biomea FUSION™

Corporate Presentation
April 2021

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OUR MISSION

Our Mission is to revolutionize drug development in order to create more effective therapies for patients in need.

Biomea Fusion is a preclinical-stage biopharmaceutical company focused on the discovery, development and commercialization of **irreversible small-molecule drugs** to treat patients with genetically defined cancers. Our discovery team is engaged in all phases of development, including target selection, small molecule design, and preclinical and clinical studies to develop innovative medicines.

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Biomea Fusion History

Portfolio of multiple irreversible inhibitors in development

2017

Biomea and A2A form Biomea Fusion to develop reversible menin Program

2018

2nd and 3rd Generation reversible molecules designed

2018

Biomea becomes a JLABS, South San Francisco resident

Johnson & Johnson INNOVATION | JLABS

Biomea builds out its proprietary irreversible binding technology

2019

Lead candidates selected for menin MLL-Fusion and menin dependent cancers

2020

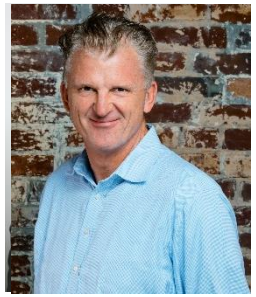
Biomea received Series A Syndicate financing of $56,000,000 to support the development of Biomea's portfolio of irreversible inhibitors

Biomea's Team

Diverse team with significant drug development experience

Thomas Butler
Chairman & CEO

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



Ramses Erdtmann
President & COO

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

Sunny Lee Ryan
EVP of Finance

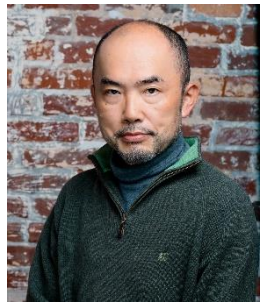
20 years in Life Science
Menlo Therapeutics
Achaogen
Alios Biopharma
Rinat Neuroscience
Genelabs Technologies
PricewaterhouseCoopers
Pepperdine University, BS Accounting

Naomi Cretcher
Chief of People

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

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



Taisei Kinoshita
VP of Biology

20 years in Life Science
Pharmacyclics
Rigel Pharmaceuticals
University of Tokyo, Ph.D. Biology

Anthony Souza
Head of IT

15 Years in Life Science
Pharmacyclics
University of Texas

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 & Management

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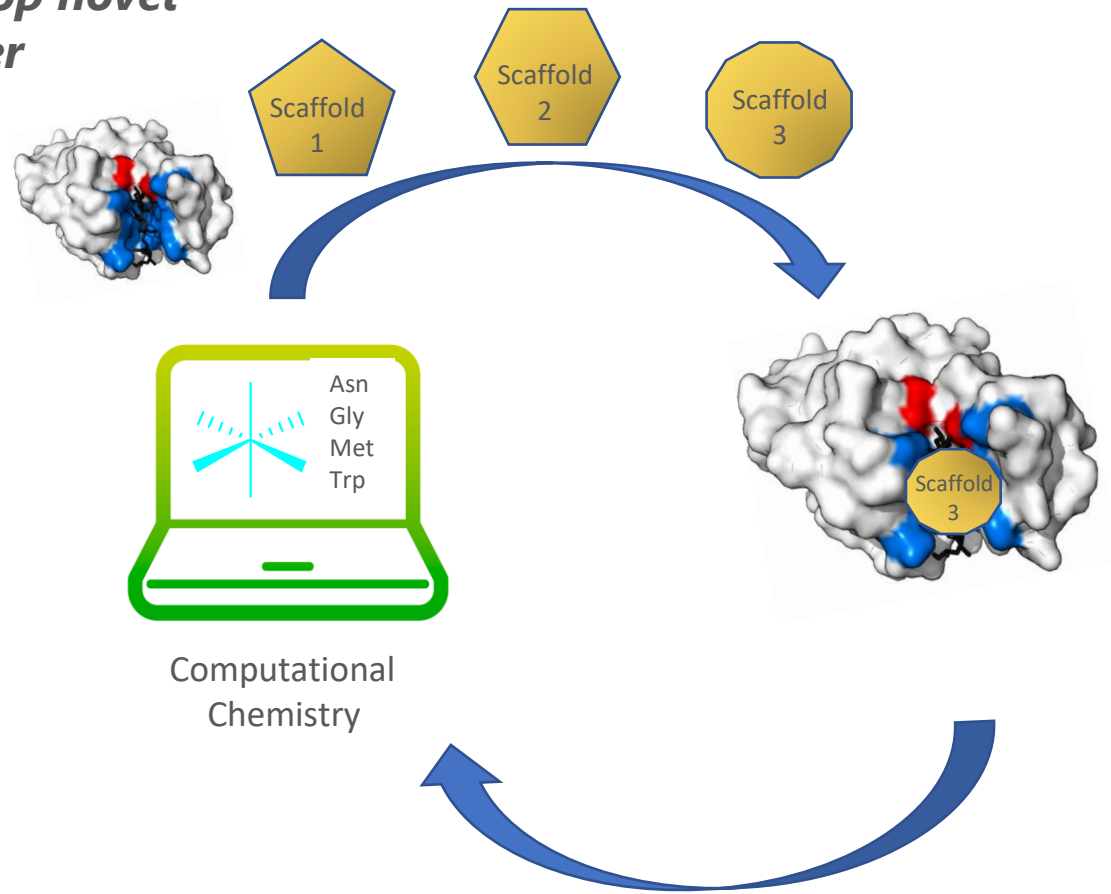
Biomea FUSION™ System Discovery Platform

We leverage our FUSION™ System to discover and develop novel irreversible inhibitors against targets essential for cancer

Our FUSION™ System Discovery Platform encompasses the following:

- ***Target selection***: Expertise in structural biology and irreversible binding chemistry.
- ***Scaffold creation:*** Computational approach to exploit unique structural elements of target proteins and create novel scaffolds***.***
- ***Molecule optimization:*** Proprietary suite of computational technologies, assays, analytical approaches, chemistry to maximize selectivity, potency, safety and convenience of our oral irreversible small molecule product candidates.



