biomea FUSION™

Corporate Brief – Q1 2023

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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 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 FOR 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

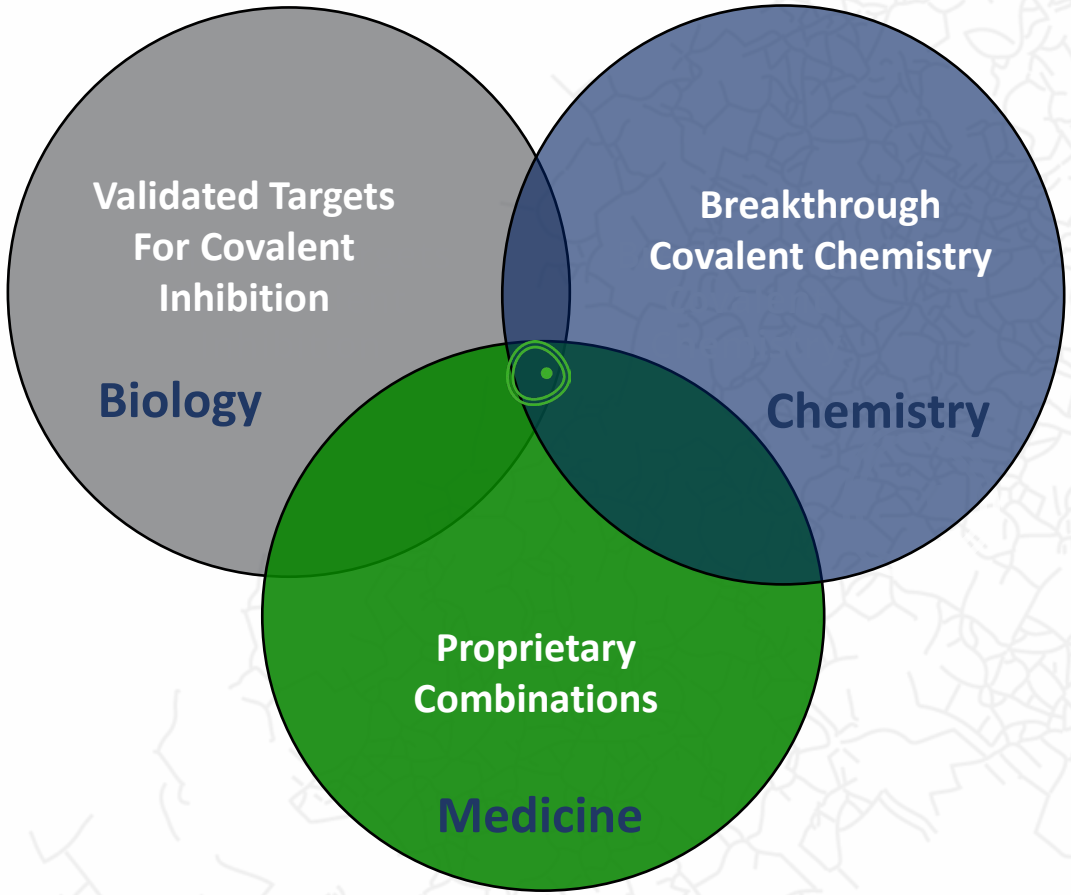
30+ years in Life Science
Biota Ltd
Cytopia Ltd.
Rigel, Inc.
Celera Genomics
Prototek Inc.
Purdue University
Ph.D. Organic Chemistry

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

Co-inventor of
ibrutinib at Celera

Biomea leverages the FUSION™ System Create a Suite of Novel Covalent Agents to Improve and Extend the Lives of Patients

Biomea's Development Principles



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

NOT ALL COVALENT SYSTEMS ARE EQUAL - We have Created the BIOMEA FUSION SYSTEM which Achieves Results- FAST

Target identification to IND candidate in 18 months

Target to Hit

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

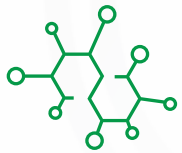
Utility:
Differentiated insights from X-ray crystal structures, identifying target cysteines

