biomea FUSION™

Corporate Presentation
August 2022

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- Experienced and Successful Management Team
- Novel FUSION™ System
- BMF-219 - Clinical Stage Lead Asset
- BMF-500 and Additional Programs Built From FUSION™ System

We Aim To Cure™

Biomea Fusion is a clinical-stage biopharmaceutical company focused on the discovery and development of 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.

Our Team – 10+ Years of Success Together

Thomas Butler
Chairman & CEO

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

- Co-inventor of FUSION system
- Co-inventor of Remdesivir at Gilead

Veklury® remdesivir 100 MG FOR INJECTION

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

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

- Co-inventor of FUSION system
- Co-lead of Ledipasvir at Gilead

HARVONI® ledipasvir / sofosbuvir

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

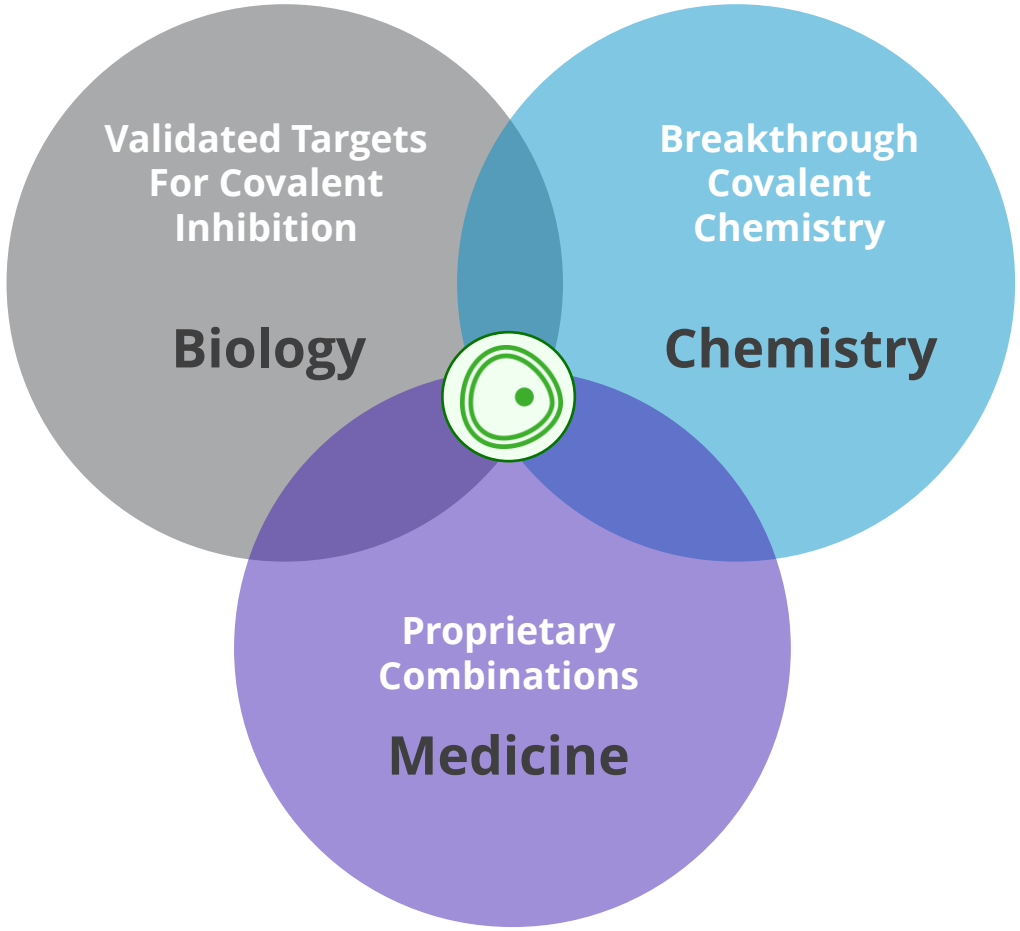
-Co-inventor of FUSION system and
- Co-inventor of ibrutinib at Celera

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

biomea FUSION™ We Aim to Cure™

Our Vision – We Are Patient Focused and Aim to Cure

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



Validated Disease Targets

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

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

Covalent Sm. Mol. Inhibitors

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

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

Proprietary Combinations

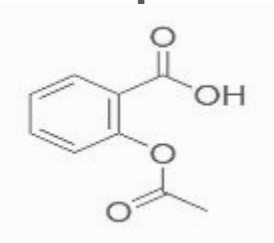
Combination therapy with non-overlapping resistance mechanisms results in more durable responses and better outcomes

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

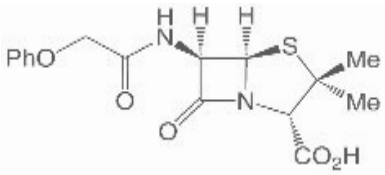
Covalent Inhibitors – a History of Medical & Commercial Success

Notable Covalent Inhibitors

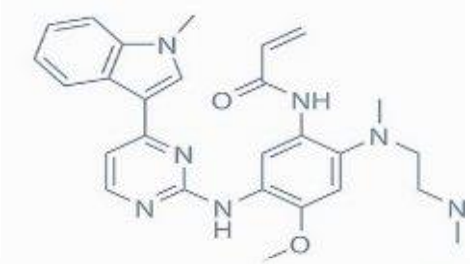
Aspirin

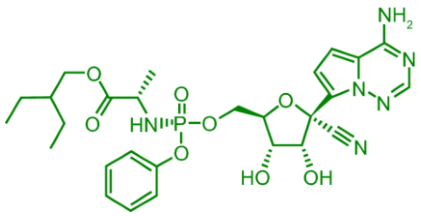


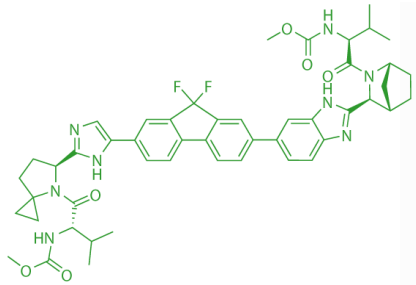
Penicillin

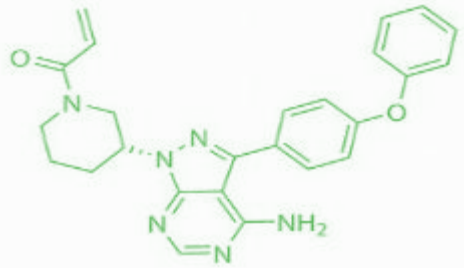


Osimertinib (TAGRISSO)









Remdesivir (VEKLURY) **Ledipasvir (HARVONI)** **Ibrutinib (IMBRUVICA)**

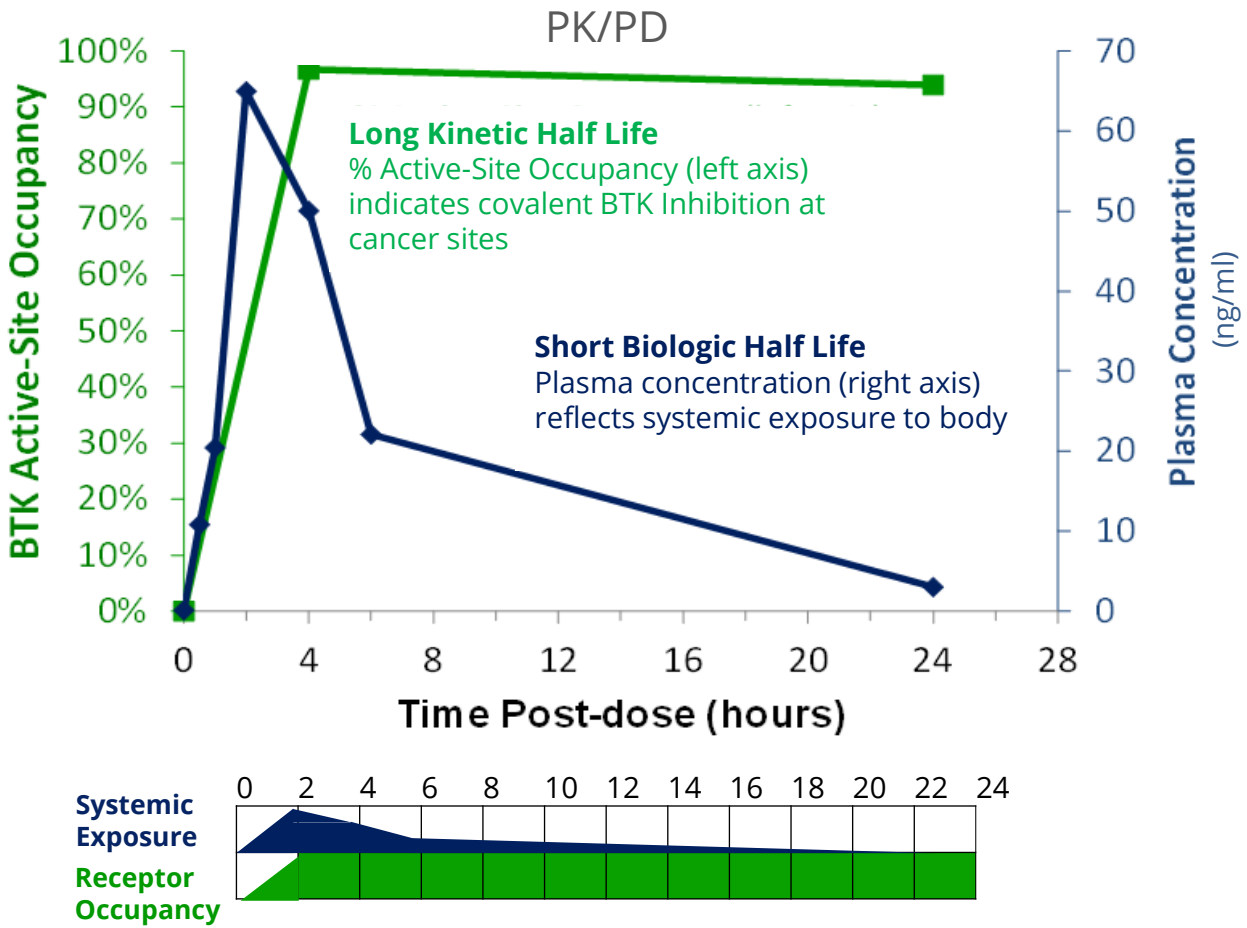
Compounds in green invented by Biomea Fusion senior leadership

- **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 COVID-19

Benefits of Covalent Inhibition

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

Ibrutinib Example –
Long Kinetic Half Life and Short Biologic Half Life



BTK: Bruton's Tyrosine Kinase

High Selectivity

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

Deep Target Inactivation

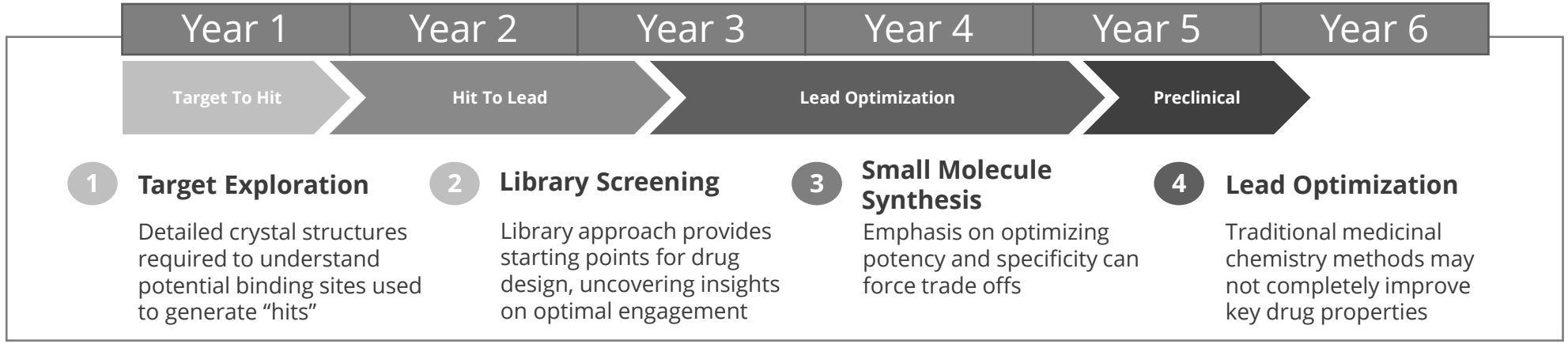
Permanent inactivation of bound protein drives target elimination through normal cellular degradation processes

Greater Therapeutic Window

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

Our Technology Platform – Covalent Inhibitors

Traditional Small Molecule Design
(Library Screening and Synthesis)



1 Target Exploration
Detailed crystal structures required to understand potential binding sites used to generate "hits"

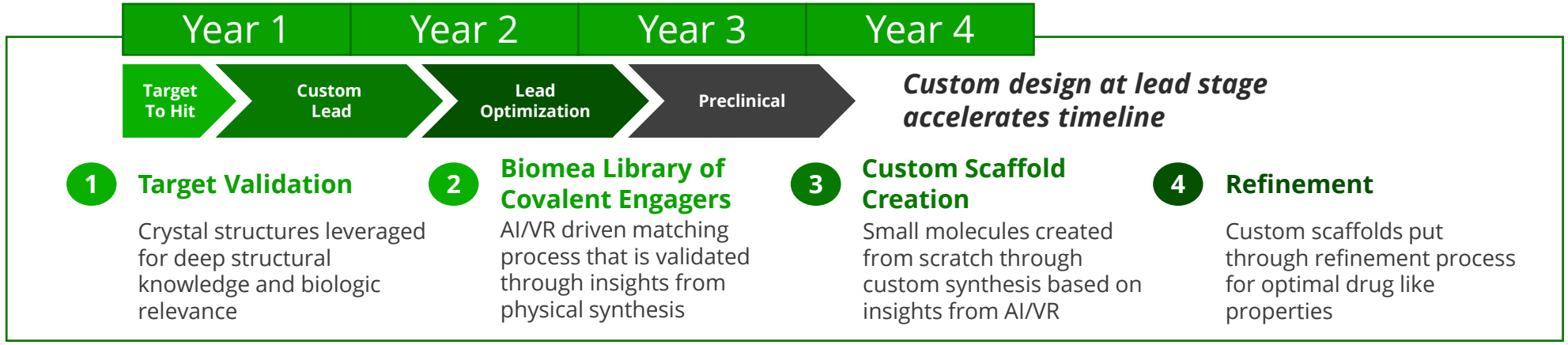
2 Library Screening
Library approach provides starting points for drug design, uncovering insights on optimal engagement

3 Small Molecule Synthesis
Emphasis on optimizing potency and specificity can force trade offs

4 Lead Optimization
Traditional medicinal chemistry methods may not completely improve key drug properties

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.