Irreversible Drugs offer several potentially significant Advantages

High Selectivity

- Irreversible drugs leverage both non-covalent and covalent interactions to drive selectivity.
- Offers greater potential selectivity versus reversible compounds, which rely on non-covalent bonding alone.
- High selectivity provides potential to reduce non-specific, off-target interactions that often lead to safety and tolerability challenges.

Deep Target-Inactivation

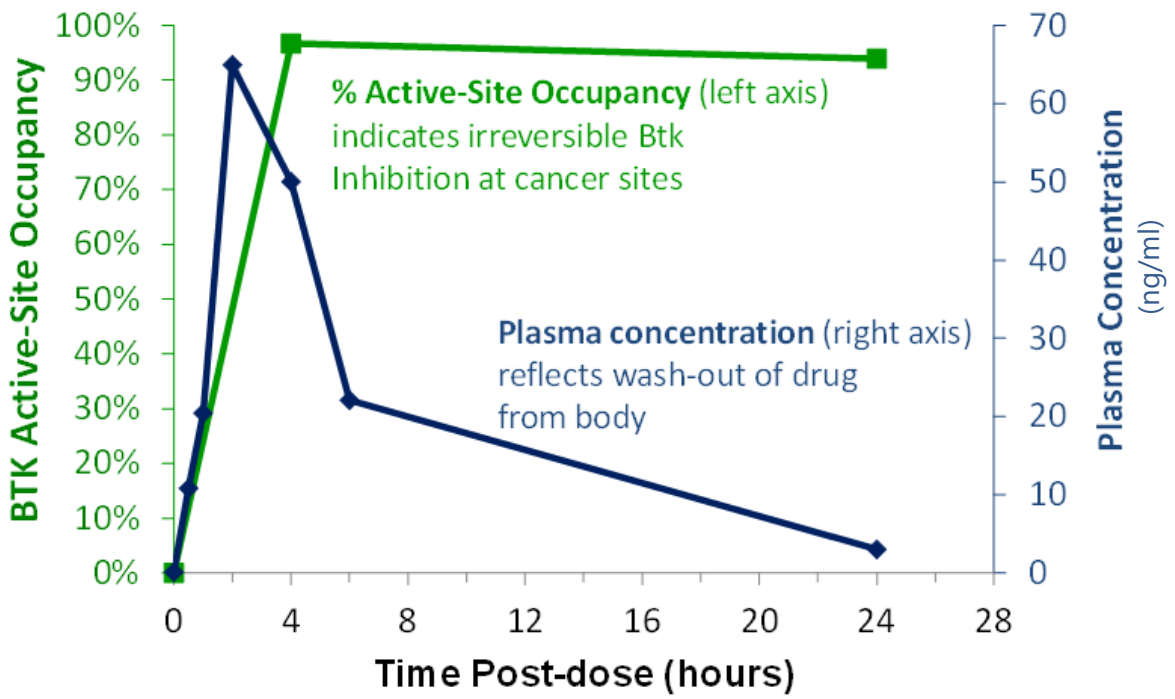
- Irreversible inhibitors can cause permanent inactivation of bound protein.
- Irreversible binding may result in the target elimination through normal cellular degradation processes.
- Target inactivation can trigger rapid apoptosis or differentiation into a normal, mature cell.

Greater Therapeutic Window

- Irreversible drugs are designed to maintain their effect in the absence of sustained drug exposure, unlike conventional reversible drugs, which typically need to be present to provide benefit.
- Uncoupling of drug effects from drug exposure can potentially enable lower drug dosing and less frequent dosing regimens versus reversible approaches.

Irreversible drugs are designed to uncouple Drug-Effects from Drug-Exposure

PK/PD – Current Commercial Drug



- The chart shows Ibrutinib, an approved, irreversible BTK inhibitor.
- Irreversible drugs can be designed to achieve nearly complete occupancy in short time, and occupancy is intended to be sustainable over 24 hours.
- Irreversible drugs are also designed to be cleared rapidly to minimize off target toxicity.
- Irreversible binding potentially offers:
  - Optimal Effect (Pharmacodynamics (PD)) / Exposure (Pharmacokinetics (PK))
  - Maximum Target Engagement
  - Better Selectivity (Lower Molecular Weight)
  - Better Drug-Like Properties (Lower Molecular Weight)

