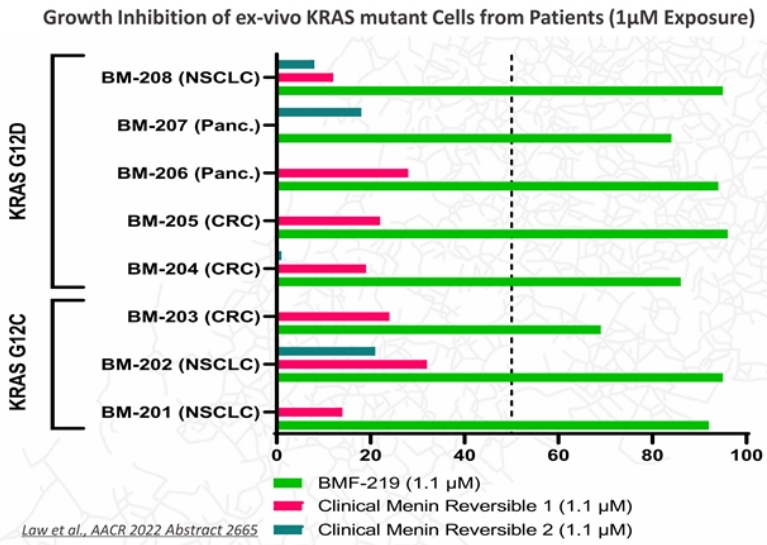
BMF-219 Produced Near Complete Inhibition of Growth at 1.1µM Across KRAS G12C, G12D, G13D, and G12V Mutant Cell Lines but not WT KRAS



- Covalent menin inhibition by BMF-219 led to robust growth inhibition, comparable to clinical G12C inhibitors in G12C cell lines
- In non-G12C cell lines, BMF-219 achieved robust growth inhibition, higher than clinical KRAS G12C inhibitors
- Clinical reversible (non-covalent) inhibitors did not achieve greater than 30% growth inhibition in any cell lines at the concentrations tested

Law et al., AACR 2022 Abstract 2665

BMF-219 Produced Near Complete Inhibition of Growth at 1.1µM in KRAS G12C and G12D ex-vivo Patient Samples

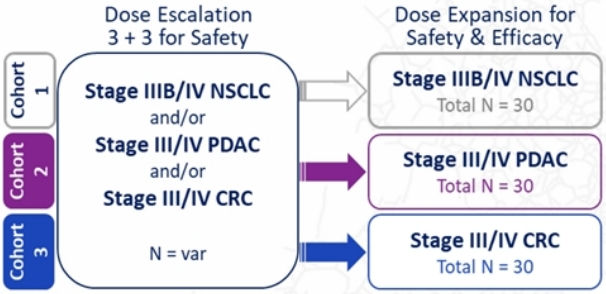


Law et al., AACR 2022 Abstract 2665

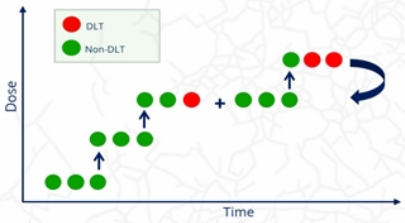
- 1.1µM exposure of BMF-219 produces robust growth inhibition in both G12C and G12D ex-vivo cell lines
- BMF-219 responses were superior to clinical reversible (non-covalent) inhibitors with respect to cell growth inhibition at the concentrations tested

COVALENT-102 (ENROLLING 3 COHORTS)

Phase I/Ib Study of BMF-219, an oral covalent menin inhibitor, in patients with KRAS Mutant, Unresectable, Locally Advanced, or Metastatic Non-Small Cell Lung Cancer (NSCLC), Pancreatic Cancer (PDAC), and Colorectal Carcinoma (CRC) (NCT05631574)



Classical 3+3 dose escalation design



Study Treatment: BMF-219

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Objectives

- Primary:
  - Determine OBD & RP2D of BMF-219 monotherapy independently for each Cohort / Indication
- Secondary:
  - Evaluate safety and tolerability of BMF-219
  - Determine PK/ PD parameters of BMF-219
  - Explore additional evidence of efficacy and antitumor activity

Abbreviations: NSCLC Non-Small Cell Lung Cancer PDAC Pancreatic Cancer CRC Colorectal Carcinoma OBD optimal biologic dose RP2D recommended phase 2 dose PK/PD pharmacokinetic/pharmacodynamic ECOG Eastern Cooperative Oncology Group var variable L prior line of systemic therapy

Novel Covalent Inhibitor of Menin

BMF-219

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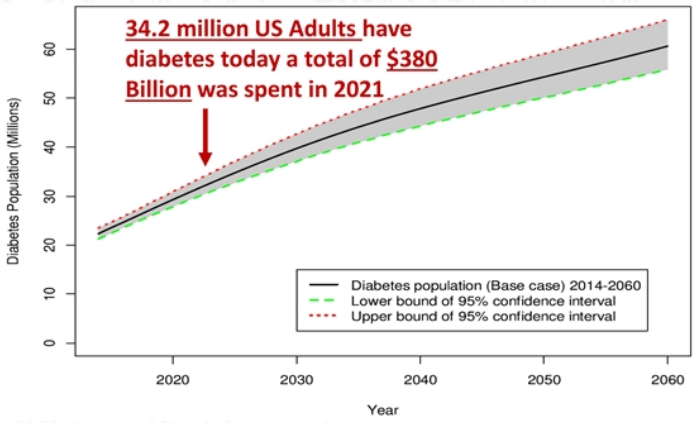
Diabetes – the biggest Epidemic of the 21st century

1 in 3 Americans will develop Diabetes in their life

- One of the largest economic burdens on the US health care system and the 7th leading cause of death in the US Source: Diabetes.org
- 80% of people with diabetes will die from this disease. Premature mortality caused by diabetes results in an estimated 12-14 years of life lost. Source: National library of Medicine 1(2): 2007 Jul PMC3068646
- In the United States $1 out of every $4 in US health care costs is being spent on caring for people with diabetes. In 2021 the US spent $380 Billion to treat diabetes.