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



Custom design at lead stage accelerates timeline

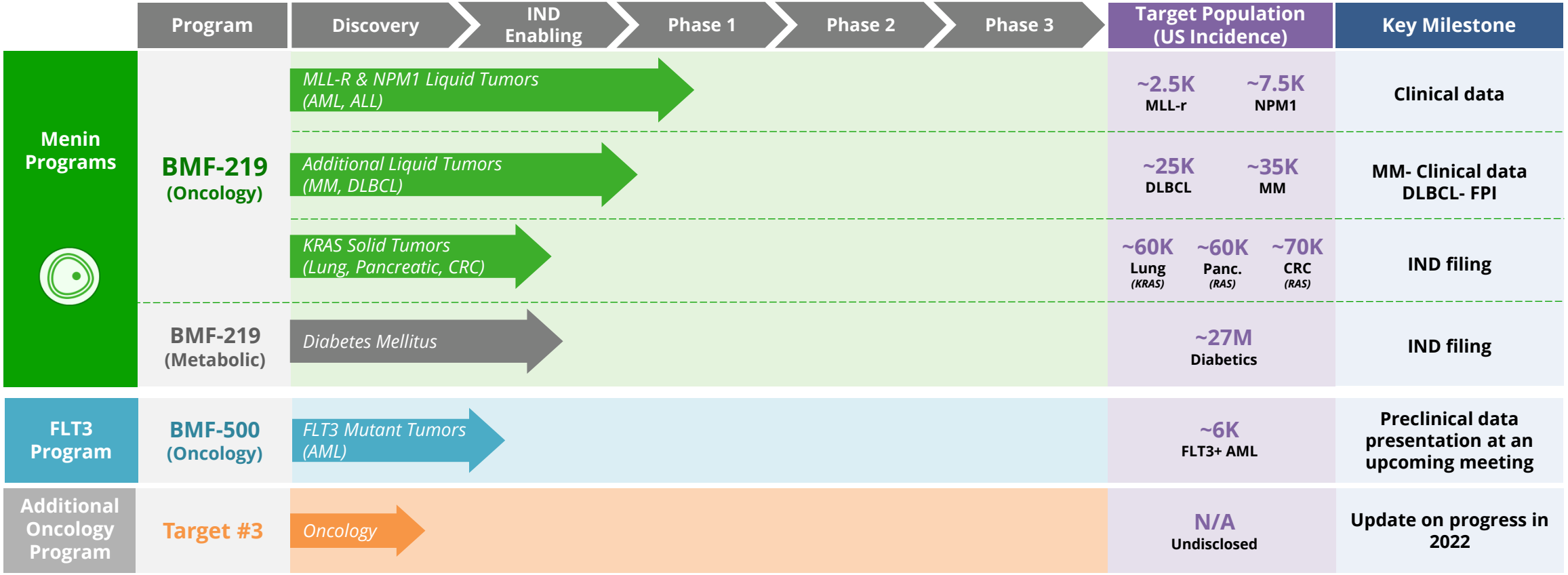
1 Target Validation
Crystal structures leveraged for deep structural knowledge and biologic relevance

2 Biomea Library of Covalent Engagers
AI/VR driven matching process that is validated through insights from physical synthesis

3 Custom Scaffold Creation
Small molecules created from scratch through custom synthesis based on insights from AI/VR

4 Refinement
Custom scaffolds put through refinement process for optimal drug like properties

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



BMF-219 → Next Generation Menin Inhibitor

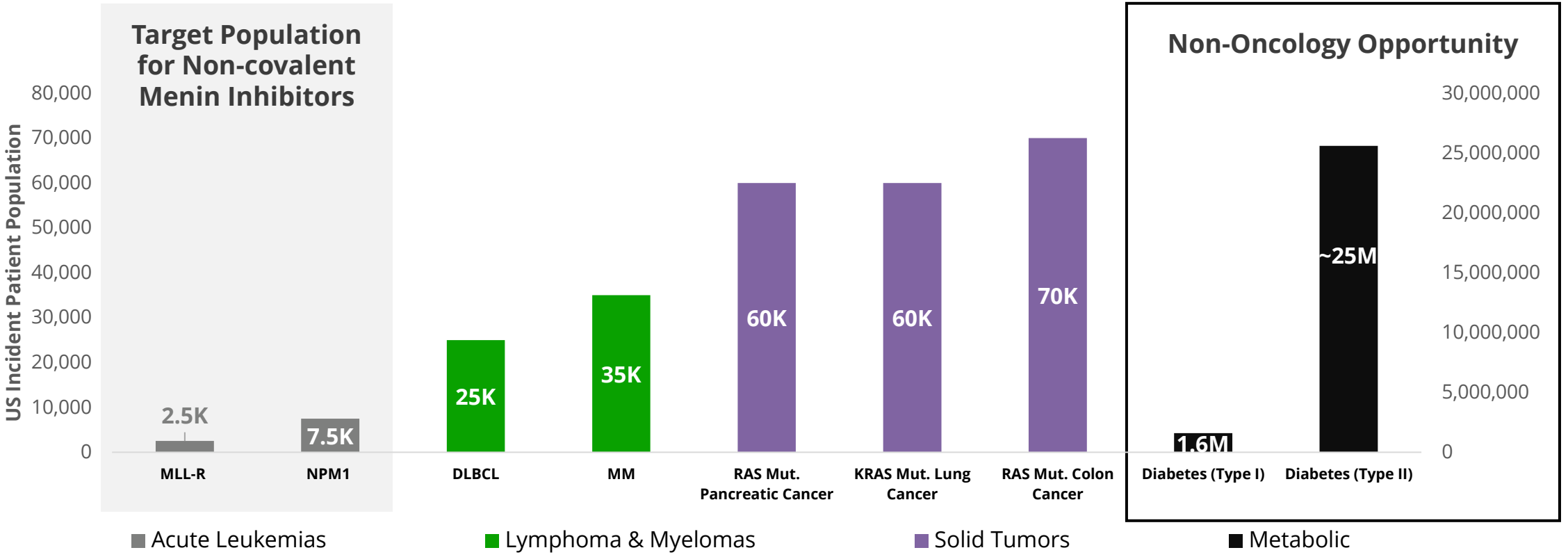
Attacks the target by forming a covalent bond

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

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

BMF-219 to Pursue Multiple Tumor Types and Diabetes in 2022

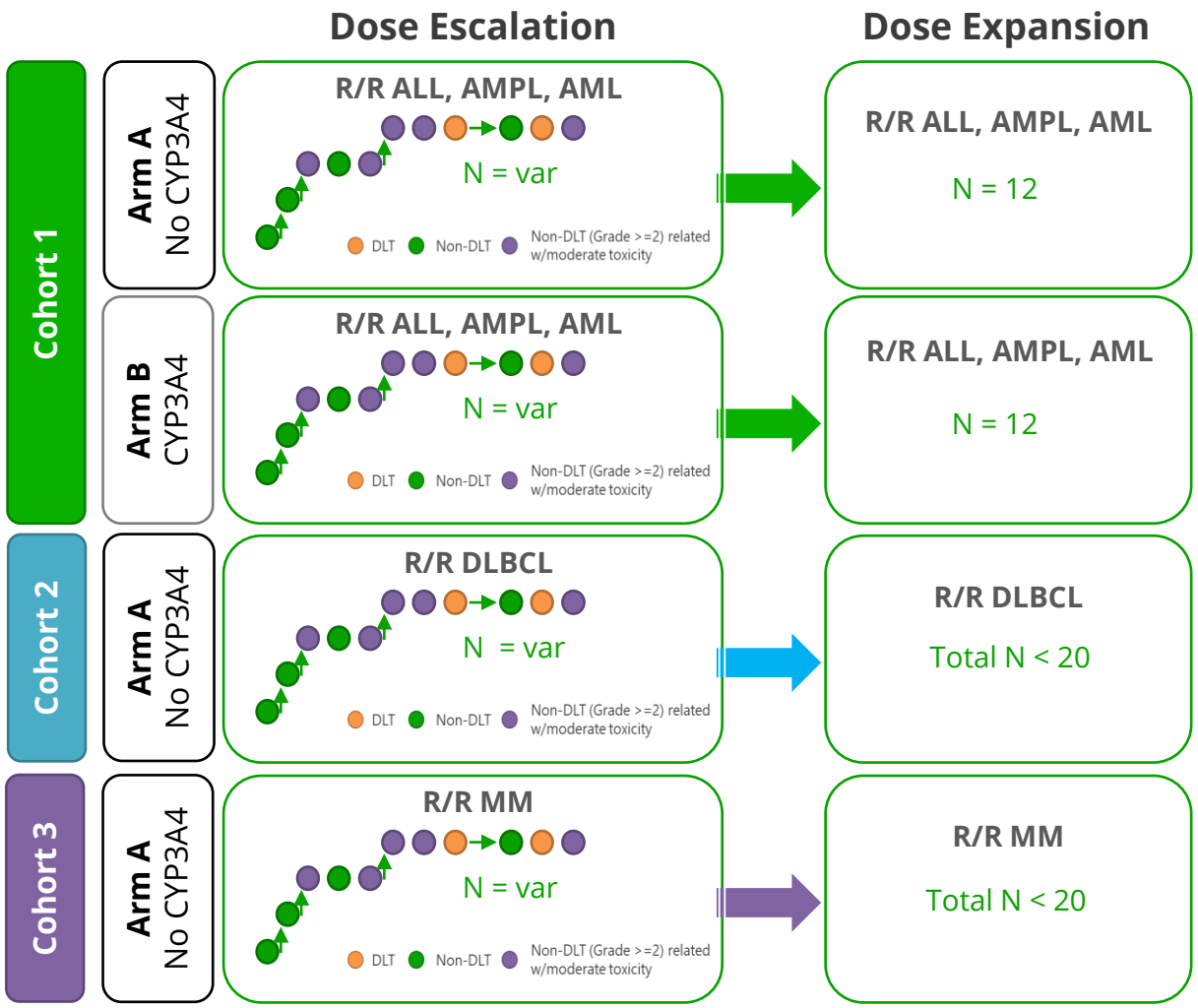
Target Patient Population for BMF-219



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

COVALENT-101

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, and r/r multiple myeloma (NCT05153330)



Accelerated titration design followed by classical 3+3

Cohorts:

- **Cohort 1** for AML/ALL patients (Arm A & Arm B)
- **Cohort 2** for R/R DLBCL with 2L – 5L of therapy
- **Cohort 3** for R/R MM with ≥ 3L of therapy
- Arm A: Starting dose 100 mg QD
- Arm B: Starting dose 25 mg QD
- Accelerated titration design followed by classical "3+3" with subsequent dose expansion for each cohort
- Food-Effect component for Cohorts 2 and 3

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

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

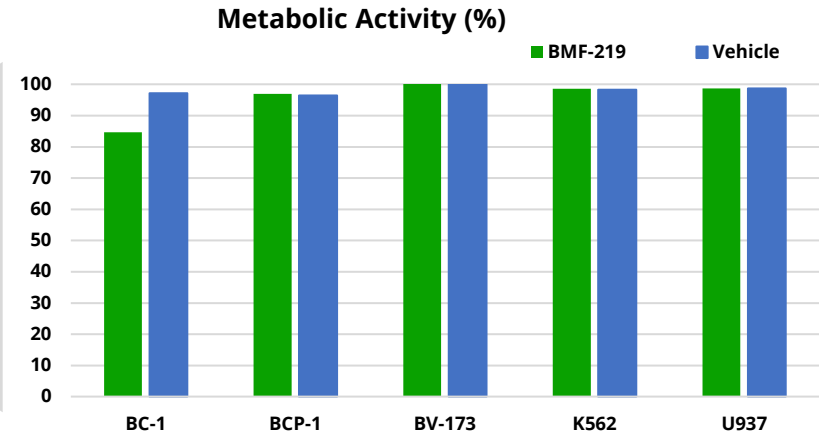
No Histopathology Findings Were Observed with BMF-219 in GLP and non-GLP IND-Enabling Toxicology Studies

✓ 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 – Novel Covalent Inhibitor of Menin