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

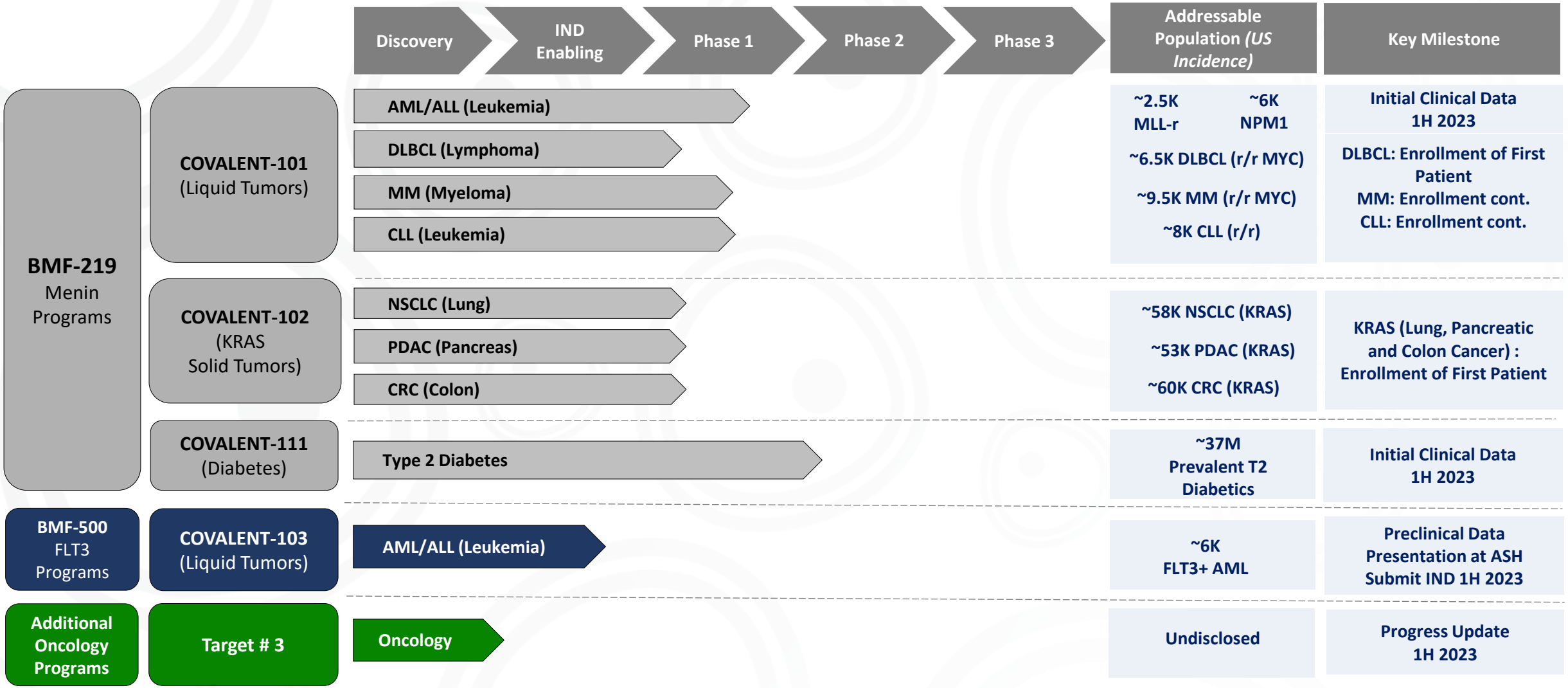
IND

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

Biomea Expanding into Eight Different Solid and Liquid Tumors as well as Type 2 Diabetes