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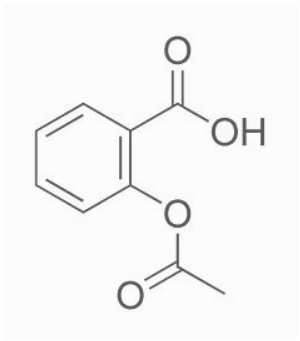
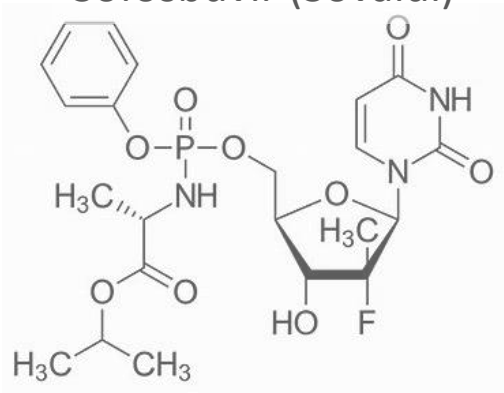
Irreversible Drugs have a long History in Medicine

Asprin was the first irreversible drug, discovered in 1899, and is to date the most used medicine in the world

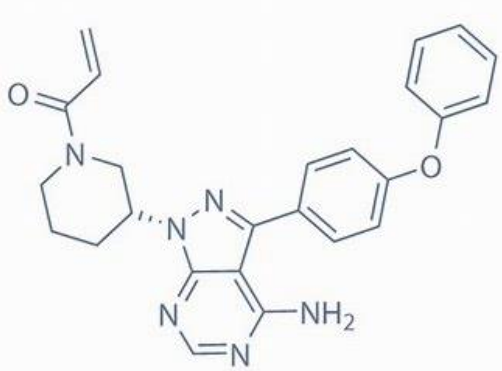
Aspirin

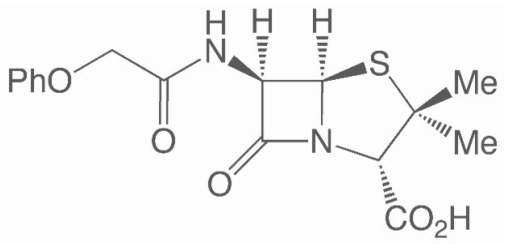


Sofosbuvir (Sovaldi)

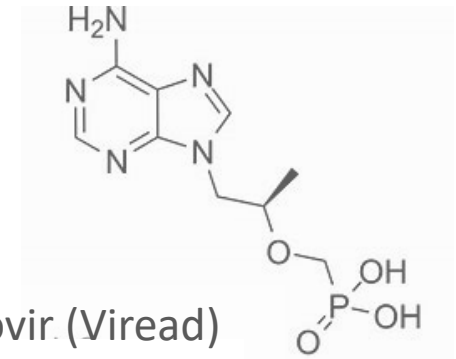


Ibrutinib (Imbruvica)

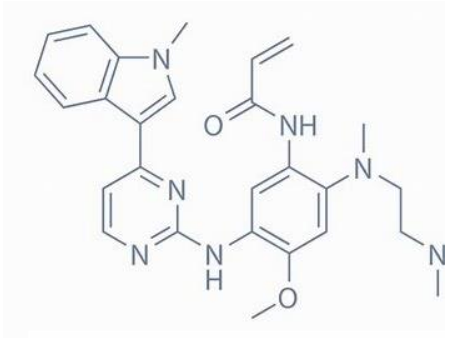




Penicillin



Tenofovir (Viread)



Osimertinib (Tagrisso)

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High Barriers to Entry to develop Irreversible Drugs

Complexity

The discovery and development of irreversible drugs has been limited by:

- Need for specialized understanding of proteome structural knowledge and medicinal chemistry capabilities, including the ability to construct complex novel chemical scaffolds.
- Limited knowledge and availability of targets as not all disease causing proteins have the properties necessary for the application of irreversible binding.