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

MYC Addicted and Driven Tumors

RAS/RAF Driven Solid Tumors

Diabetes

BMF-219: In Acute Leukemia

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

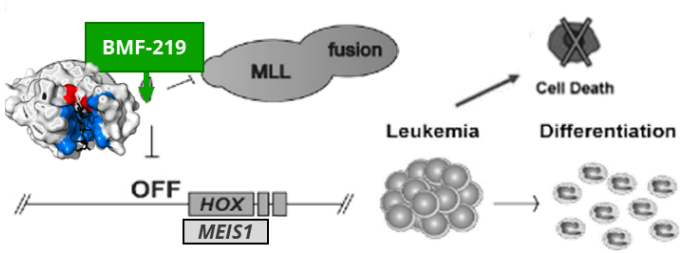
Key Facts

Estimated Target Population

Acute Leukemia (Mutation)	Estimated US Patient Population (Annual Incidence)
MLL-r	~2,500
NPM1 mutant	~7,500
Ras Driven	~6,500

MOA

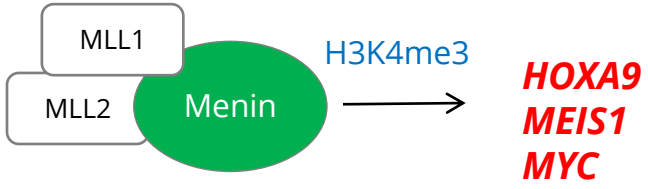
BMF-219 covalently blocks menin / MLL interaction



- 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

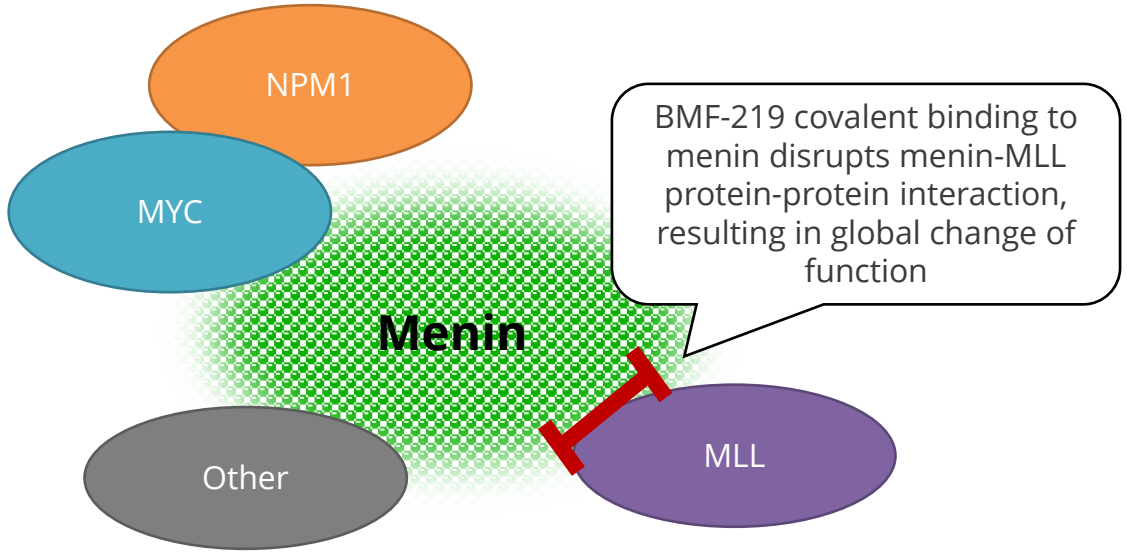
Menin / MLL interaction can modify chromatin, activating key leukemic genes



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

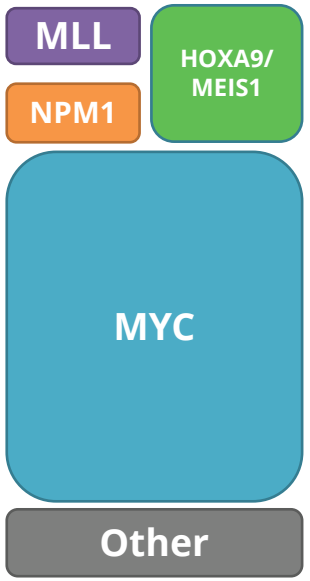
BMF-219 Has the Potential to Impact Important Binding Partners Involved in Multiple Tumors

Mechanism of Action



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

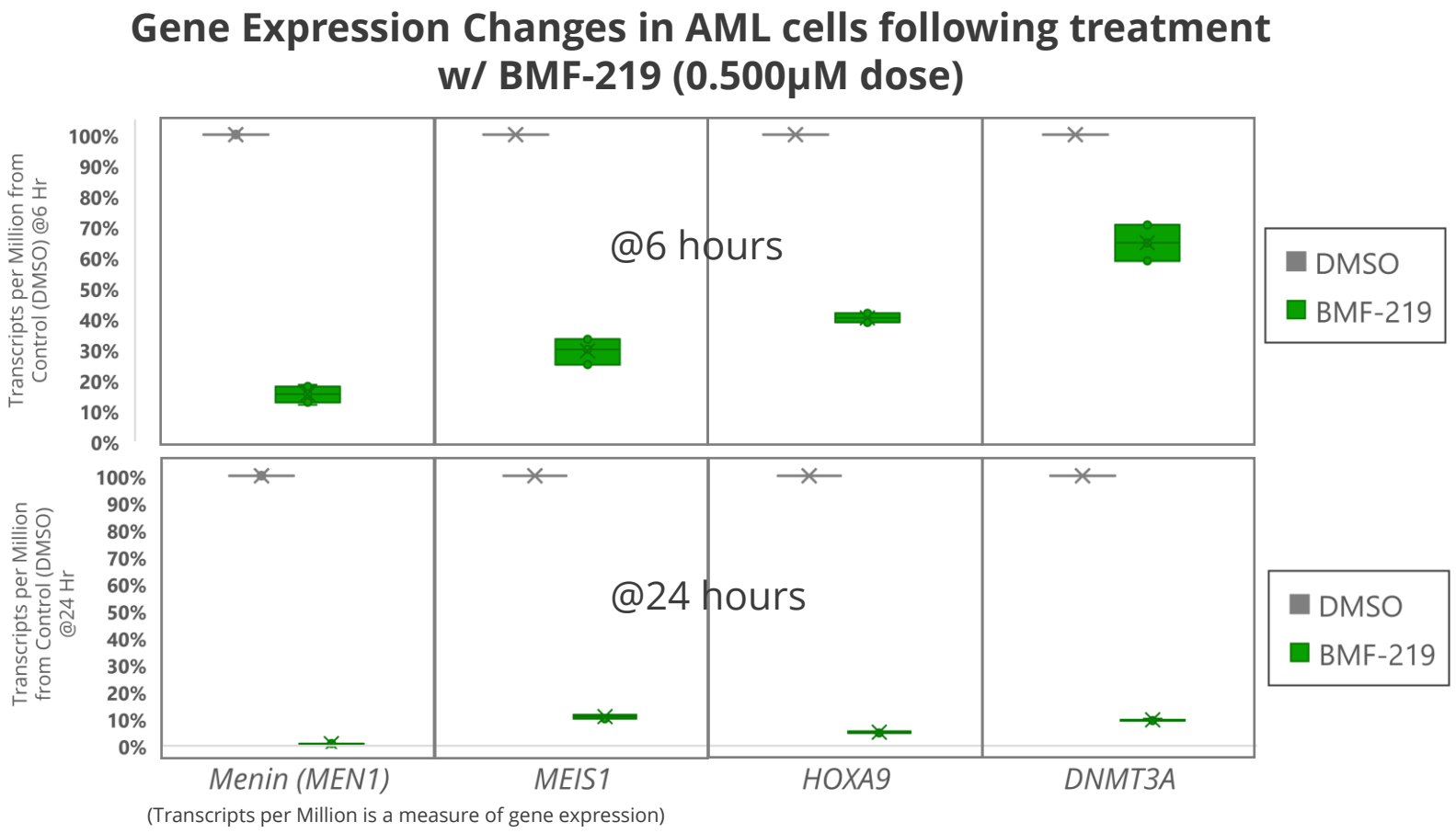
Target Patient Population



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

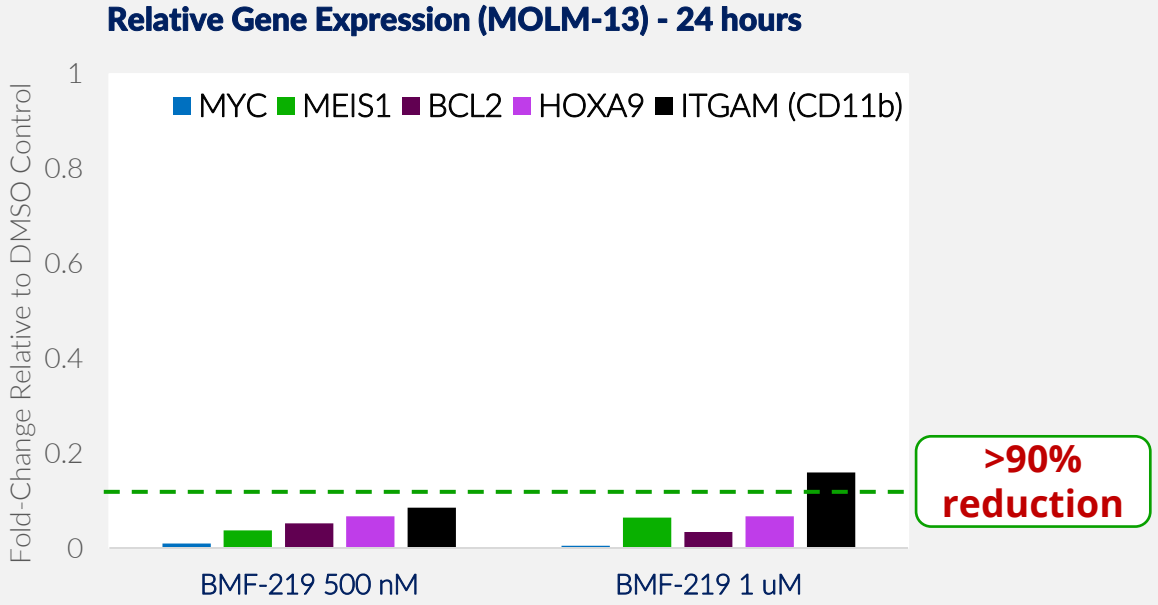
BMF-219 has the potential to address additional patient populations that are dependent on menin or some of its binding partners

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

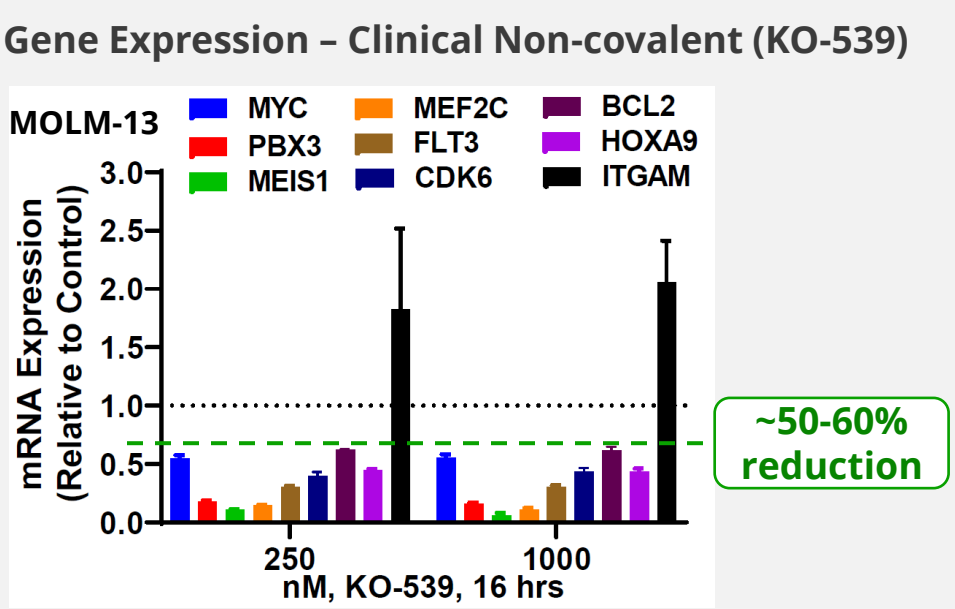


- Covalent inhibitor, BMF-219, downregulates expression of Menin (via the target *MEN1* gene) and critical leukemogenic genes (e.g. *MEIS1* and *HOXA9*)
  - *MEIS1* is a gene that can be an accelerator of leukemic transformation (along with *HOXA9*)
  - *HOXA9* is a gene involved in myeloid differentiation 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 Displayed Superior Impact on Key Gene Signatures in MLL-rearranged AML Cell Line