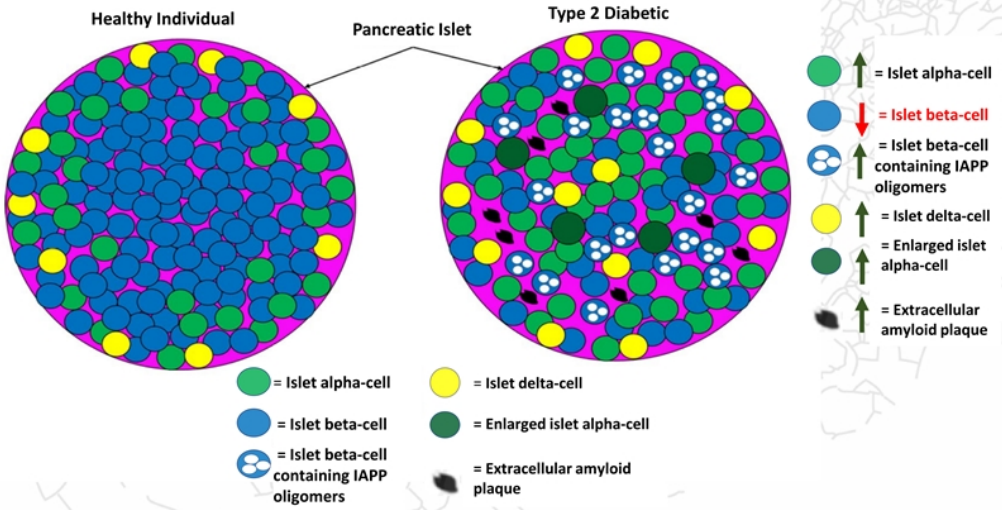


- According to the CDC, worldwide 463 million adults have diabetes. In the United States alone, 34.2 million adults have diabetes, 10.5% of the population. 96 million adults (more than 1 in 3) in the US have pre-diabetes.

= ***Diabetes is an uncontrolled disease despite the availability of current medication. There is a significant need for the treatment and care of diabetes patients.***

Diabetes – the biggest Epidemic of the 21st century

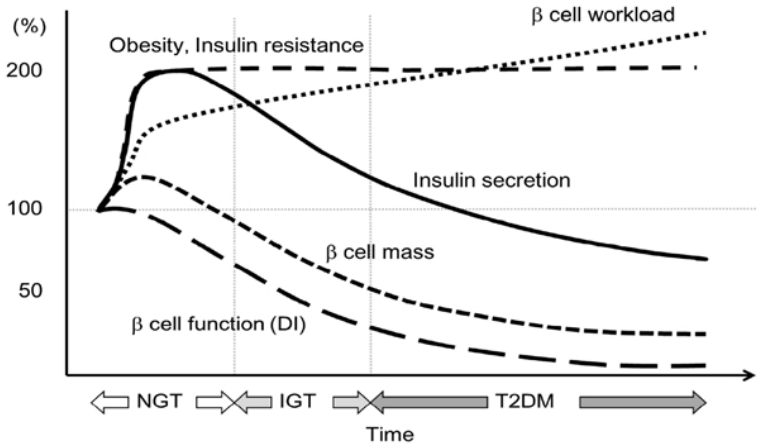
Types 2 Diabetes Progression: Beta Cell Loss



- Type 1 and Type 2 Diabetes results in Beta Cell Loss and a Reduction in Beta Cell Mass
- Standard of Care Agents are not addressing the Loss of Beta Cells
- Type 1 and Type 2 Diabetes Patients remain un-controlled and continue to progress

*Int. J. Mol. Sci. 2016, 17, 744; doi:10.3390/ijms17050744

Diabetes Progression of Type 1 and Type 2 Driven by Beta Cell Loss



Prior Paradigm		
	Type 1 diabetes	Type 2 diabetes
	β cell destruction β cell mass ↓↓ Insulin secretion ↓↓	Obesity Insulin resistance Hyperinsulinemia
Current Paradigm		
	Type 1 diabetes	Type 2 diabetes
	β cell destruction β cell mass ↓↓ Insulin secretion ↓↓	β cell loss β cell mass ↓ Insulin secretion ↓
Causes	Autoimmune	Insulin resistance β cell overwork

Insulin Resistance leads to an increase in Beta Cell Workload which ultimately leads to Beta Cell Failure and Death and the Progression of Type 2 Diabetes.