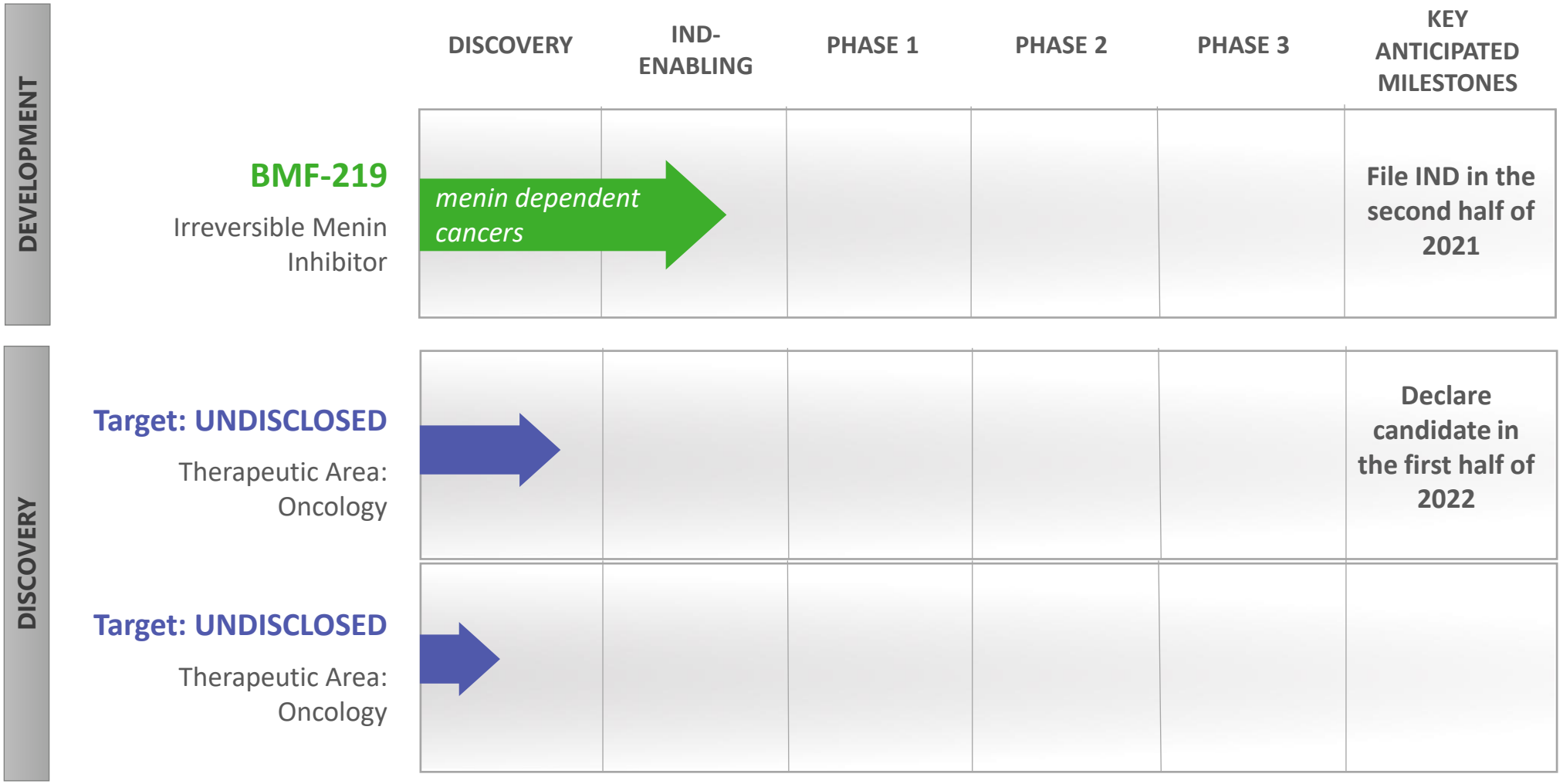
Safety and Toxicity

While the irreversible binding modality can provide a high degree of selectivity, potential risks have presented barriers:

- Irreversible molecules with promiscuous binding profiles can pose risk of significant off-target interactions and safety concerns.
- Drug developers, without the experience and specific capabilities required to develop irreversible binders, have historically not pursued irreversible drugs.

Biomea's Pipeline of Irreversible Proprietary Assets

We are building a platform of irreversible inhibitors in multiple tumor types



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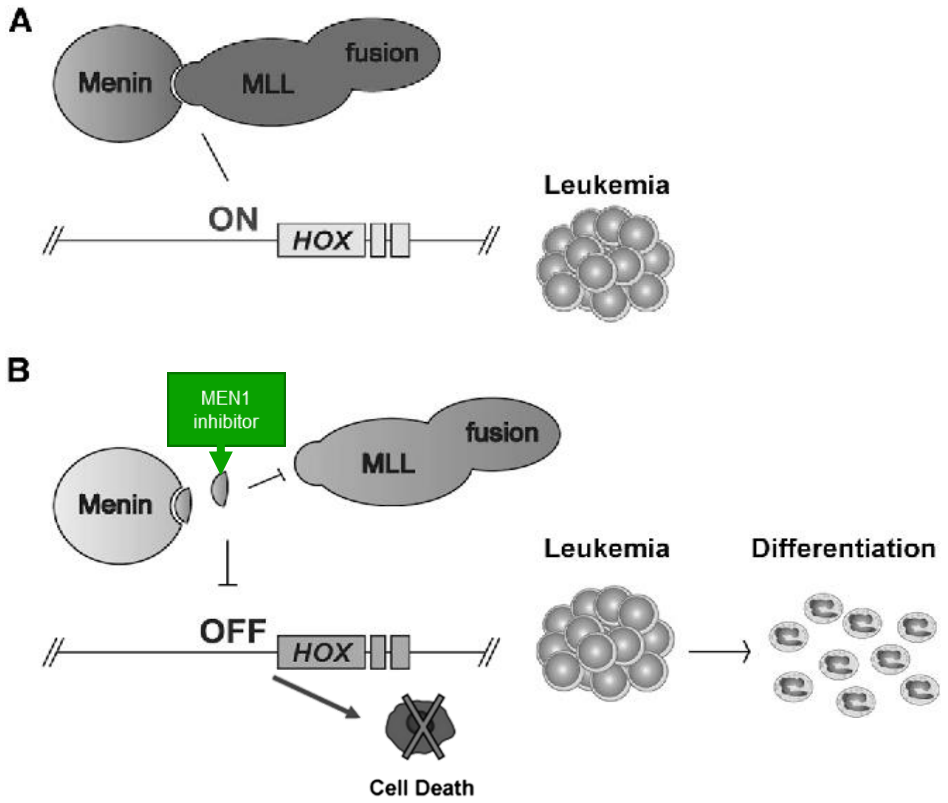
Menin – a Protein important to transcriptional Regulation