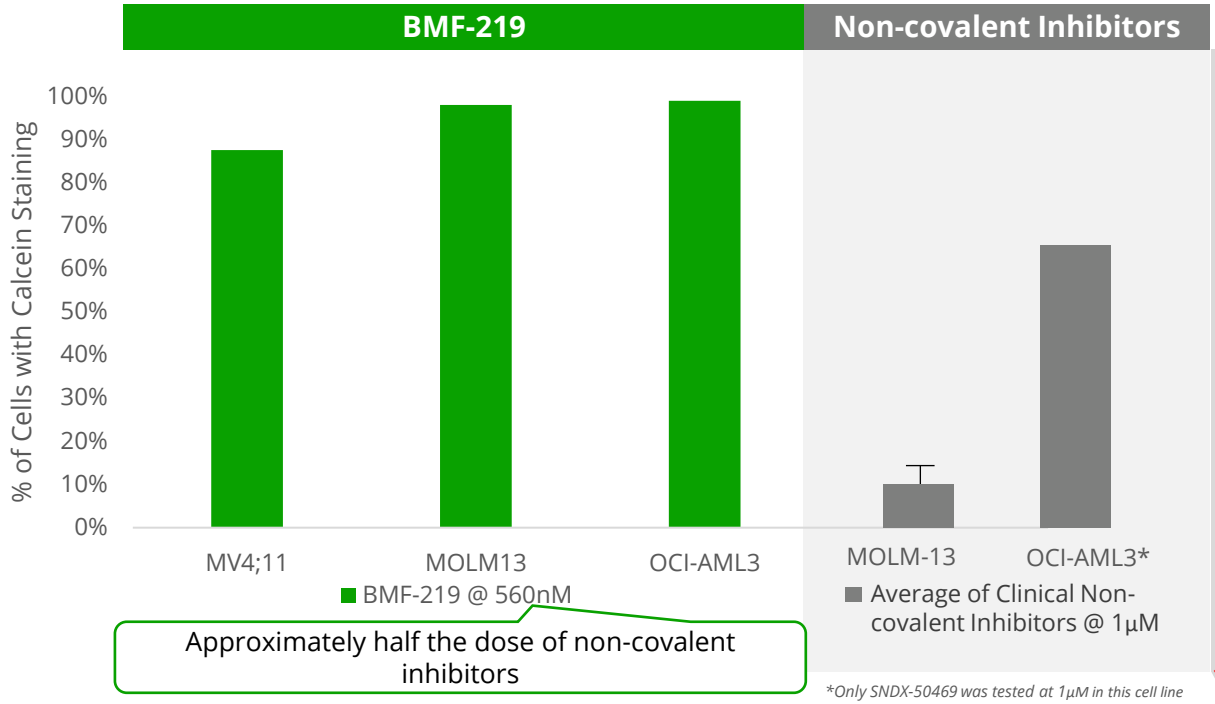
Somanath et al., ASCO 2022 Abstract 7541



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

- Differentiation marker, ***ITGAM (CD11b)*, expression increases *2 to 3-fold* at 6 hours, followed by *~8 to 10-fold* reduction** at 24 hours with BMF-219
- ***MEIS1* expression is reduced *~10 to 20-fold* at 24 hrs** with BMF-219
- ***HOXA9* expression decreases *~15-fold* at 24 hrs** with BMF-219
- ***BCL2* expression decreases *~20 to 30-fold* at 24 hrs** post-treatment with BMF-219
- ***MYC* expression is reduced *~100 to 200-fold* at both 6 and 24 hrs** post-treatment with BMF-219

BMF-219 Exerted Superior Cell Killing of AML Cell Lines at Half the Dose vs Non-Covalent Menin Inhibitors



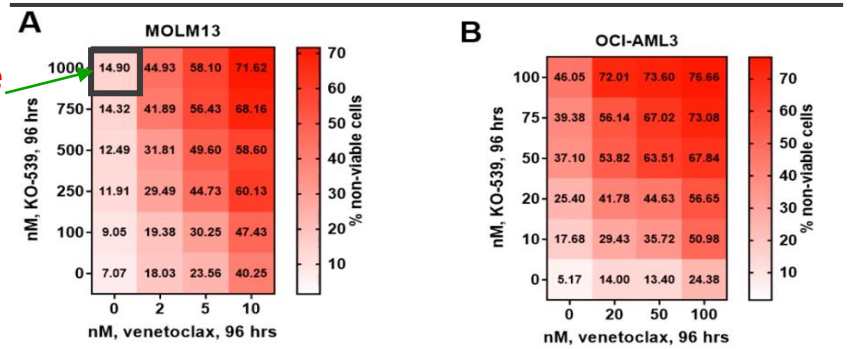
- **BMF-219 killed >90% of AML cells in MLL-rearranged and NPM1 mutant cell lines at 4 days post-treatment**
- **Non-covalent menin inhibitors generally report significantly less cell killing of AML cell lines as a single agent**

15% effective @ 1uM

12% effective @ 1uM

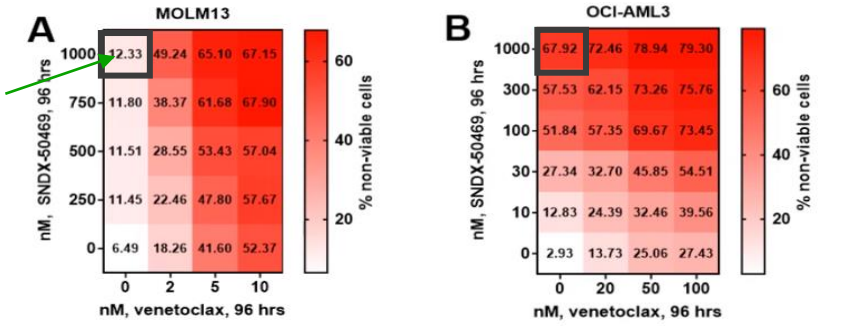
Source Data from ASH 2021 Publications

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



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

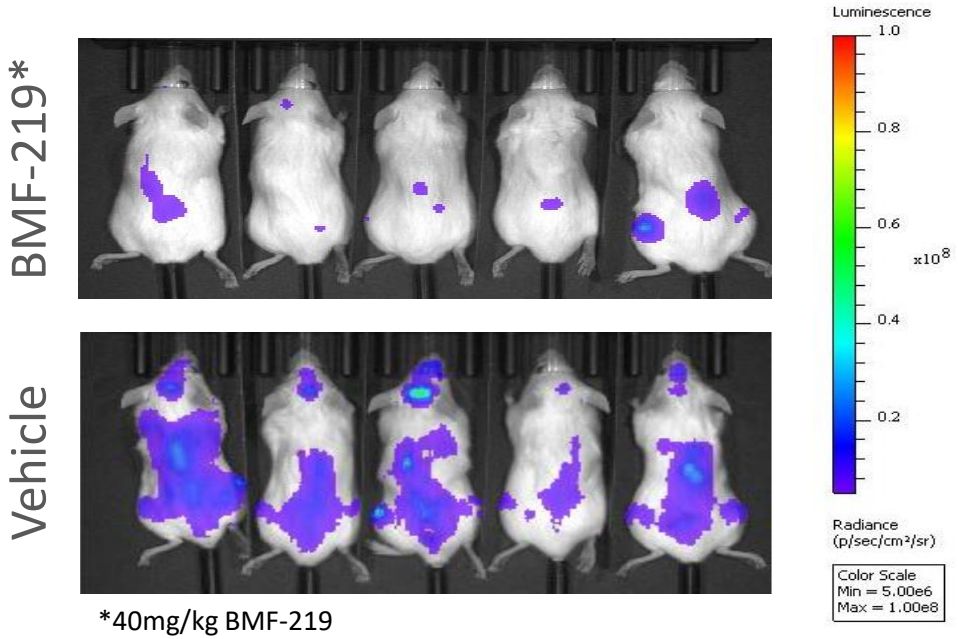
SNDX-50469 is 12% effective @ 1µM in MOLM-13 cells



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

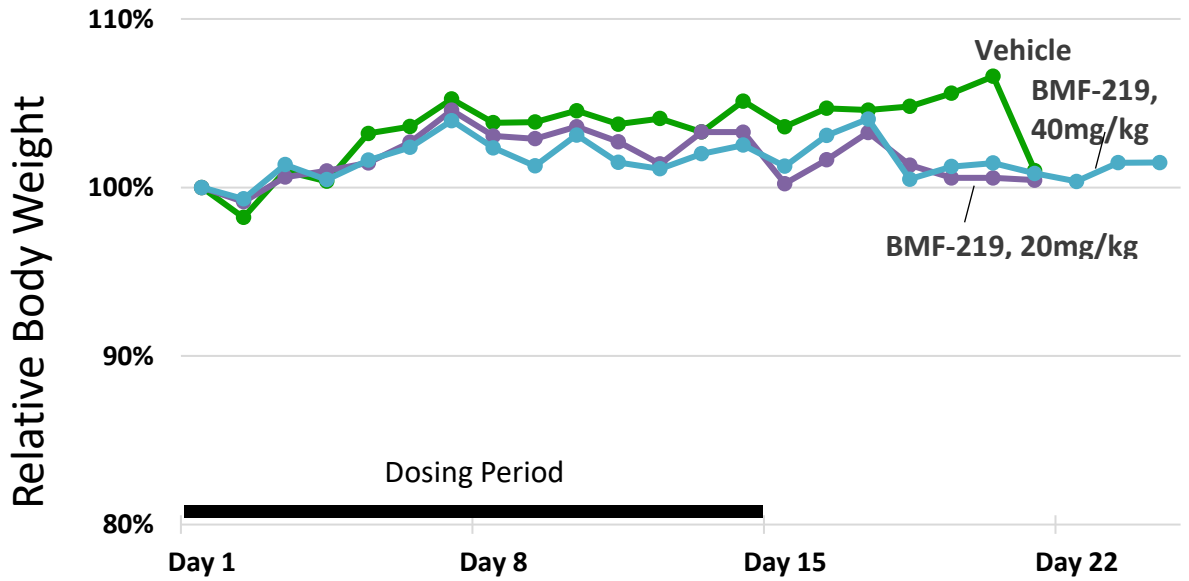
BMF-219 Achieved Significant Survival Benefit in A Disseminated Leukemia Xenograft Model

Anti-Tumor Effect



*40mg/kg BMF-219

Body Weight



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

BMF-219 – Novel Covalent Inhibitor of Menin

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

MLL Fusion & NPM1 Driven Tumors

MYC Addicted and Driven Tumors

Expansion into r/r diffuse large b cell lymphoma and r/r/ multiple myeloma

RAS/RAF Driven Solid Tumors

Diabetes

BMF-219: In Diffuse Large B-cell Lymphoma (DLBCL) and Multiple Myeloma (MM)

Development Stage: Phase I Clinical Trial (COVALENT-101) enrolling patients with relapsed/refractory DLBCL and MM

Key Facts

Estimated Target Population

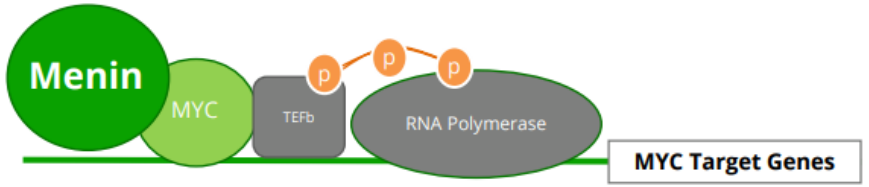
Disease	Estimated US Patient Population (Annual Incidence)
DLBCL	~25,000
MM	~35,000

- MYC addiction tends to increase with stage and line of therapy
- ~20-50% MYC dysregulation or translocations in newly diagnosed MM patients
- ~50-70% of advanced r/r MM patients have MYC dysregulation
- ~10,000 (40%) of DLBCL patients are Double and Triple Hit and Double expressors (BCL2 and MYC overexpression)
- >50% of relapsed/refractory DLBCL are double expressors

MOA

Menin complexes with MYC in the expression of MYC target genes. BMF-219 robustly decreases MYC gene expression and genomic function.

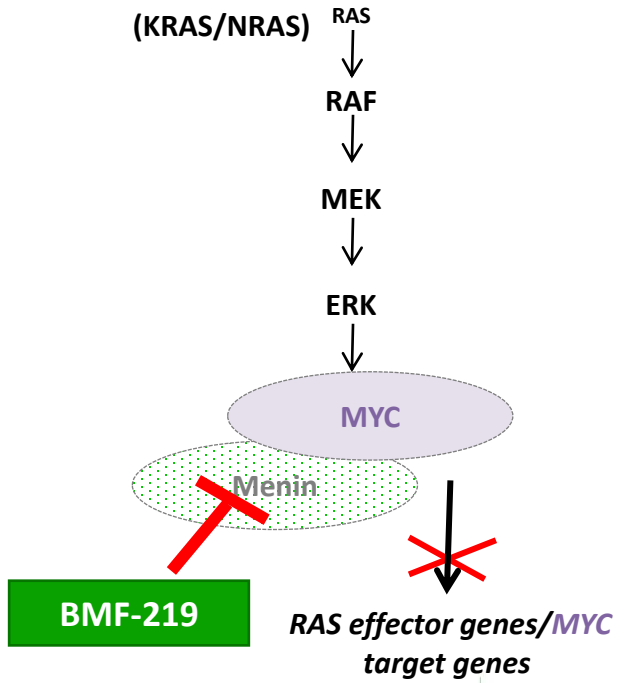
(Blood (2021) 138 (Supplement 1): 4318.)