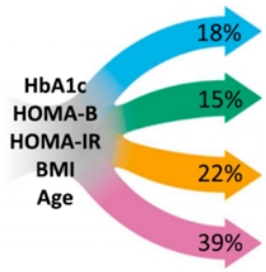
Type 1 and Type 2 Diabetes results in Beta Cell Loss and Reduction in Beta Cell Mass

Int. J. Mol. Sci.* **2016, *17*, 744; doi:10.3390/ijms17050744

Diabetes – the biggest Epidemic of the 21st century

Diabetes Patient Segments

		Patient Population	Proposed BMF-219 MOA
Pre-Diabetes	**Initial Decline in Glycemic Control** Increasing HbA1c, Increasing Insulin Resistance Decreasing beta cell numbers and function	90M	Beta Cell Preservation Beta Cell Growth
T2D	**SIDD = Severe Insulin Deficient Diabetes** Low insulin secretion, poor metabolic control, increased risk of retinopathy and neuropathy	6.3M	Beta Cell Reactivation Beta Cell Growth
	SIRD = Severe Insulin Resistant Diabetes Insulin resistance, obesity, late onset, increased risk of nephropathy and fatty liver	5.3M	Beta Cell Reactivation Beta Cell Preservation
	MOD = Mild Obesity-Related Diabetes Obesity, early onset	7.7M	Beta Cell Reactivation Beta Cell Growth
	MARD = Mild Age-Related Diabetes Late onset, low risk of complications	13.65M	Beta Cell Reactivation Beta Cell Preservation
T1D	**Initial Diagnosis/Disease – Stage 2/Stage 3** Increasing HbA1c, Initial Reduction in Insulin Significant Decrease in beta cell numbers	1.5M	Beta Cell Growth Beta Cell Preservation



BMF-219 Value Proposition in Diabetes

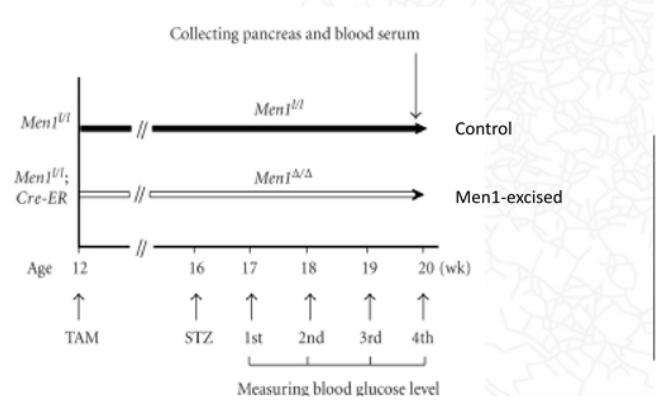
First in class molecule with paradigm shifting potential for the treatment of diabetes

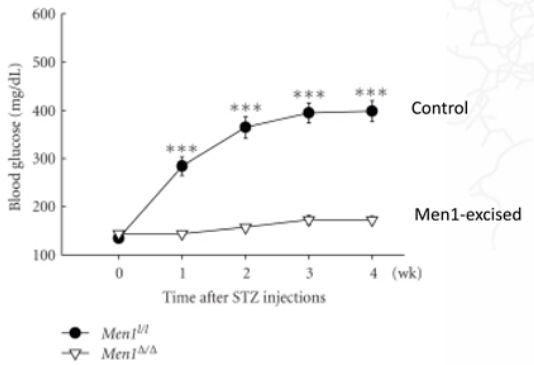
Oral Treatment for the Regeneration, Preservation, and Reactivation of Beta Cells

- **Disease modification** as the first treatment to potentially provide a functional cure of diabetes via restoration of beta cell homeostasis
- **Synergistic with GLP-1** based treatments while potentially insulin sparing. Potential utility in:
  - Prevention of T2D (90M prediabetic patients in the US)
  - 90% of T2D patients with beta cell impact
  - 50% of T2D patients on SOC but not at target A1C
  - T1D
  - Diabetic patients at risk for hypoglycemia
- **Potential reduction** in insulin dependance
- **MOA could positively impact**
  - NASH, CKD, CV benefit
  - Weight loss as monotherapy or in combination
  - Patients at risk for hypoglycemia under current SOC

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

MEN1 Excision Prevents Development of 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**

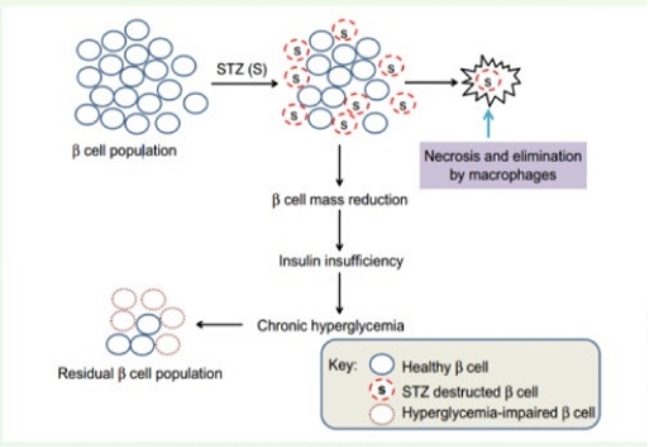
Sources: Yang et al. (2010) Deletion of theMen1Gene Prevents Streptozotocin-Induced Hyperglycemia in Mice. Experimental Diabetes Research, 2010, 1–11. doi:10.1155/2010/876701

First Development Success with BMF-219 in Type II Diabetes

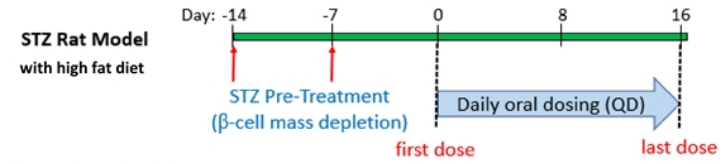
STZ Rat Model Study Design

The Streptozotocin (STZ)-Induced Rat Model

Only direct insulin injection shows an effect in this model



Study Design



Treatment groups (n=10/group):