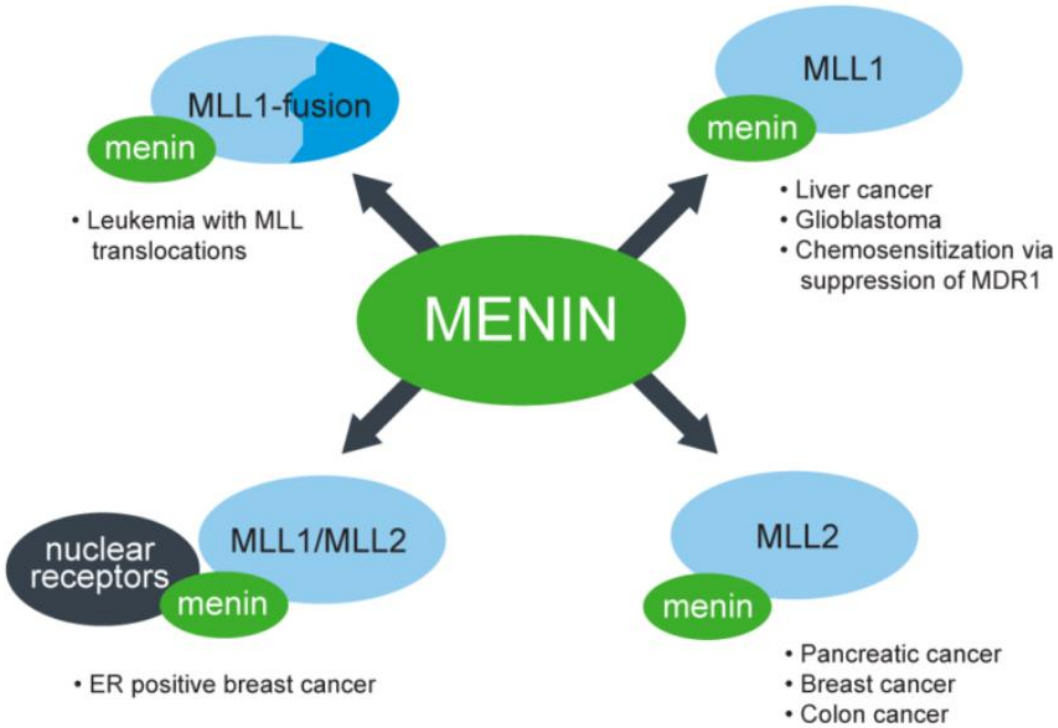
Menin impacts major processes such as cell cycle control, apoptosis, and DNA damage repair

Liquid Tumor Role



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

Solid Tumor Role



Source: Cierpicki & Grambacka, Future Med. Chem. (2014)

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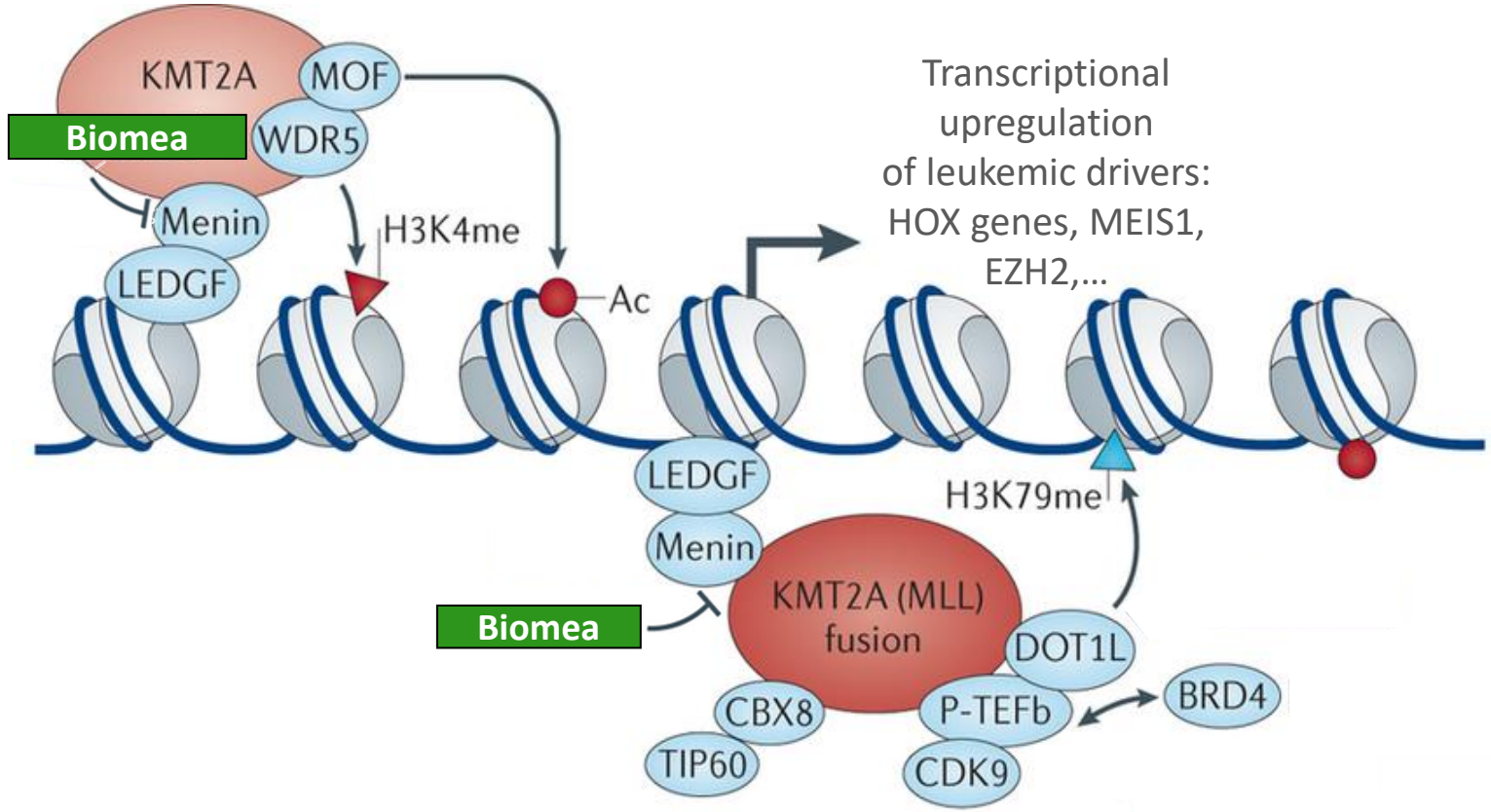
Menin-MLL Interaction