Pipeline



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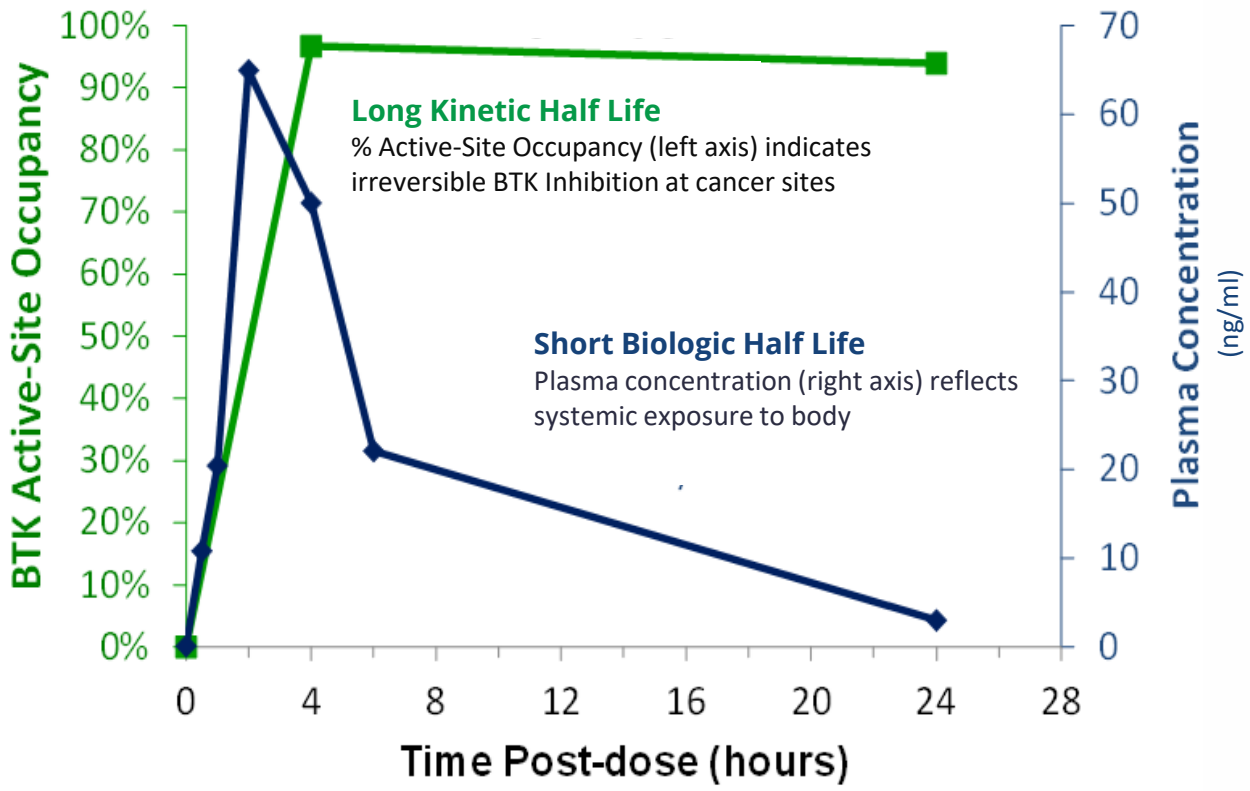
Imbruvica – a Covalent Inhibitor with Long Kinetic but very Short Biological Half Life



High Selectivity

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

Deep Target Inactivation

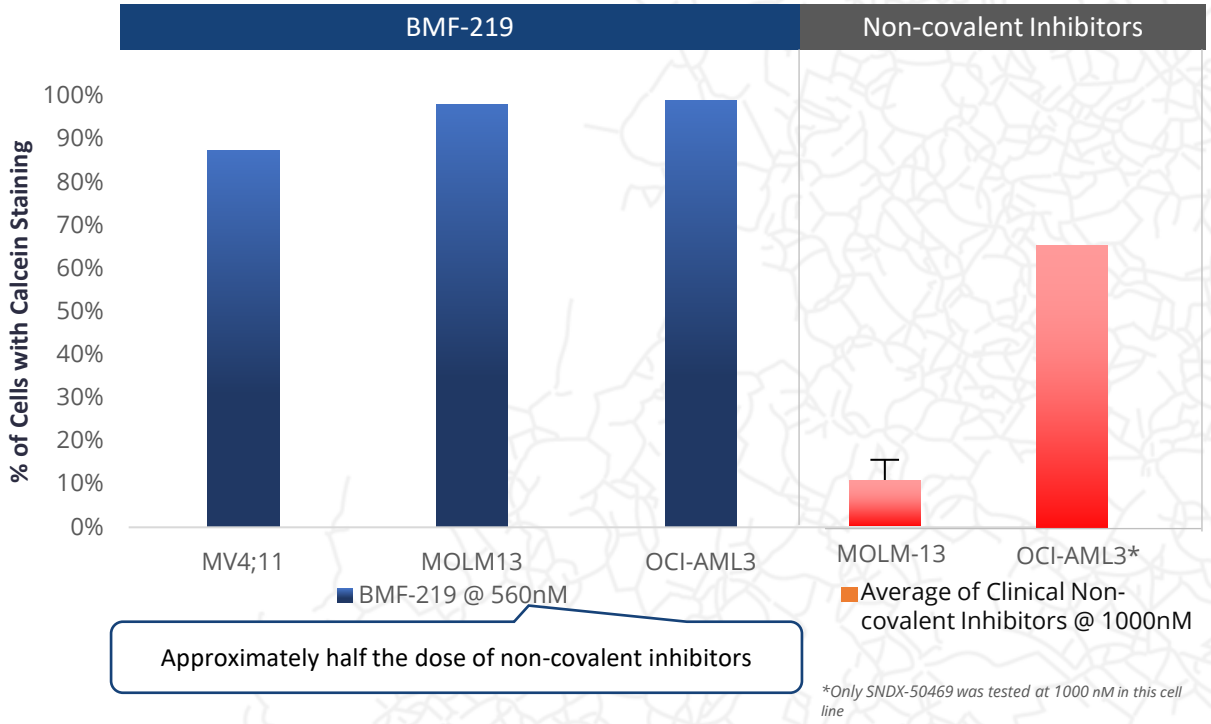
Permanent inactivation of bound protein drives target elimination through normal cellular degradation processes