1. Vehicle
2. BMF-219 175 mg/kg
3. Pioglitazone 30 mg/kg

Rats monitored for the following parameters through dosing include: OGTT, blood glucose levels

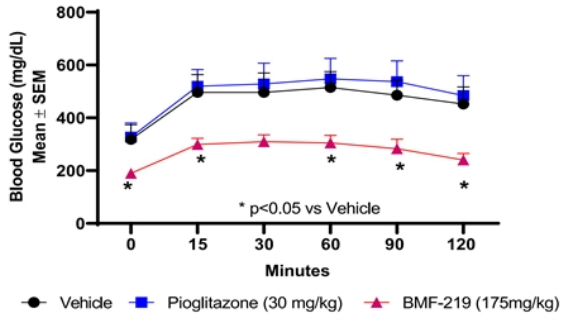
STZ treatment typically results in ~50% Beta Cell Loss

First Development Success with BMF-219 in Type II Diabetes

BMF-219 Demonstrates Strong Efficacy in Beta Cell Loss Animal Model (STZ Rat)

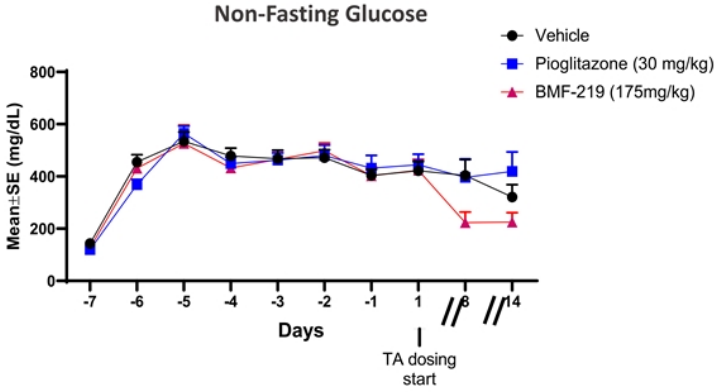
BMF-219 Achieves Glycemic Control in STZ (Beta Cell Loss) Rat Model

Oral Glucose Tolerance Test (Day 17)



BMF-219 achieves lower glucose level than pioglitazone at all timepoints in OGTT (day 17) in STZ rat model

Non-Fasting Glucose

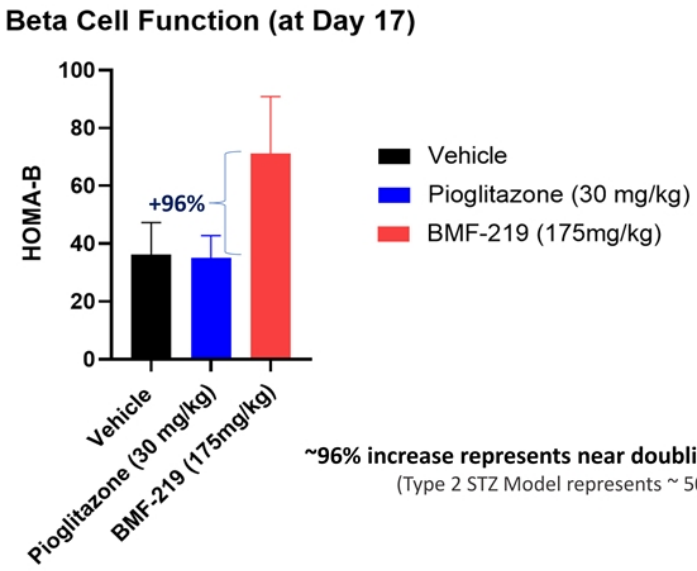


BMF-219 achieves lower non-fasting glucose than pioglitazone at day 8 and day 14 in STZ rat model

Butler et al., ADA 2022 (P-851)

First Development Success with BMF-219 in Type II Diabetes

BMF-219 Demonstrates Recovery of Beta Cell Activity

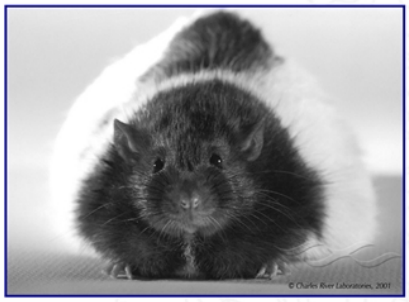


- HOMA-Beta, a measurement of Beta Cell Function, was analyzed using 4-hr fasting glucose and insulin levels in animal plasma.
- BMF-219 displayed a significant level of Beta Cell function compared to vehicle at Day 17 in a Beta Cell Type 2 Diabetes Model.
- This data supports the observed results from the Beta Cell Mass Quantitative Analysis using IHC. Importantly, Beta Cell Function is observed despite cessation of dosing.

~96% increase represents near doubling of beta cell function
(Type 2 STZ Model represents ~ 50% Beta Cell Destruction)

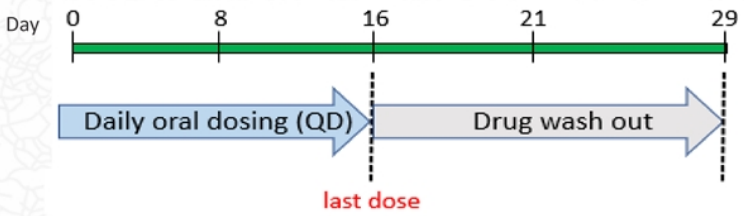
Zucker Diabetic Fatty Rat - a Model of Insulin Resistance

The ZDF Rat



- The ZDF rat is a model of pancreatic exhaustion, thus mimicking some aspects of human diabetes.
- Pioglitazone and metformin provide therapeutic efficacy in this model.
- The ZDF rat is a translatable model for studying the development of T2D.