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

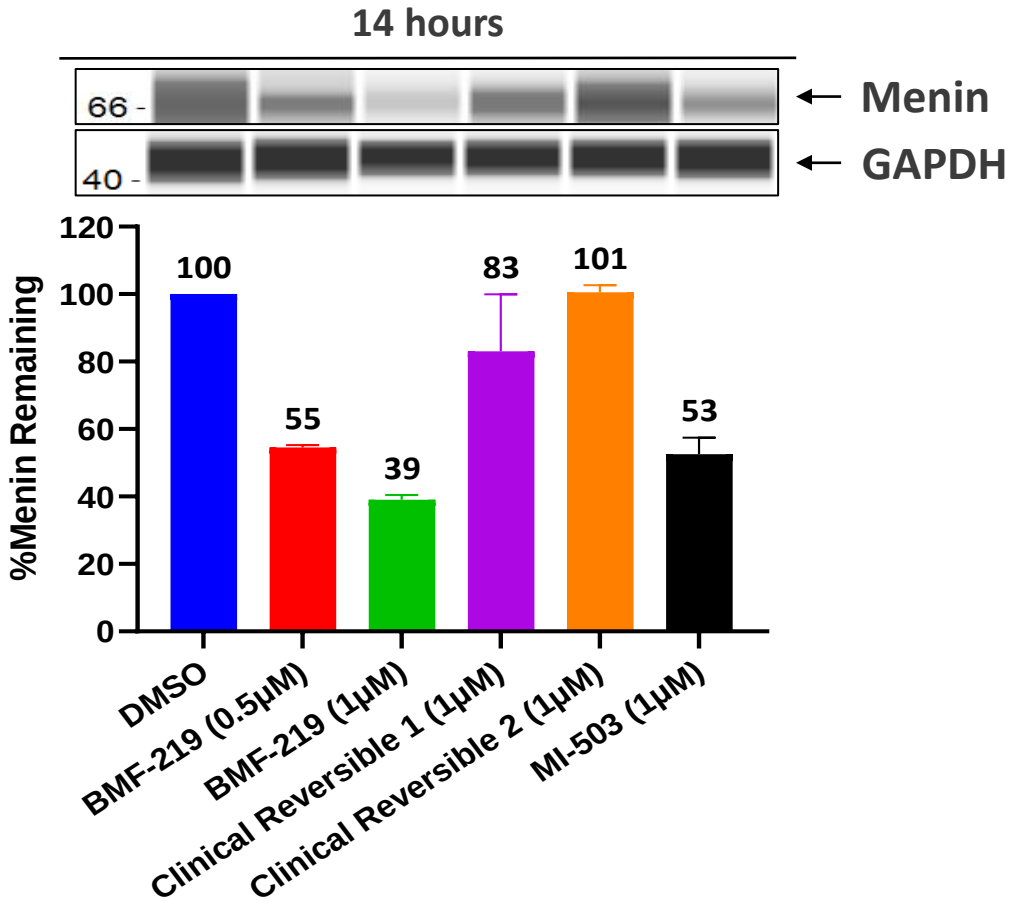
Relevant Pathway

Tumor leverages MAPK pathway



BMF-219 Significantly Reduces Menin Protein in DLBCL Cell Line

Menin Protein Levels in BMF-219 TOLEDO (DLBCL-DHL) cell line



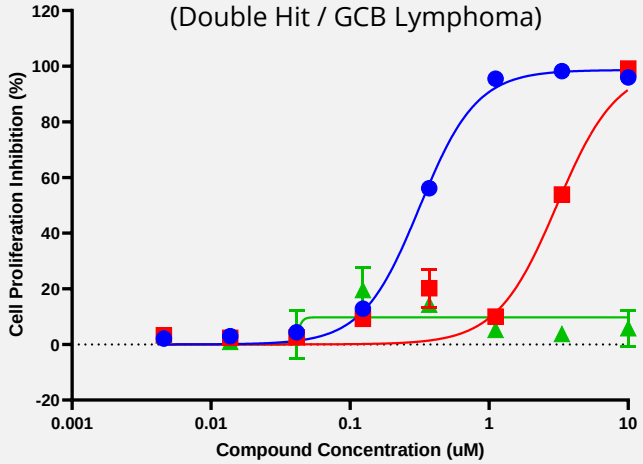
- Covalent inhibitor, BMF-219, at 1μm concentration achieves >60% reduction of menin protein at 14hrs
- Clinical reversible (non-covalent) inhibitors of menin achieved less than 20% reduction of menin protein at the same concentration

Somanath et al., AACR 2022 Abstract 2654

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

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

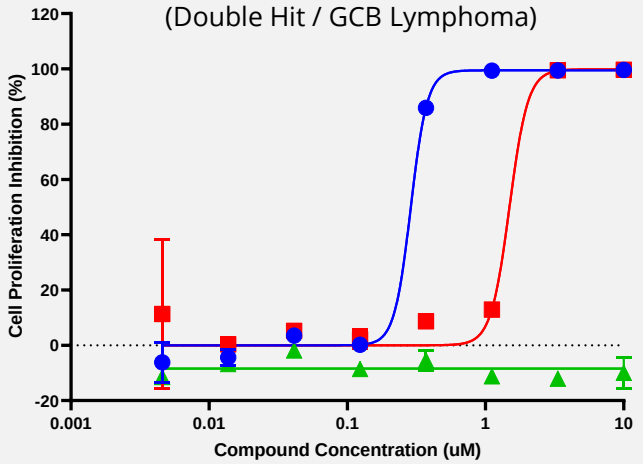
DB
(Double Hit / GCB Lymphoma)



	IC50 (µM)	%Max
BMF-219	0.316	98.64
Clinical Non-covalent Inhibitor-1	3.07	100
Clinical Non-covalent Inhibitor-2	No Response	9.7

DB and Toledo cells were incubated with compounds for 4 days

TOLEDO
(Double Hit / GCB Lymphoma)



	IC50 (µM)	%Max
BMF-219	0.2877	99.47
Clinical Non-covalent Inhibitor-1	1.49	99.84
Clinical Non-covalent Inhibitor-2	No Response	-8.4

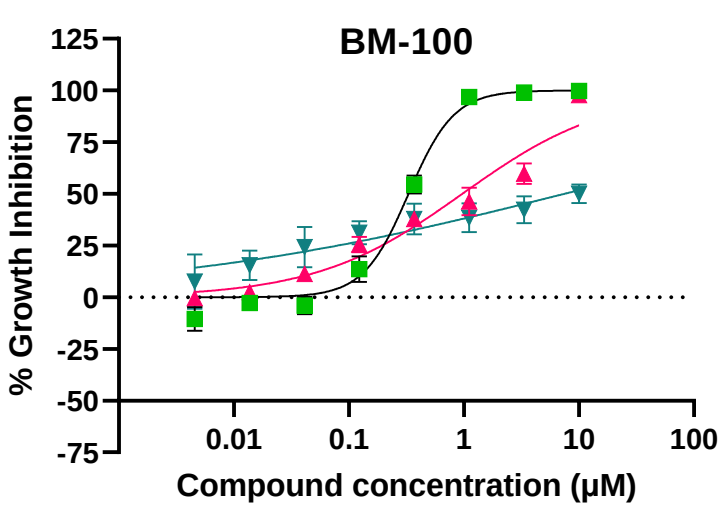
Cell Lines	Cell Type	Translocations
DB	GCB-DLBCL	MYC/BCL2
TOLEDO	GCB-DLBCL	MYC/BCL2

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

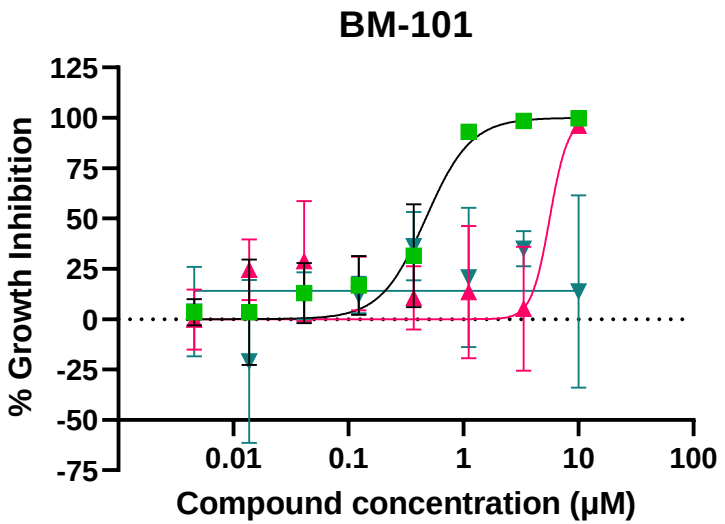
- **Covalent menin inhibition by BMF-219 led to marked growth inhibition in multiple DLBCL cell lines**
- **We believe this is due to disruption of Menin-MYC**
- **One of the clinical stage non-covalent menin inhibitors tested displayed activity, but at 5-10x higher conc.**
- **The other clinical non-covalent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

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

THL - Responded, then progressed on R-EPOCH



MYC Amplified DLBCL - Responded, then progressed on R-CHOP



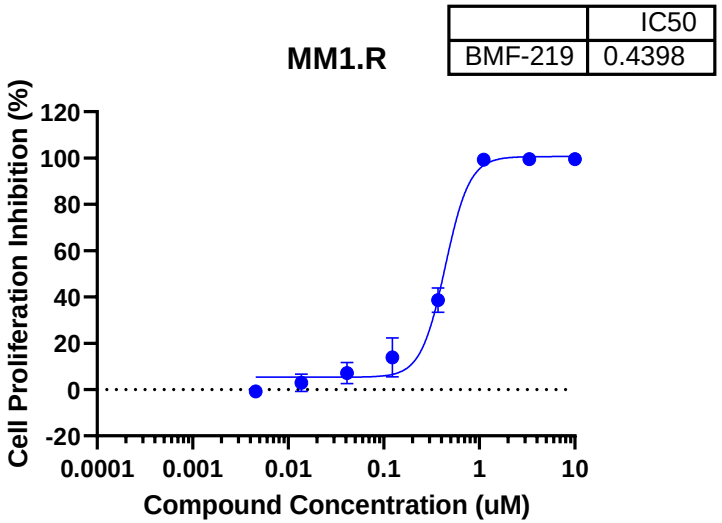
BMF-219 Clinical Reversible 1 Clinical Reversible 2

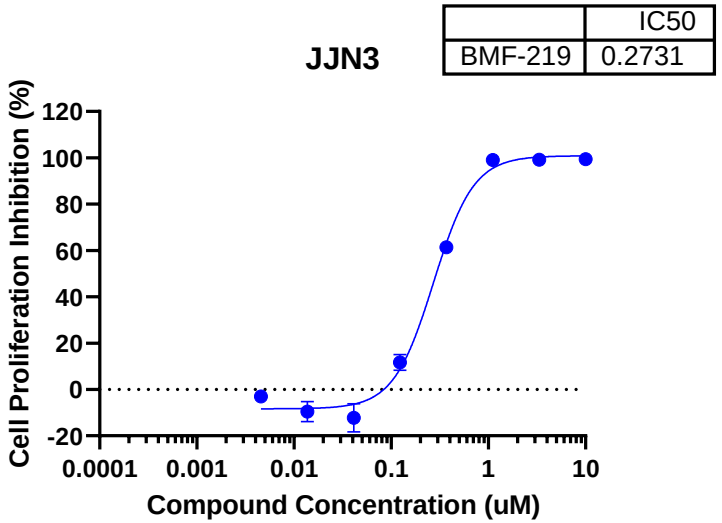
	Growth Inhibition IC_{50} (µM)	
Treatment	BM100	BM101
BMF-219	0.250	0.151
Clinical Reversible-1	0.969	5.63
Clinical Reversible-2	6.31	Max killing <30%

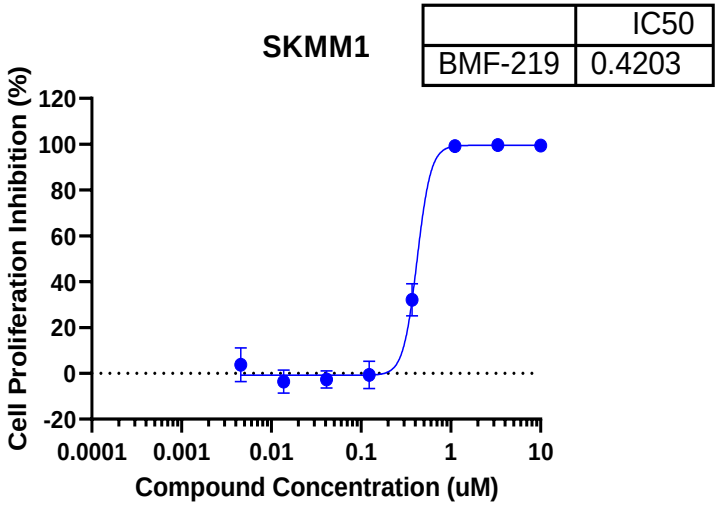
- ~1µM exposure of BMF-219 produces robust growth inhibition in both THL (triple hit lymphoma) and MYC amplified DLBCL ex-vivo cell lines
- BMF-219 responses were superior to clinical reversible (non-covalent) inhibitors with respect to cell growth inhibition at the concentrations tested

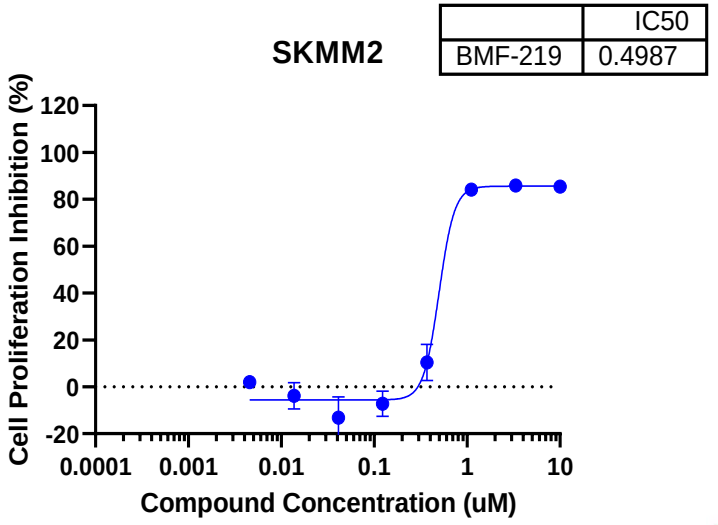
Somanath et al., AACR 2022 Abstract 2654