Greater Therapeutic Window

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

First Development Success with BMF-219 in Acute Myeloid Leukemia

BMF-219 Exerted Superior Cell killing of the Target AML Cell at Half the Dose vs Reversible Competitive Drugs



*Only SNDX-50469 was tested at 1000 nM in this cell line

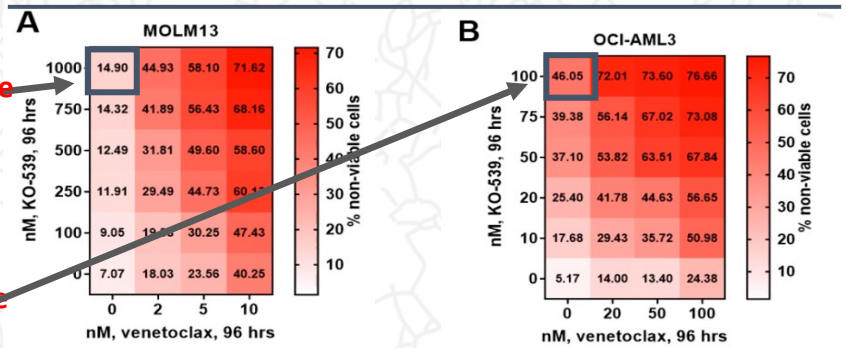
- BMF-219 **killed >90% of AML cells** in MLL-rearranged and NPM1 mutant cell lines at 4 days post-treatment
- Non-covalent menin inhibitors generally report significantly less cell killing of AML cell lines as a single agent

Source Data from ASH 2021 Publications

KO-539 is 15% effective @ 1000nM in MOLM-13 cells and 46% effective @ 1 100nM in OCI-AML3 cells

15% effective @ 1000nM

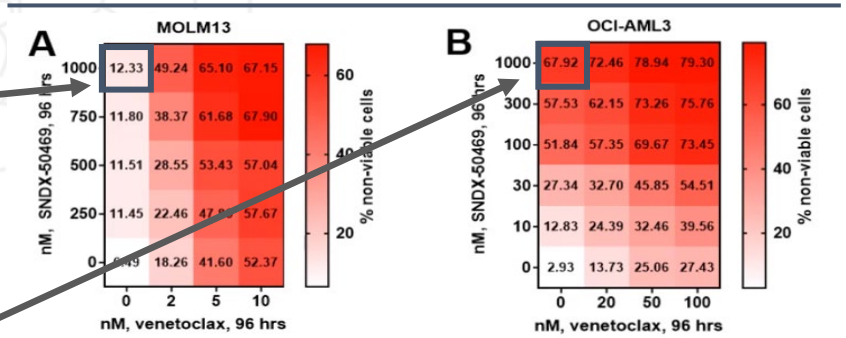
46% effective @ 100nM



SNDX-50469 is 12% effective @ 1000nM in MOLM-13 cells And 68% effective @ 1000nM in OCI-AML3 cells

12% effective @ 1000nM

68% effective @ 1000nM



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

BMF-219 Exerts Potent Lethality Against DLBCL (Toledo & U2932) & MM Cell Lines (SKMM1 & OPM2)