Study Design



Rats monitored for the following parameters through dosing and washout phases include:
Body weight, fasting blood glucose, blood insulin, C-peptide, and OGTT

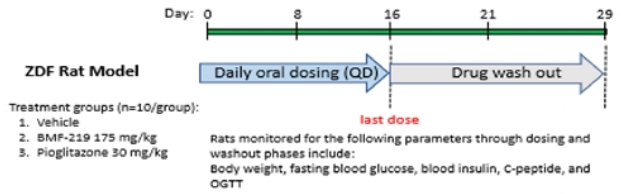
Treatment groups (n = 10/group):

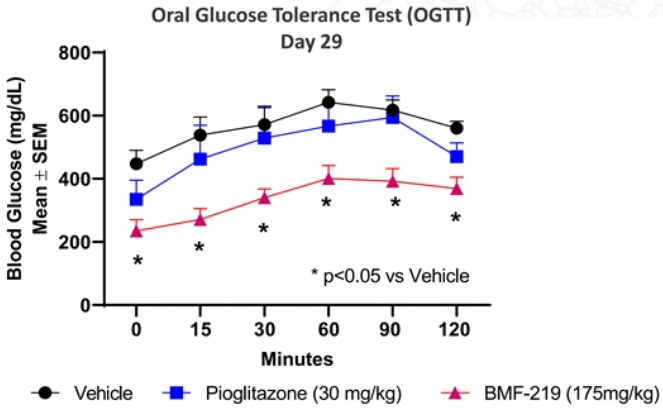
1. Vehicle
2. BMF-219 175 mg/kg
3. Pioglitazone 30 m g/kg

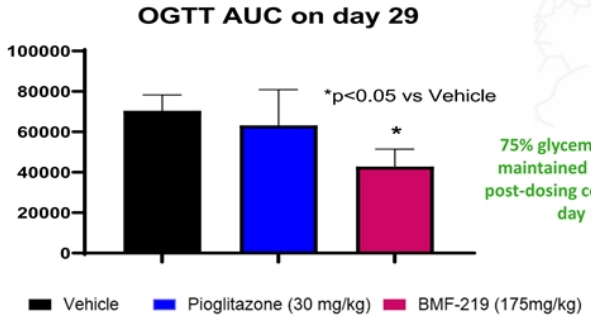
First Development Success with BMF-219 in Type II Diabetes

BMF-219 Displays Durable Glycemic Control during Drug Washout and Two Weeks after the Last Dose

After 2-week Drug Washout





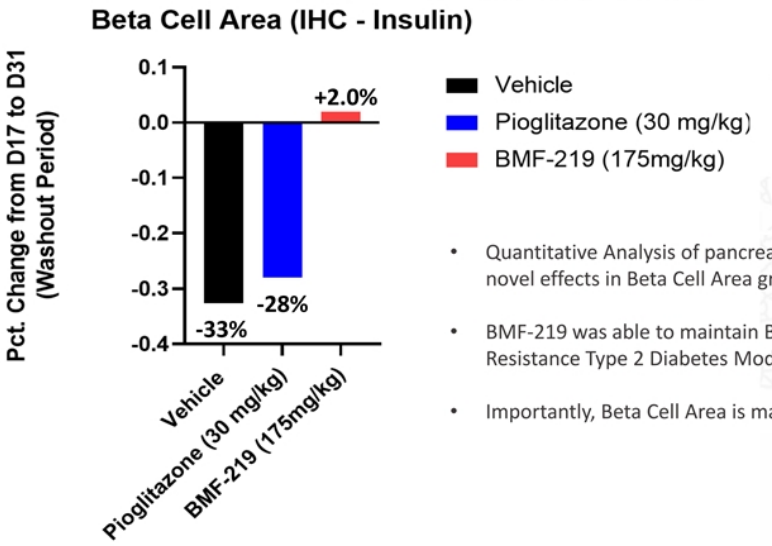


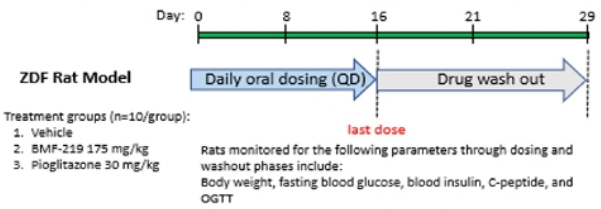
75% glycemic control maintained on day 29 post-dosing compared to day 15

ZDF rats treated with BMF-219, pioglitazone or vehicle control for 16 days were monitored for blood glucose levels by OGTT on day 29, ~2 weeks after administration of the last dose, displaying an AUC reduction of 40%, ($p<0.05$).