BMF-219 Exerts >99% Lethality Against Representative MM Cell Lines





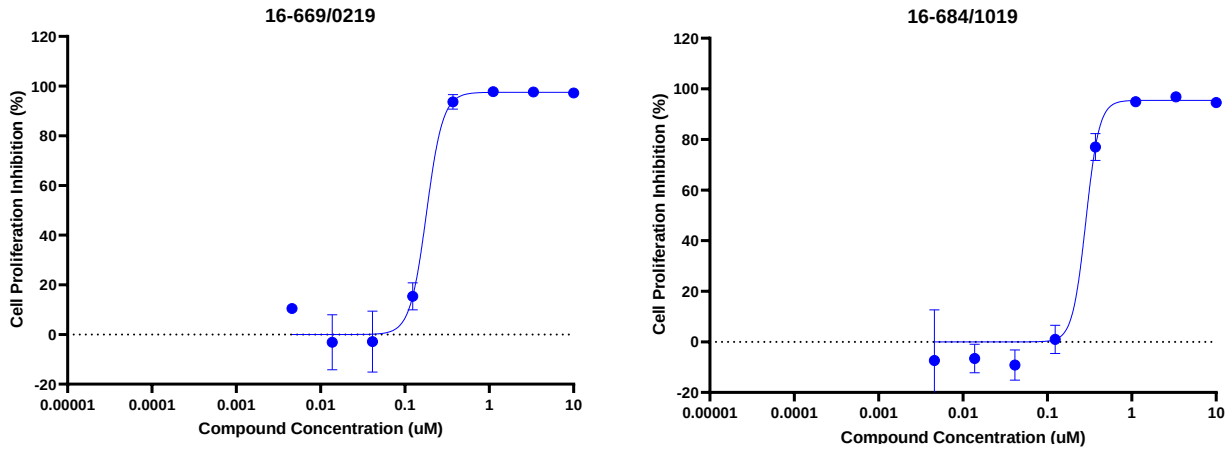




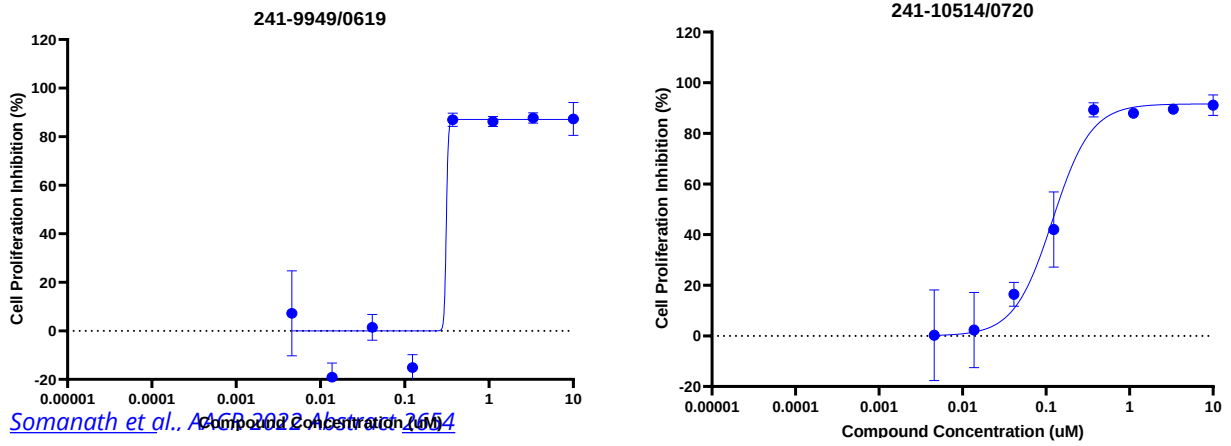
Somanath et al., AACR 2022 Abstract 2654

BMF-219 Exhibits Comparable Potency Against Newly Diagnosed and Multiply Relapsed/Refractory MM Patient Derived Samples

Newly Diagnosed



Relapsed/Refractory



Multiple Myeloma Specimen ID	Treatment Status	Prior Therapy and Response	Translocation	IC50 (µM)
16-669/0219	Newly Diagnosed	None	No data	0.1799
16-684/1019	Newly Diagnosed	None	No data	0.2856
241-9949/06-19	Refractory	VCD N4 (resistant)	p53 deletion	0.3116
241-10514/0720	Refractory	VCD N 4 (responded)	p53 deletion-negative	0.1199
		High dose CPH (SC-mobilization) (responded)		
		Consolidation (AutoSCT, double transplant)		
		Bortezomib- maintenance (resistant)		
		RVD #4 (resistant)		
		PRD #4 (resistant)		

Somanath et al., ASCO 2022 Abstract 2654

BMF-219 – Novel Covalent Inhibitor of Menin

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

MLL Fusion & NPM1 Driven Tumors

MYC Addicted and Driven Tumors

RAS/RAF Driven Solid Tumors

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

Diabetes

BMF-219: In KRAS Mutant Solid Tumors (Lung, Colon, Pancreatic)

Development Stage: IND Stage in relapsed/refractory KRAS mutant Solid Tumors

Key Facts

Estimated Target Population

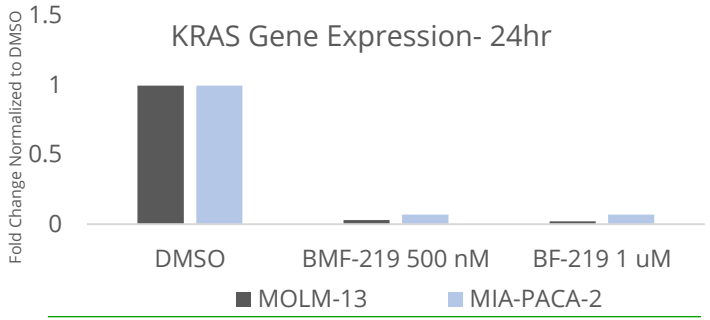
Tumor Type (KRAS Mutant)	Estimated US Patient Population (Annual Incidence)
Lung (NSCLC)	~60,000
Colon (CRC)	~70,000
Pancreatic	~60,000

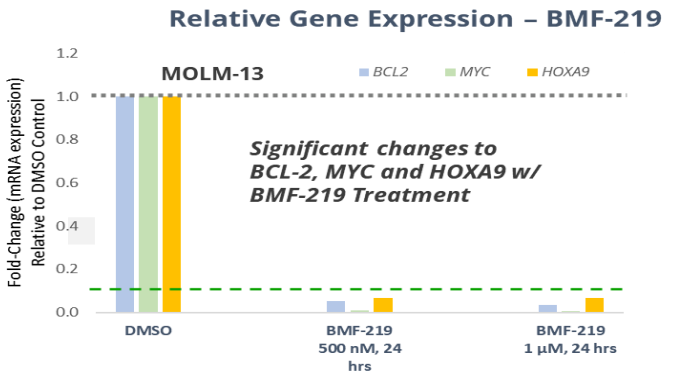
- MYC is a major downstream effector of the MAPK pathway in KRAS-activated tumors
- BMF-219 robustly decreases MYC gene expression and genomic function and drives cell killing in numerous MYC driven ex-vivo tumor samples.

MOA

BMF-219 inhibits the menin/ MYC interaction and downregulates expression of MYC and MYC target genes, including KRAS

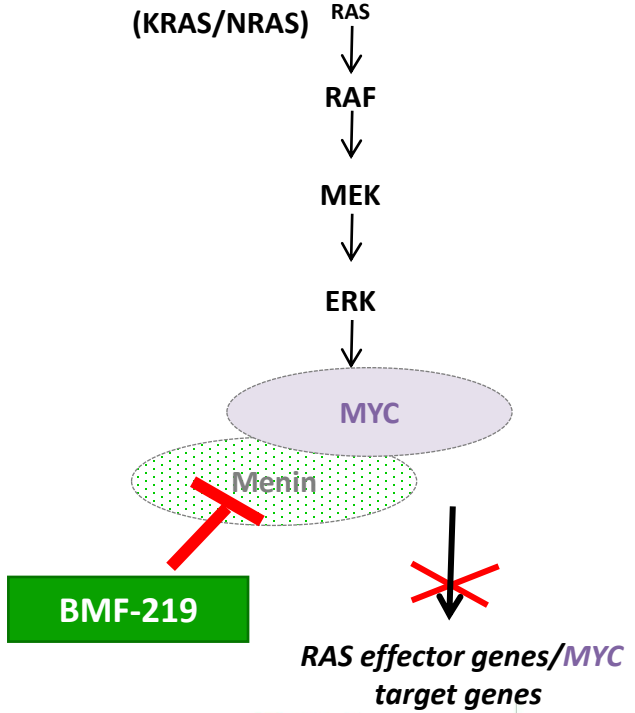
(Blood (2021) 138 (Supple. 1): 4318.)



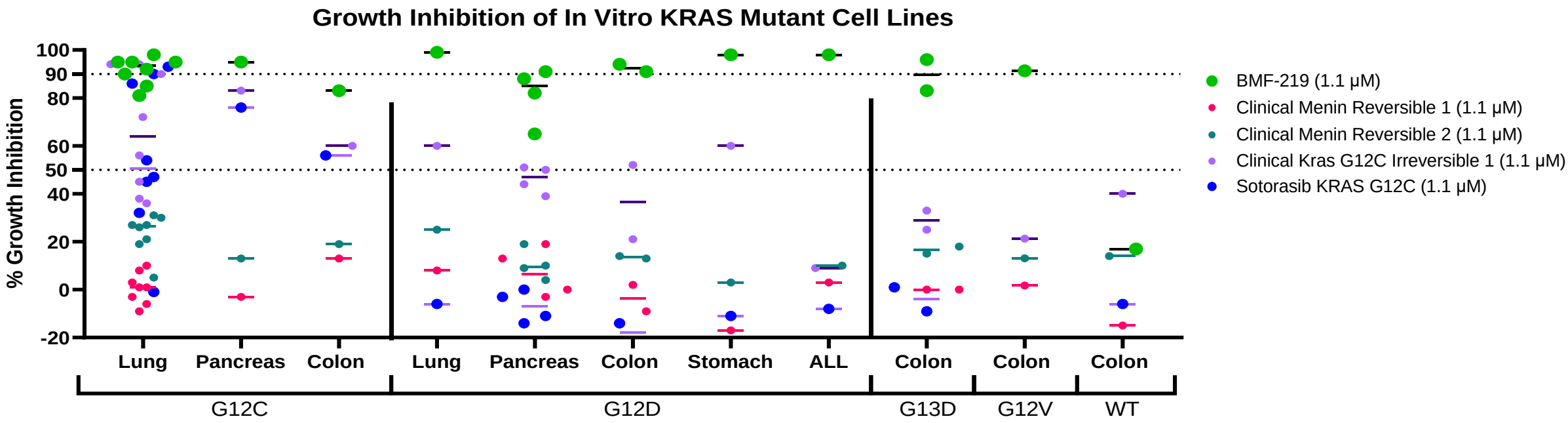


Relevant Pathway

Tumor leverages MAPK pathway



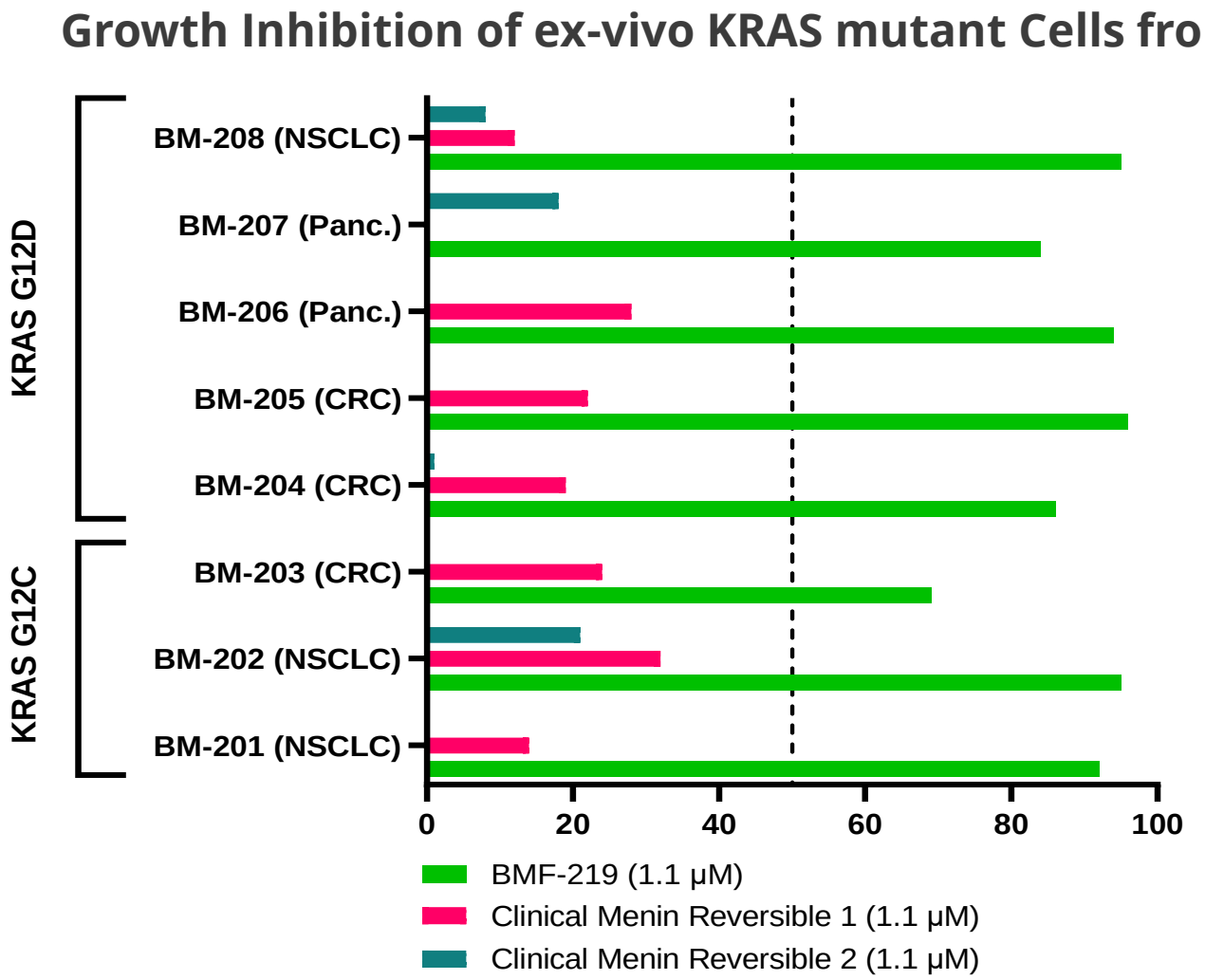
BMF-219 Produced Near Complete Inhibition of Growth at 1.1µM Across KRAS G12C, G12D, G13D, and G12V Mutant Cell Lines