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

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

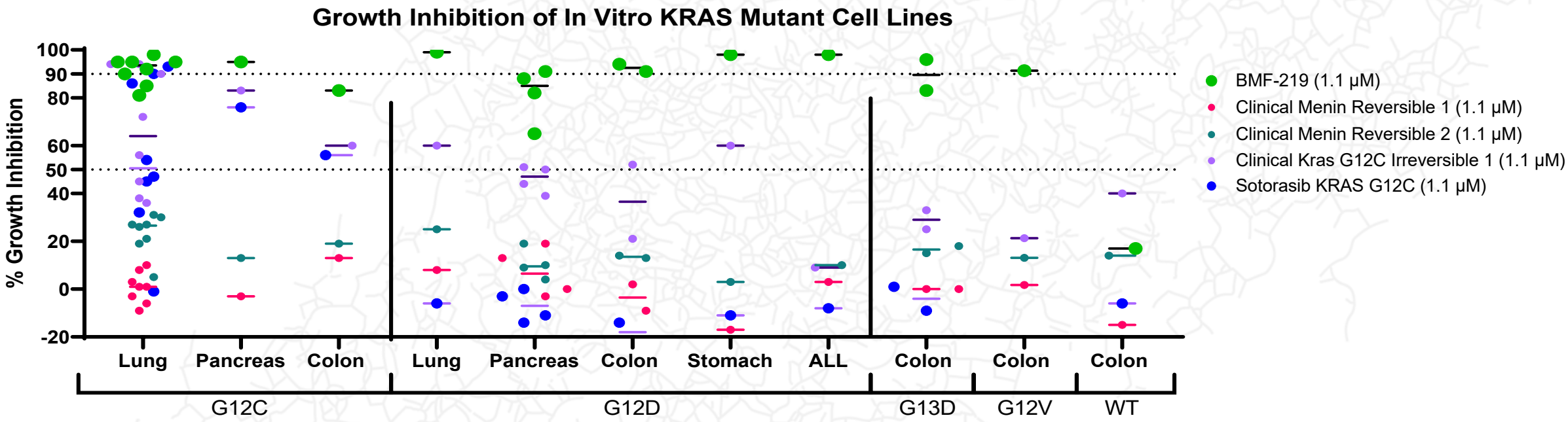
Lu et al., IMS 2022

To measure cell killing, cells were cultured in the presence of menin inhibitor for 72hr or 14hr and viable cell count measure by CTG readout. The % cell killing relative to untreated cultures was measured at 72hr and 14hr. Data tabulated was averaged from 2 independent experiments.

BMF-219 at 1 uM induced potent killing inducing 80-97% cell death following 72 hr drug treatment. In comparison, the reversible menin inhibitors MI-503 and a clinical reversible menin inhibitor were significantly less effective (20-35% cell killing with 3 uM MI-503)