First Development Success with BMF-219 in Type II Diabetes

BMF-219 Increases B-islets in Pancreas Sections of ZDF Diabetic Model

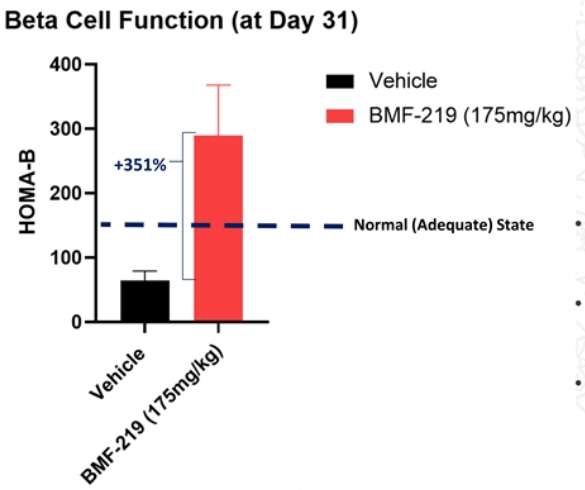




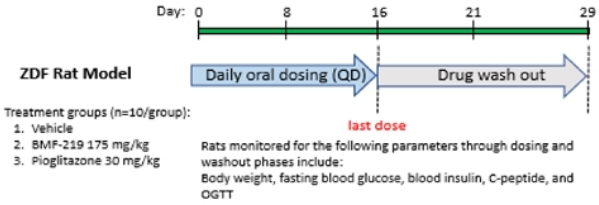
- Quantitative Analysis of pancreatic islet tissue cross sections shows BMF-219 treated animals show novel effects in Beta Cell Area growth and maintenance.
- BMF-219 was able to maintain Beta Cell function and prevent Beta Cell Area Loss in an Insulin Resistance Type 2 Diabetes Model.
- Importantly, Beta Cell Area is maintained, despite cessation of dosing.

First Development Success with BMF-219 in Type II Diabetes

BMF-219 Demonstrates Strong B-cell Activity - Supporting Quantitative Analysis



O.J. Fasipe et al. / Can J Diabetes 44 (2020) 663e669

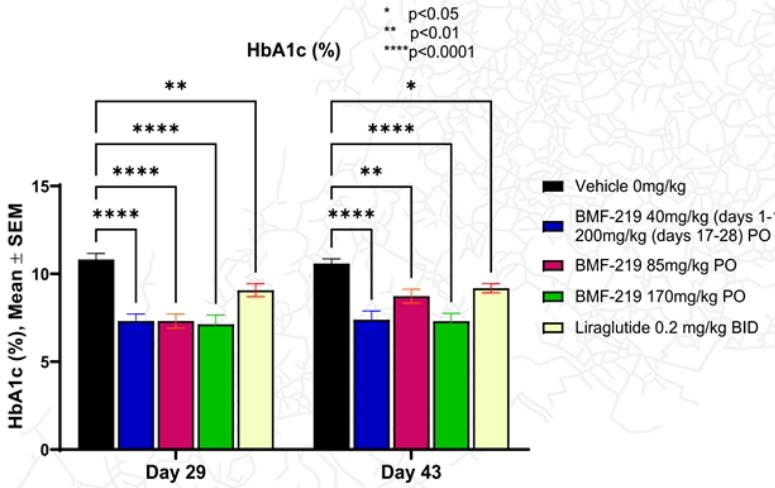


- HOMA-Beta, a measurement of Beta Cell Function, was analyzed using 4-hr fasting glucose and insulin levels in animal plasma.
- BMF-219 displayed a significant level of Beta Cell function compared to vehicle at Day 31 in an Insulin Resistance Type 2 Diabetes Model.
- This data supports the observed results from the Beta Cell Area Quantitative Analysis using IHC. Importantly, Beta Cell Function is observed despite cessation of dosing.

First Development Success with BMF-219 in Type II Diabetes

BMF-219 Demonstrates Strong Efficacy in Insulin Resistant Animal Model (ZDF Rat)

BMF-219 Reduces HbA1c After 28 days of Treatment and Maintains Effect After 14-day Washout



Somanath et al., ADA 2022 (113-LB)

BMF-219 demonstrated significant decrease in HbA1c (-3.5% at day 29) vs. control starting on day 21 of treatment

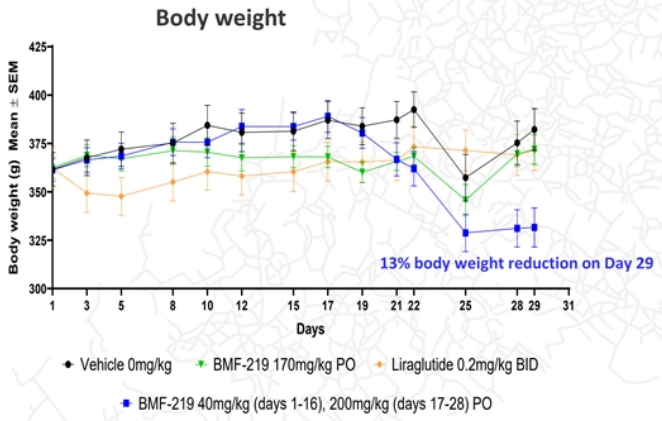
BMF-219 treated group demonstrated significant weight reduction starting at day 25