- **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 Samples



- 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

Law et al., AACR 2022 Abstract 2665

BMF-219: In Chronic Lymphocytic Leukemia (CLL)

Development Stage: Preclinical Validation

Key Facts

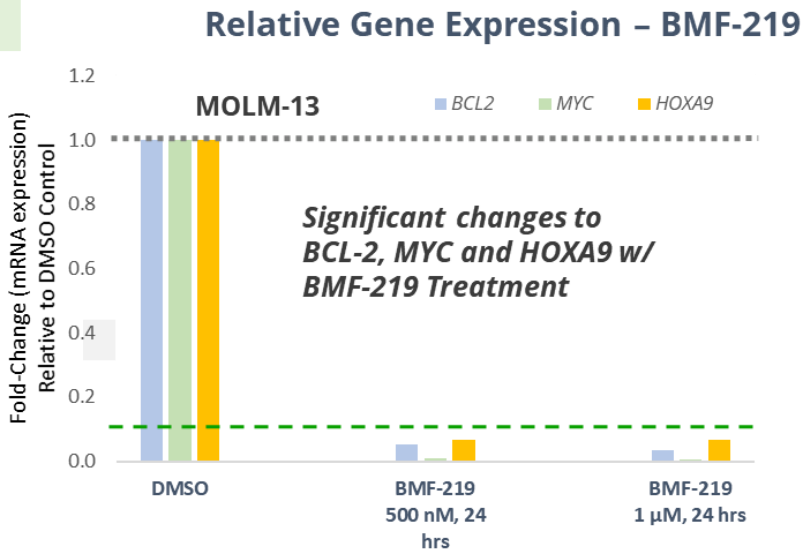
Estimated Target Population

Disease	Estimated US Patient Population (Annual Incidence)
CLL	~20,000

- A major driving feature of CLL is overexpression of the anti-apoptotic marker, BCL2.

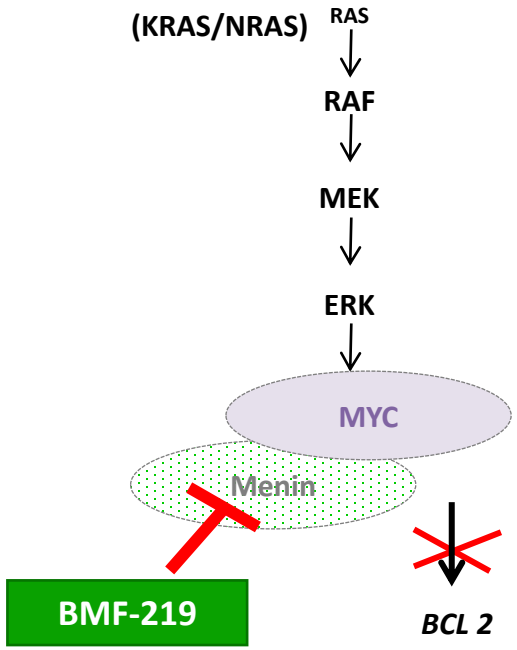
MOA

Menin complexes with MYC in expression of MYC target genes. BMF-219 robustly decreases MYC gene expression and downregulates the expression of BCL2 in cells.



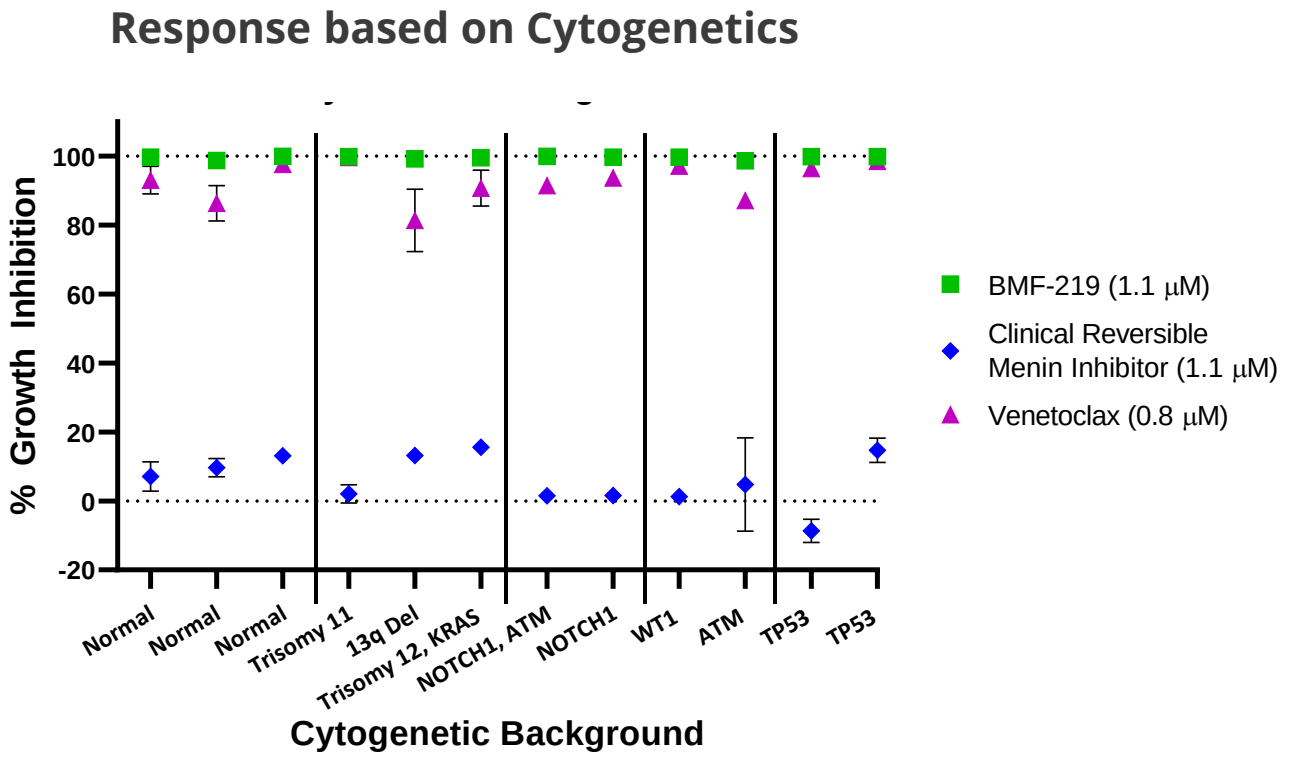
Relevant Pathway

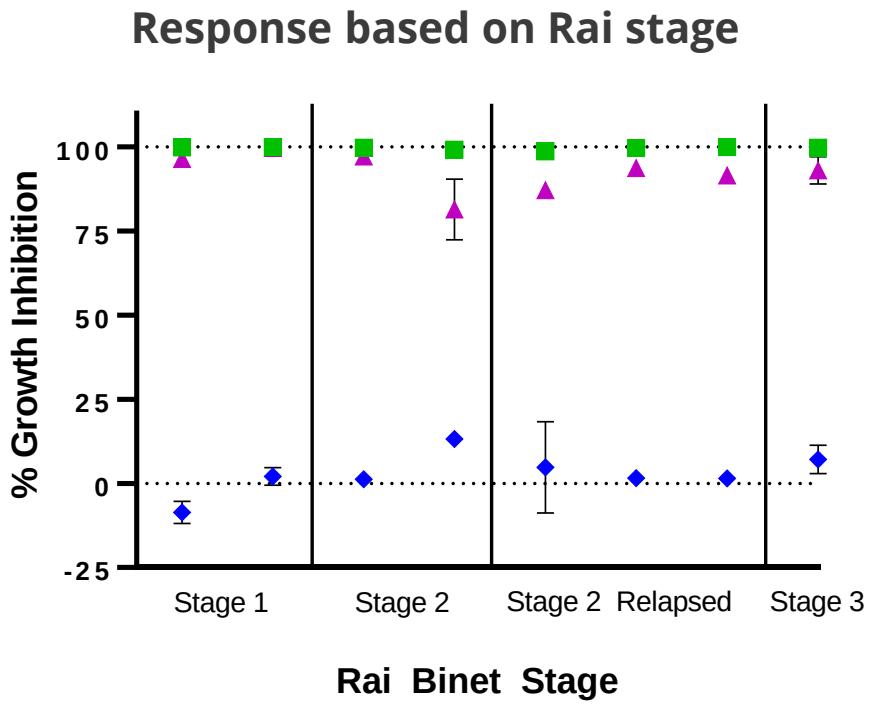
Tumor leverages MAPK pathway



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

BMF-219 – Novel Covalent Inhibitor of Menin

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

MLL Fusion & NPM1 Driven Tumors

MYC Addicted and Driven Tumors

RAS/RAF Driven Solid Tumors

Diabetes

Pathway and clinical validation of covalent menin inhibition

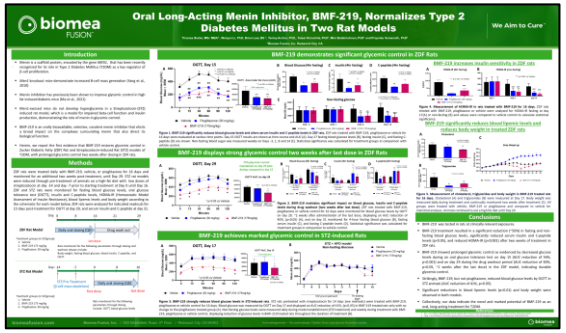
BMF-219 Ameliorated Diabetes in Two Animal Models Presented at ADA 2022

Results

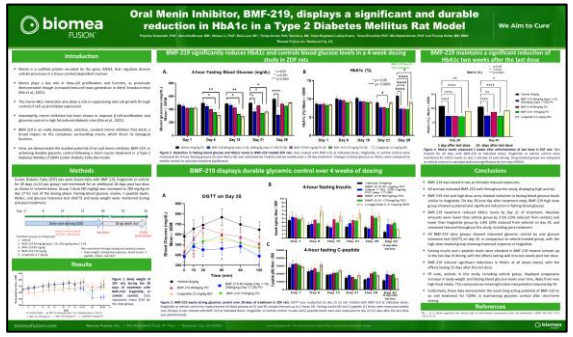
BMF-219 was able to normalize glucose levels in the majority of diabetic animals after as little as two weeks of treatment. The majority of the effect was maintained despite complete washout of BMF-219

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

Poster Presentations



Oral Long-Acting Menin Inhibitor, BMF-219, Normalizes Type 2 Diabetes Mellitus in Two Rat Models



Oral Menin Inhibitor, BMF-219, displays a significant and durable reduction in HbA1c in a Type 2 Diabetes Mellitus Rat Model

Next Steps

File IND in H2 2022

Conduct Additional Translational Work

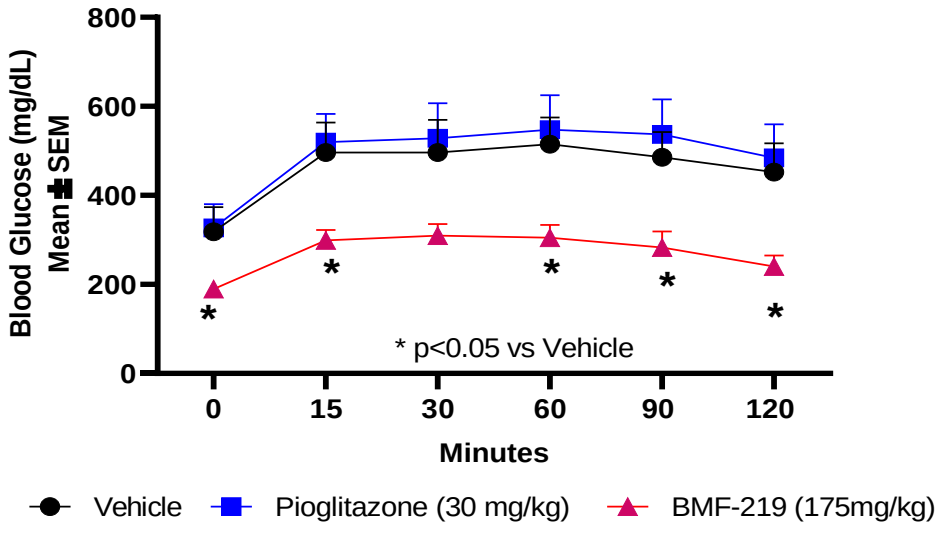
Present Data at 2022 International Conference