First Development Success with BMF-219 in KRAS Mutant Solid Tumors

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

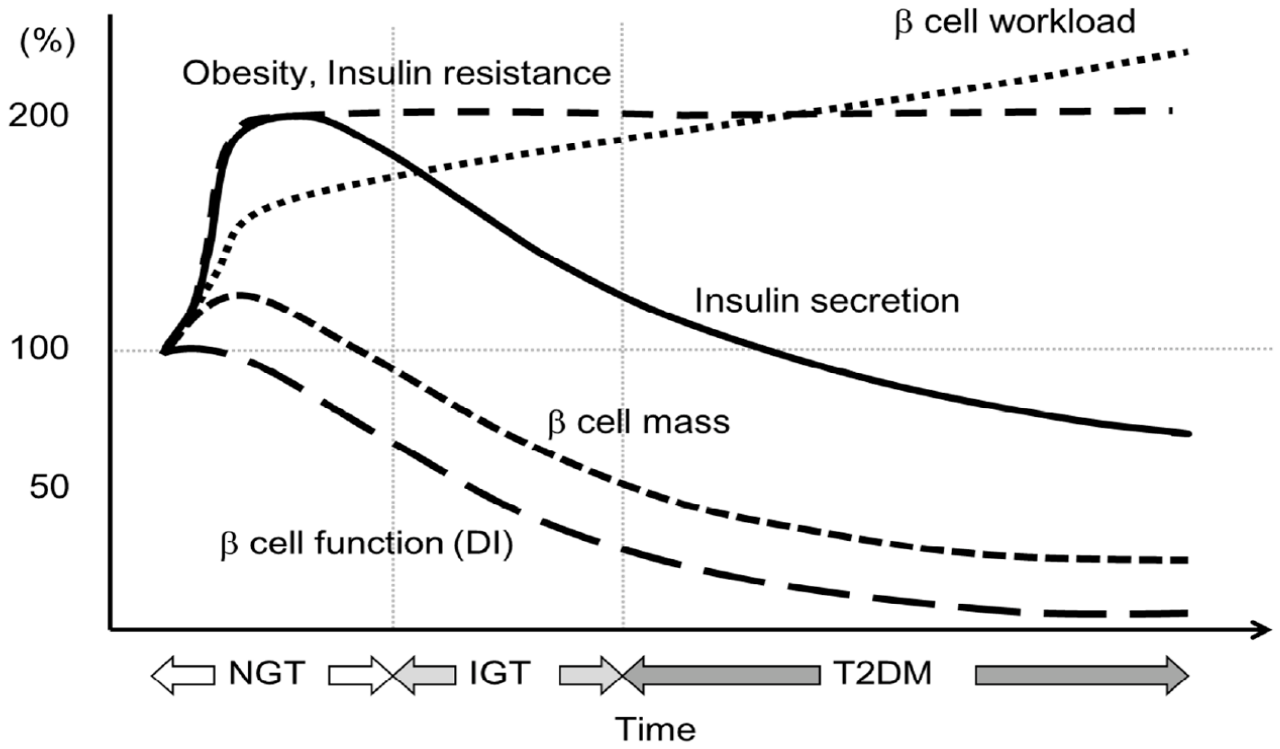


- Covalent menin inhibition by BMF-219 led to robust growth inhibition, comparable to clinical G12C inhibitors in G12C cell lines
- In non-G12C cell lines, BMF-219 achieved robust growth inhibition, higher than clinical KRAS G12C inhibitors
- Clinical reversible (non-covalent) inhibitors did not achieve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

Law et al., AACR 2022 Abstract 2665

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

BMF-219 represents a new, novel MOA, to re-establish the pool of beta cells to restore glycemic control



	Type 1 diabetes	Type 2 diabetes
Prior Paradigm	β cell destruction β cell mass ↓↓ Insulin secretion ↓↓	Obesity Insulin resistance Hyperinsulinemia
Current Paradigm	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.