HbA1c reduction in BMF-219 highest dose groups maintained through washout period

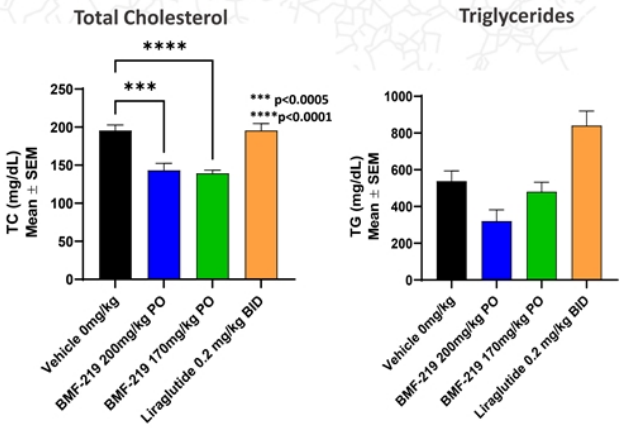
First Development Success with BMF-219 in Type II Diabetes

BMF-219 Treated Groups Display Body Weight and Cholesterol Reduction

BMF-219 200 mg/kg group reduces body weight during treatment in ZDF rats



BMF-219 reduces blood lipemic levels measured on Day 29



First Development Success with BMF-219 in Type II Diabetes COVALENT – 111 (Enrolling)

A Phase 1/2 Randomized, Double-Blind, Placebo-Controlled Single and Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BMF-219, an Oral Covalent Menin Inhibitor, in Healthy Adult Subjects and in Adult Subjects with Type 2 Diabetes Mellitus

Phase 1 (SAD)

SAD C1 to SAD C4 (HVs)
Total N=40
Dose [100, 200, 400, and 600 mg]

Phase 2 (MAD)

MAD C1 (HVs)
Total N = 16

MAD C2 to MAD C8 (T2D)
Total N=108

Dose [100, 200, 300, 400, 600 mg]

In the Phase 2, COVALENT-111 will enroll subjects with a HbA1C of 7-10% despite being on standard of care, up to three agents of therapy.

Study Treatment: BMF-219

- A covalent small molecule menin inhibitor, administered orally daily in 28 day cycles

Primary Objective:

- Evaluate safety and tolerability of BMF-219

Secondary Objectives:

- Evaluate PK of BMF-219
- Evaluate the effect on BMF-219 on glycemic parameters (HbA1C, PG) and few additional parameters using OGTT, 7-day CGM
- Evaluate the changes in beta cell function
- Evaluate impact on lipid parameters, body weight etc.

Exploratory Objectives:

- To assess the durability of response to glycemic parameters

Second Development Success with BMF-500

BMF-500 A Third Generation FLT3 Inhibitor

Generation of FLT3 Inhibitor	First Generation FLT3 / multi-kinase Inhibitors			Second Generation FLT3 Inhibitors			Third Generation FLT3 Inhibitors
Products	**Midostaurin** *(FDA Approved as RYDAPT)*	**Lestaurtinib** *(Failed in clinical trials)*	**Sorafenib** *(FDA Approved as NEXAVAR)*	**Quizartinib** *(FDA Rejected due to Cardiotox)*	**Gilteritinib** *(FDA Approved as XOSPATA)*	**Crenolanib** *(Phase 3 in US)*	**BMF-500** *(Covalent Inhibitor, Preclinical)*
Benefits	• *In vitro* potency against FLT3 • Oral route of administration			• More selective for FLT3	• Improved PK properties	• Improved potency D835 • Reduced KIT inhibition	• Drives cell death • Improved FLT3 potency and selectivity • Improved activity in known resistance mechanisms • Limited impact on cKIT at projected physiological dose
Challenges	• Poor kinase selectivity • Challenging pharmacokinetic (PK) profile • Low steady state free drug concentration • Low potency resulting from challenging PK at tolerable doses			• Adverse Events • QTc impact • Cytopenia	• Drives Differentiation • Myelo-suppression • Frequent Dose Adj • QTc impact	• TID Dosing • F619 Resistance • Drives Differentiation	• Limited history of covalent FLT3 experience in the clinic • Novel scaffold with emerging profile
Kinome Selectivity							 BMF-500

Sources: Levis M. (2017). Midostaurin approved for FLT3-mutated AML. *Blood*, *129*(26), 3403–3406. https://doi.org/10.1182/blood-2017-05-782292; Drugs@FDA.gov

BMF-500 Highly Effective FLT3 Inhibitor Against Resistance Mutations

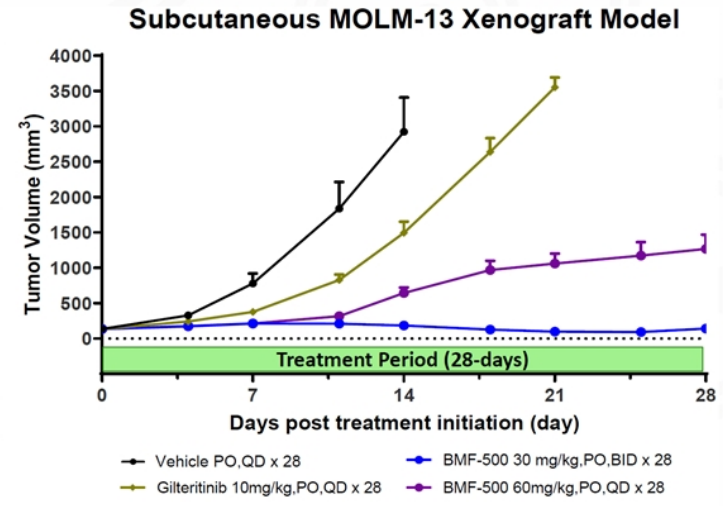
NanoBRET Target Engagement Assay, IC_{50} (nM)