Schematic of key proteins and their interactions in the regulation of gene transcription

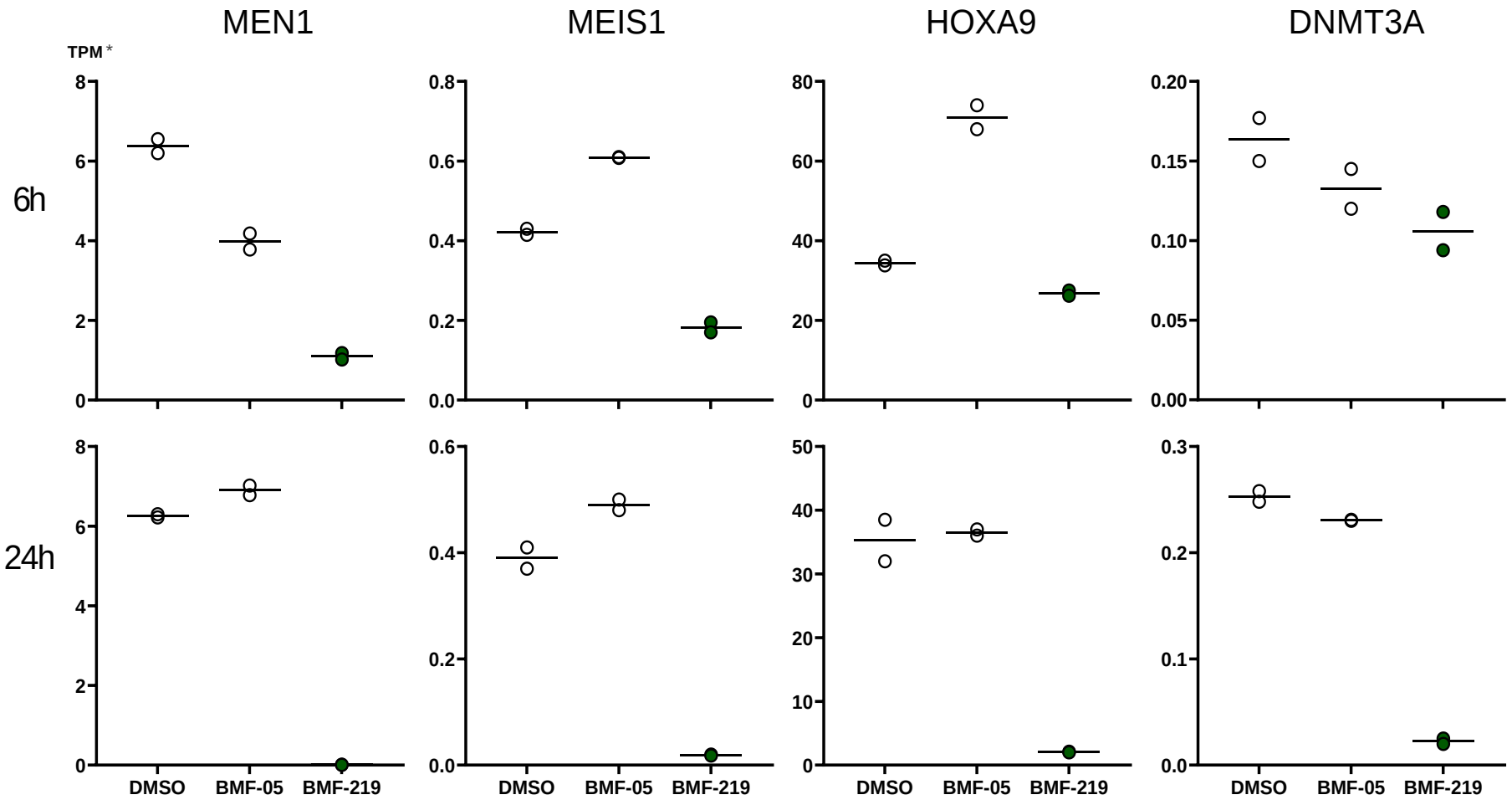
- Inhibition of the menin-MLL interaction leads to reduction in *MEN1* transcription, resulting in down regulation of *MEIS1*, *HOXA9* and *DMNT3A*, and differentiation of leukemic cells into myeloid cells.

- BMF-219, is intended to irreversibly inhibit the interaction between menin and wild type MLL and MLL fusions.