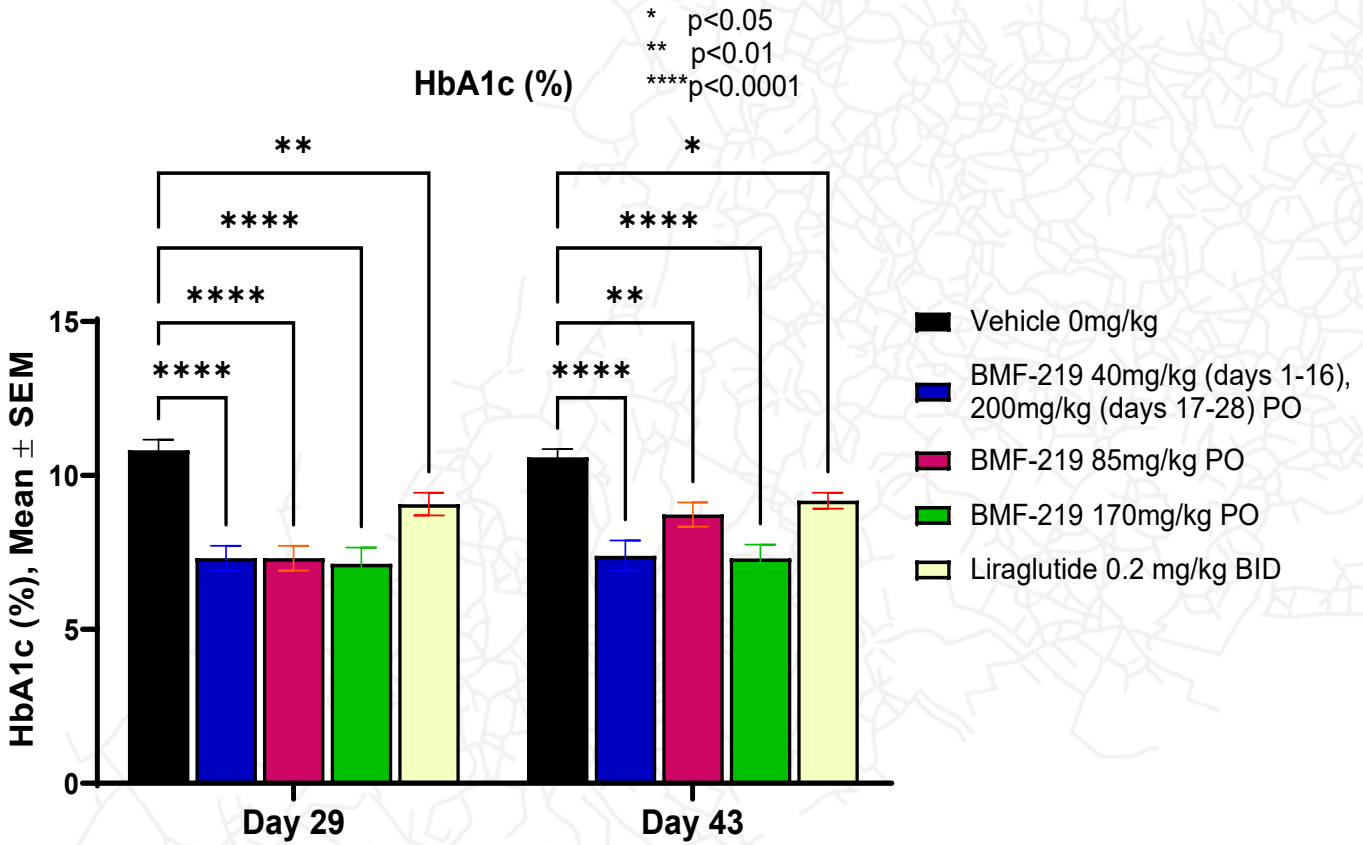
Type 1 and Type 2 Diabetes results in Beta Cell Loss and Reduction in Beta Cell Mass. Current therapy has no to marginal improvement in Beta Cell Mass.

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

First Development Success with BMF-219 in Type II Diabetes

BMF-219 Demonstrates Strong Efficacy in Insulin Resistant T2DM Animal Model (ZDF Rat)

BMF-219 Reduces HbA1c After 28 days of Treatment and Maintains Effect After 14-day Washout (ZDF Rat Model)



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

Clinical Trials

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Program	Molecule	Trial Name	Patient Number	Status and Milestones
Menin	**BMF-219** Oncology	**COVALENT-101 (NCT05153330)** Hematologic Malignancies **Enrolling Now** AML/ALL, DLBCL, MM, CLL	Approximately 140 Patients across 4 Cohorts	**Trial Status:** Enrolling all Cohorts in Dose Escalation **Data:** 1 H 2023 **Dataset:** To include patients in the Acute Leukemia Cohort reporting initial safety, tolerability, and efficacy

BMF-219's ability to disrupt multiple binding partners of menin results in potent activity across multiple tumor types.

AML/ALL: BMF-219 displays in preclinical models differentiated tumor cell killing capacity
DLBCL: BMF-219 displays in preclinical models MYC disruption and potent activity in MYC-driven tumors
MM: BMF-219 displays in preclinical models MYC disruption and potent activity in MYC-driven tumors
CLL: BMF-219 displays in preclinical models key biomarker disruption and potent activity in R/R CLL tumors

Clinical Trials

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Program	Molecule	Trial Name	Patient Number	Status and Milestones
Menin	**BMF-219** Oncology	**COVALENT-102 (NCT05631574)** KRAS Mutant Solid Tumors **Enrolling Soon** NSCLC, PDAC, CRC	Approximately 120 Patients across 3 Cohorts	**Trial Status:** Site Activation **Data:** To be determined **Dataset:** To be determined

BMF-219's ability to disrupt multiple binding partners of Menin results in potent activity across multiple tumor types Including those driven by RAS.