Butler et al., ADA 2022 (P-851)
Somanath et al., ADA 2022 (113-LB)

BMF-219 Demonstrates Preclinical Proof of Concept in Challenging Diabetes Model, outperforming pioglitazone
(as presented at ADA 2022)

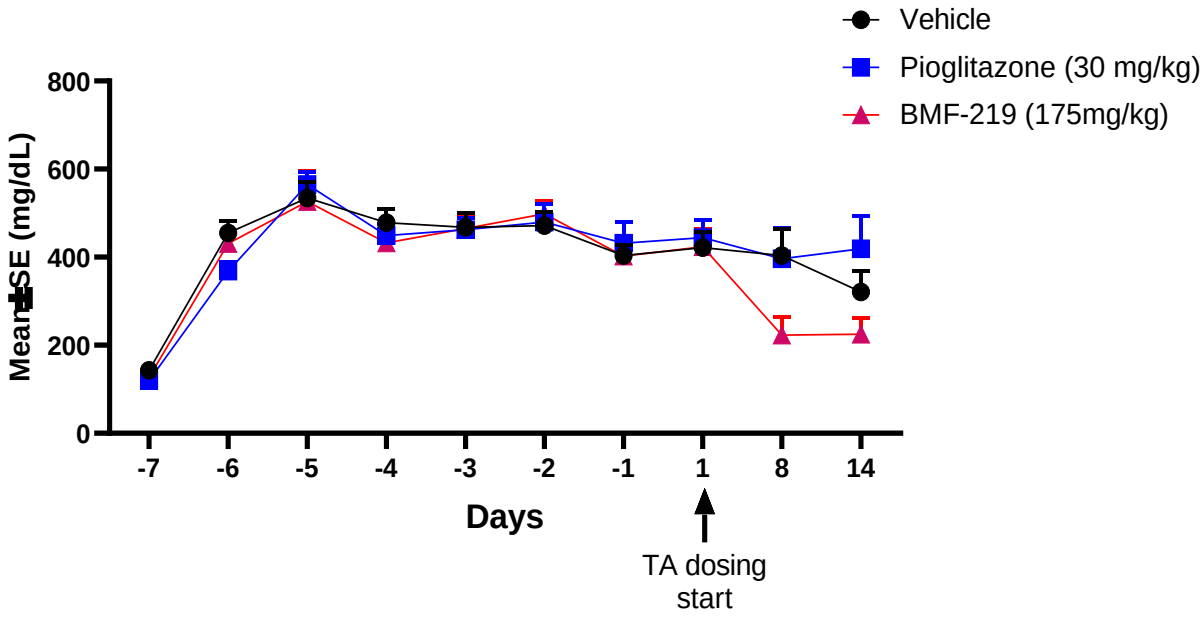
BMF-219 Achieves Glycemic Control in STZ Rat Model

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

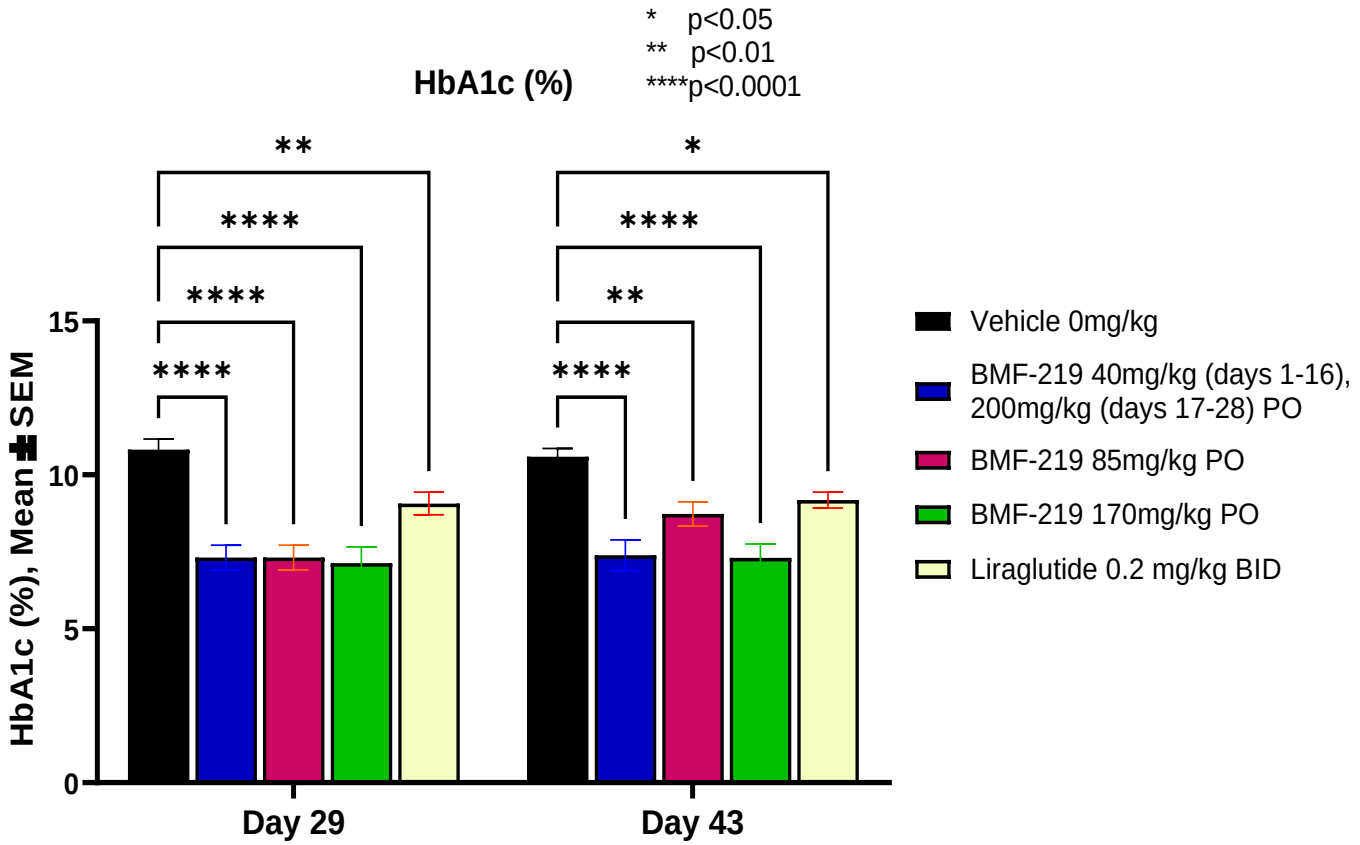


BMF-219 achieves lower non-fasting glucose than pioglitazone at day 8 and day 14 in STZ rat model

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

BMF-219 significantly reduces HbA1c and controls blood glucose levels in a 4-week dosing study in ZDF rats
(as presented at ADA 2022)

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



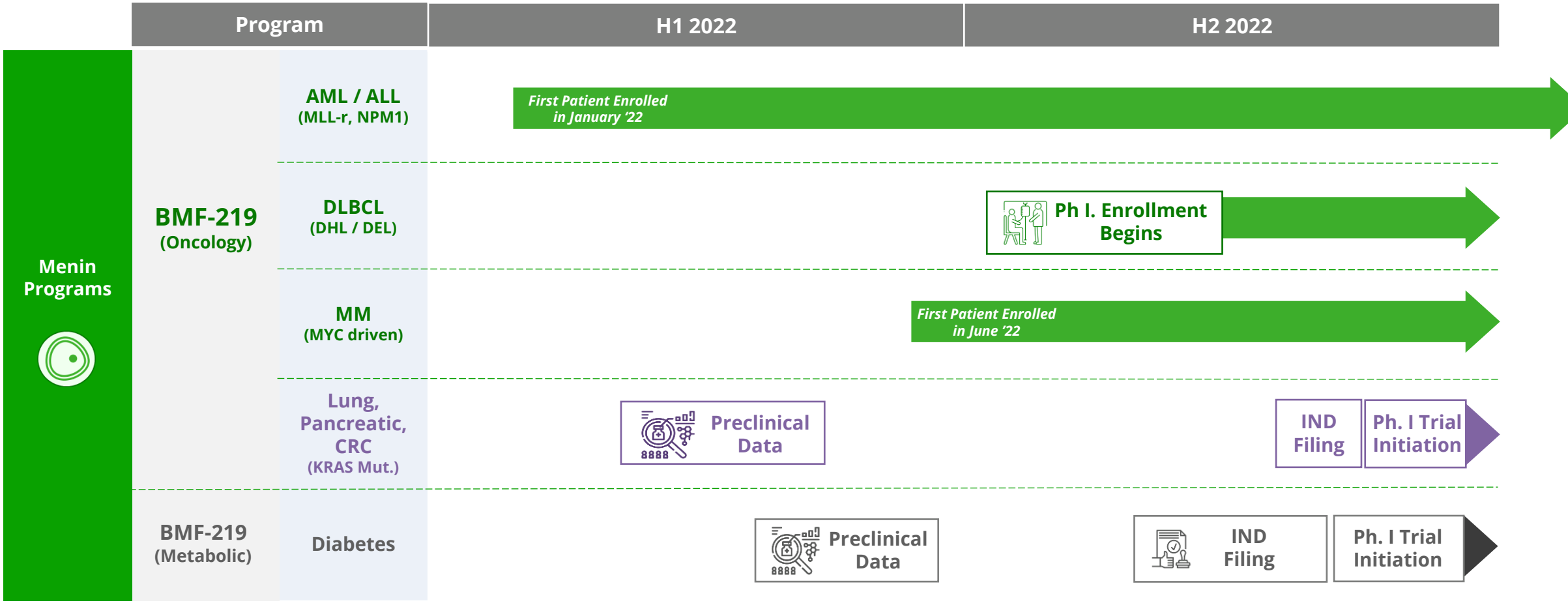
BMF-219 demonstrated significant decrease in HbA1c (-3.5% at day 29) vs. control starting on day 21 of treatment

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

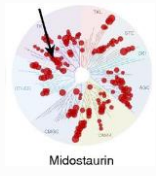
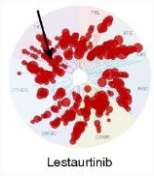
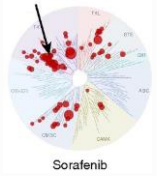
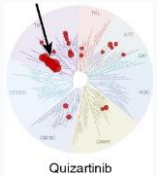
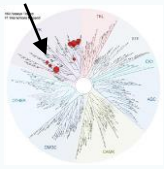
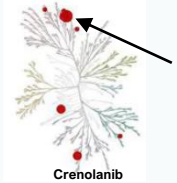
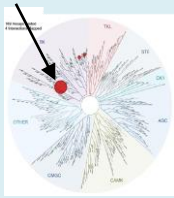
HbA1c reduction in BMF-219 highest dose groups maintained through washout period

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

BMF-219 Clinical Study Plan – Enrolling up to 7 Tumor Types and Diabetic Patients in 2022



History of FLT3 Inhibitors: Third Time's The Charm

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
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	
Kinome Selectivity	 Midostaurin	 Lestaurtinib	 Sorafenib	 Quizartinib	 Gilteritinib	 Crenolanib	 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

Biomea Fusion – *WE AIM TO CURE*

- **Established FUSION™ platform technology for discovery of covalent inhibitors**
- **Lead molecule (BMF-219) with best-in-class potential and favorable safety profile**
- **Initiate studies with BMF-219 in up to 7 tumor types (liquid and solid) in 2022**
- **Significant addressable market and scarcity of effective treatment options for clinically targeted tumor types**
- **IND enabling work in progress for diabetic patients**
- **Announced second pipeline asset: BMF-500, pM potent covalent FLT3 inhibitor**
- **Capitalized into 2024**

Near Term Milestones – Biomea Fusion (NASDAQ: BMEA)

BMF-219 – Liquid Tumors

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

BMF-219 – Solid Tumors

Additional Preclinical Data in KRAS Mutant Tumors	Completed
IND Filing	Q4 2022

Menin Inh. – Diabetes

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

BMF-500 – AML

IND Filing	To Be Announced

Additional Program

3rd Pipeline Candidate Announced	To Be Announced

Company Financials

Detailed Financials (unaudited)

	Three Months Ended June 30,	
	2022	2021
Operating expenses:		
R&D	$ 12,582	$ 5,224
G&A	$ 4,892	$ 3,211
Total Operating Expenses	$ 17,474	$ 8,435
Loss from operations	$ (17,474)	$ (8,435)
Interest and other income, net	$ 216	$ 36
Net loss	$ (17,258)	$ (8,399)
Other comprehensive loss:		
Changes in unrealized gain on short term investments, net	$ 6	17
Comprehensive loss	$ (17,252)	$ (8,382)
Net loss per common share, basic and diluted	$ (0.59)	$ (0.33)
Weighted-average number of common shares used to compute basic and diluted net loss per common share	29,196,398	25,161,038

$150M

Cash, cash equivalents, and investments as of the end of Q2 2022


Thank You