Modified after Rao & Dou (2015). Hijacked in cancer: the KMT2 (MLL) family of methyltransferases. Nat.Rev.Cancer. 15: 334-346

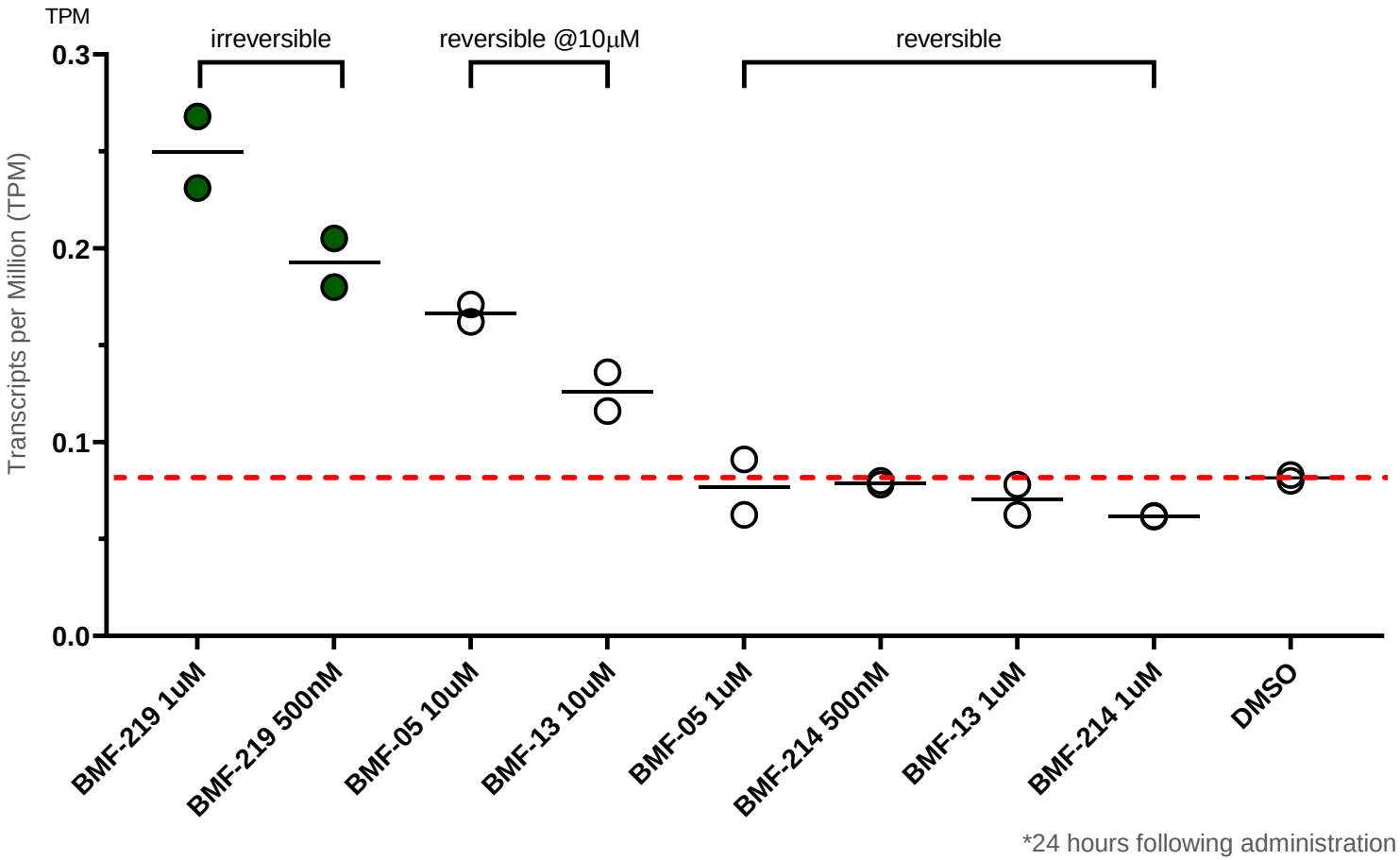
BMF-219 has demonstrated rapid Reduction in Menin dependent Gene Expression = Target Engagement



*TPM (Transcripts per Million, a measure of gene expression)

- Molecular responses following treatment with BMF-219 in MOLM-13 cells (an acute myeloid leukemia cell line with a KMT2A-MLLT3 fusion).
- A reversible inhibitor (BMF-05) showed minimal impact on signature genes at these time points as measured in Transcripts per Million (TPM), consistent with published findings.
- Our irreversible inhibitor BMF-219 caused rapid and notable effect, showing up to 80% reduction in readout genes by 6 hours and approximately 95% reduction at 24 hours.

BMF-219 has demonstrated Dose Dependent Cell Differentiation



*24 hours following administration

- Dose dependent elevation of myeloid differentiation marker (ITGAM) at 24 hours after administration of BMF-219 demonstrated target engagement in MOLM-13 cells.
- Comparable exposures of reversible menin inhibitors (BMF-05, BMF-13, BMF214) reflected no change from vehicle controls.
- Reversible inhibitors were able to upregulate ITGAM at 10-fold increase in exposure. This supports:
  - Hypothesis for the role of menin in cancer cell proliferation and
  - Highlights potential need for high clinical exposures for reversible inhibitors in order to achieve sufficient menin suppression to affect the disease.