KRAS G12C:	BMF-219 displays in preclinical models differentiated tumor cell killing capacity versus adegrasib and sotorasib.
KRAS G12D,V,X:	BMF-219 displays in preclinical models MYC disruption and potent activity in KRAS-driven tumors
KRAS G13 D,X:	BMF-219 displays in preclinical models MYC disruption and potent activity in KRAS-driven tumors.
KRAS pan mutations:	BMF-219's activity is independent of the activating mutation of KRAS across multiple tumor types.

BMF-219 in preclinical models have shown great tissue exposure in the target organs being explored in the study.

Clinical Trials

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Program	Molecule	Trial Name	Patient Number	Status and Milestones
Menin	**BMF-219** Metabolic Diseases	**COVALENT-111 Type 2 Diabetes** a double blinded, randomized, placebo-controlled Phase I/II study **Enrolling Now** Type 2 Diabetes Patients	Approximately 110 Patients with Type 2 Diabetes across 5 Dosing Cohorts	**Trial Status:** Enrolling first Dosing Cohorts in Dose Escalation **Data:** 1 H 2023 **Dataset:** HV patients (Safety and Tolerability) and T2DM patients (Safety, Tolerability, and Efficacy)

BMF-219 is orally administered, with the goal of being a novel long-acting treatment that achieves and maintains glycemic control in type 2 diabetes.

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.

Preclinical Highlights:

- BMF-219 displays in preclinical animal experiments significant glycemic control, outperforming liraglutide in reduction of fasting blood glucose by Day 29 and by OGTT on day 25.
- BMF-219 significantly reduces HbA1c levels (3.5%) in preclinical animal experiments during treatment and after drug washout.
- BMF 219 treatment restores HOMA-B scores in preclinical animal experiments to normal state indicating restored beta-cell function.
- BMF-219 significantly reduced in preclinical experiments body weight (13% at 4 weeks of treatment) and reduced blood lipemic levels

Coming Soon

Clinical Trials

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Program	Molecule	Trial Name	Patient Number	Status and Milestones
FLT3	**BMF-500** Oncology	**COVALENT-103** Acute Myeloid Leukemia **Planned Enrollment** R/R Acute Leukemia	In Planning	**Trial Status:** IND enabling Studies **Data:** To be determined **Dataset:** To be determined

BMF-500 demonstrated to be a novel FLT3 inhibitor with best-in-class potential, given its efficacy, durability, and selectivity in comparison to existing FLT3 inhibitors

BMF-500 demonstrated in preclinical models potent FLT3 inhibition and high selective cell killing against AML cells harboring FLT3 activating mutations, including MV4-11 and MOLM-13, and engineered cells expressing FLT3 internal tandem duplications (FLT3-ITD) and/or FLT3 tyrosine kinase domain (TKD) mutations.

BMF-500 is a highly potent and selective, covalent, small molecule inhibitor of FLT3, that binds irreversibly to a reactive cysteine in the kinase active site. BMF-500 is a picomolar inhibitor with markedly improved potency and selectivity over gilteritinib, a reversible inhibitor of FLT3.

Multiple Clinical Read Outs over the coming Quarters

Near Term Milestones – Biomea Fusion (NASDAQ: BMEA)

			Key Milestones	Expected Timeline
BMF-219 Menin Programs	**COVALENT-101** (Liquid Tumors)	AML/ALL (Leukemia)	Phase I: Clinical Data in AML	1H 2023
		DLBCL (Lymphoma)	Initiation of Phase I additional Cohort in DLBCL	In Progress
		MM (Myeloma)	Enrolling in Phase I additional Cohort in MM	In Progress
		CLL (Leukemia)	Enrolling in Phase I additional Cohort in CLL	In Progress
	COVALENT-102 (KRAS Solid Tumors)	NSCLC (Lung)	Initiation of Phase I/Ib KRAS Study in CRC, PDAC, NSCLC	In Progress
		PDAC (Pancreas)		
		CRC (Colon)		
	COVALENT-111 (Diabetes)	Type 2 Diabetes	Healthy Volunteers of PI/II COVALENT-111 Trial Phase II: Clinical Data in Type 2 Diabetes	Completed 1H 2023
BMF-500 FLT3 Programs	**COVALENT-103** (Liquid Tumors)	AML/ALL (leukemia)	Preclinical Data Presentation IND Filing	ASH 2022 1H 2023
Additional Oncology Programs	**Target # 3**	Oncology	Progress Update	1H 2023

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THANK YOU

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