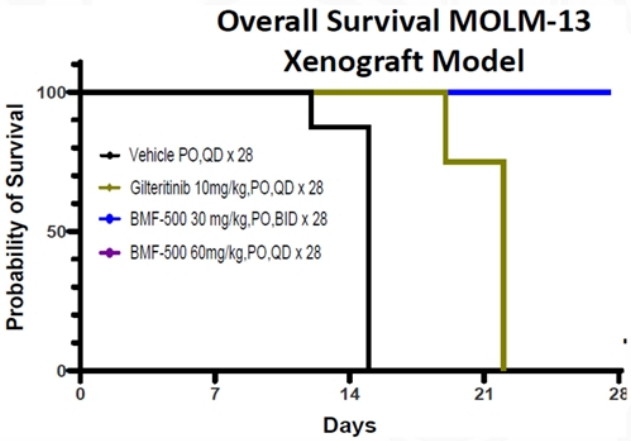
Cmpd ID	FLT3 WT	FLT3 (D835H)	FLT3 (D835V)	FLT3 (D835Y)
BMF-500	0.31	0.18	0.22	0.25
Gilteritinib	23.4	1.45	1.1	1.4

FLT3 Inhibitor Resistance Mutations Coverage, IC_{50} (nM)

Cmpd ID	FLT3-ITD	FLT3-ITD-D835Y	FLT3-ITD-F691L
BMF-500	2 nM	5 nM	7 nM
Gilteritinib	7 nM	19 nM	98 nM

BMF-500 Highly Potent and Durable FLT3 Inhibitor

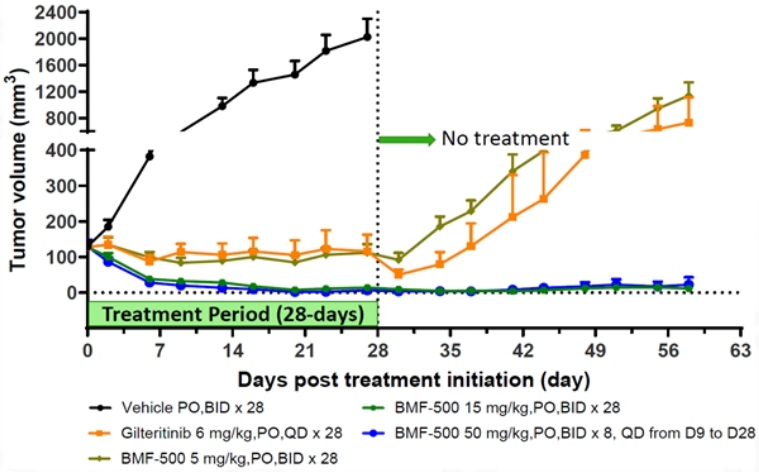




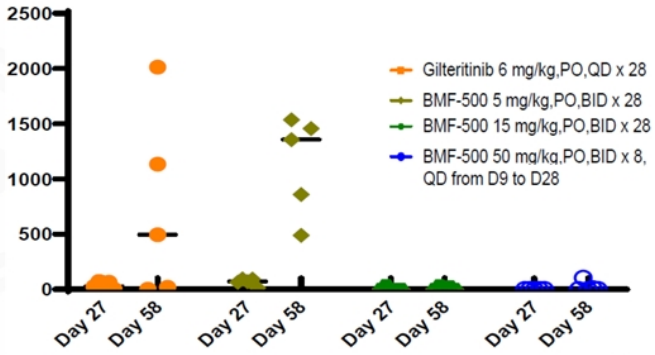
Second Development Success with BMF-500

BMF-500: Highly Potent and Durable FLT3 Inhibitor

Subcutaneous MV-4-11 Xenograft Model



Individual Tumor Volume MV-4-11 Xenograft Model



biomea FUSION We Aim to Cure

2023 : Exploring 8 Different Tumor Types and Type II Diabetes in the Clinic

- [ ] Present initial Phase II clinical data in Type 2 Diabetes: 1Q 2023
- [ ] Present initial Phase I clinical data in AML: 1H 2023
- [ ] Continue enrolling patients in trials exploring BMF-219 utility in KRAS driven Solid Tumors (PDAC, NSCLC, CRC) and Liquid Tumors (AML/ALL, MM, CLL, DLBCL)
- [ ] File IND for BMF-500: 1H 2023
- [ ] Initiate Phase I trial for BMF-500: 1H 2023
- [ ] Announce third pipeline asset from FUSION™ platform technology : 1H 2023

- [x] Cash as of 30 Sept 2022 $133.8M - Capitalized into 2024

As of September 30, 2022

Company Financials (NASDAQ: BMEA)

	Three Months Ended Sept 30	
	2022	2021
Operating expenses:		
R&D	$ 18,242	$ 7,886
G&A	$ 5,242	$ 4,752
Total Operating Expenses	$ 23,484	$ 12,638
Loss from operations	$ (23,484)	$ (12,638)
Interest and other income, net	$ 594	$ 32
Net loss	$ (22,890)	$ (12,606)
Other comprehensive loss:		
Changes in unrealized gain on short term investments, net	$ 4	-
Comprehensive loss	$ (22,886)	$ (12,606)
Net loss per common share, basic and diluted	$ (0.78)	$ (0.43)
Weighted-average number of common shares used to compute basic and diluted net loss per common share	29,319,042	29,001,213

Cash as of 31 June 2022	$ 150.2M
Net Cash Burn Q3	$ 16.4M
Cash as of 30 Sept 2022	**$ 133.8M**

THANK YOU

biomea FUSION | We Aim to Cure™

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