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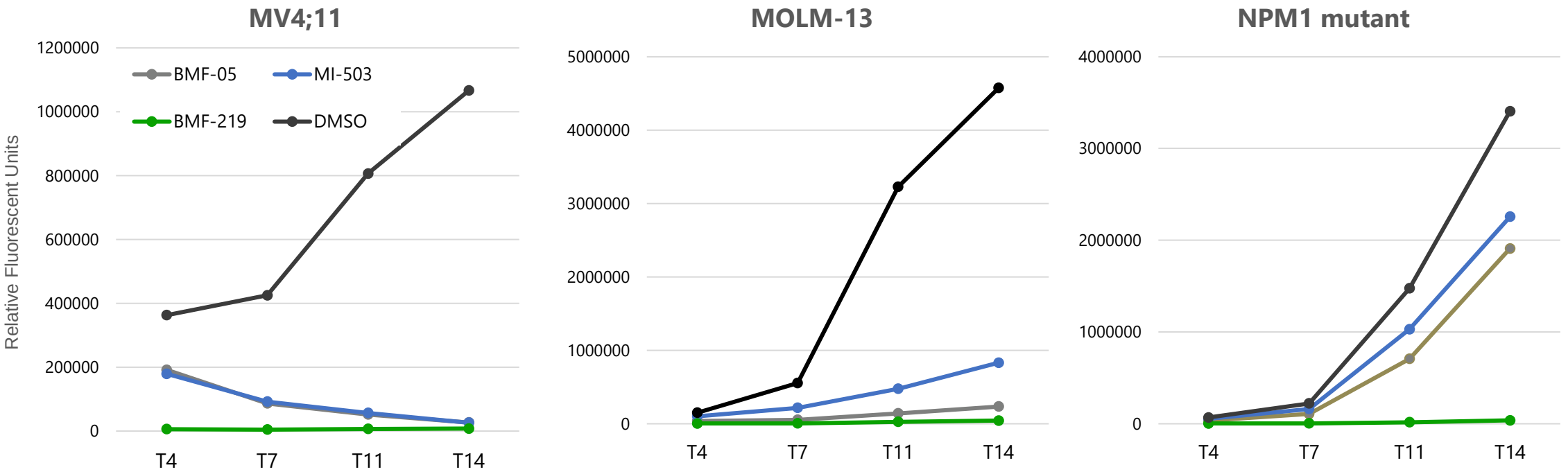
BMF-219 has demonstrated superior, rapid and durable Responses in Leukemia Cell Lines



- BMF-219 demonstrated rapid shut down of metabolic activity, sustained over the 14-day study duration.
- BMF-219 responses were superior to tested reversible menin inhibitors (BMF-05, MI-503) with respect to both onset and durability of metabolic suppression.

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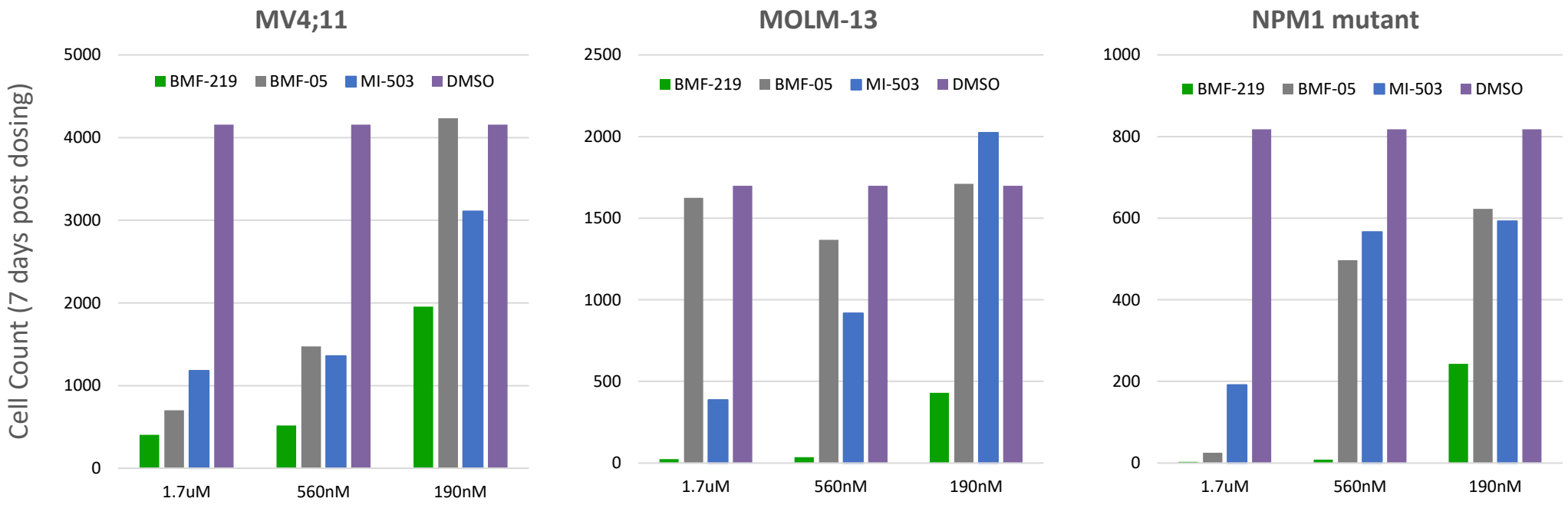
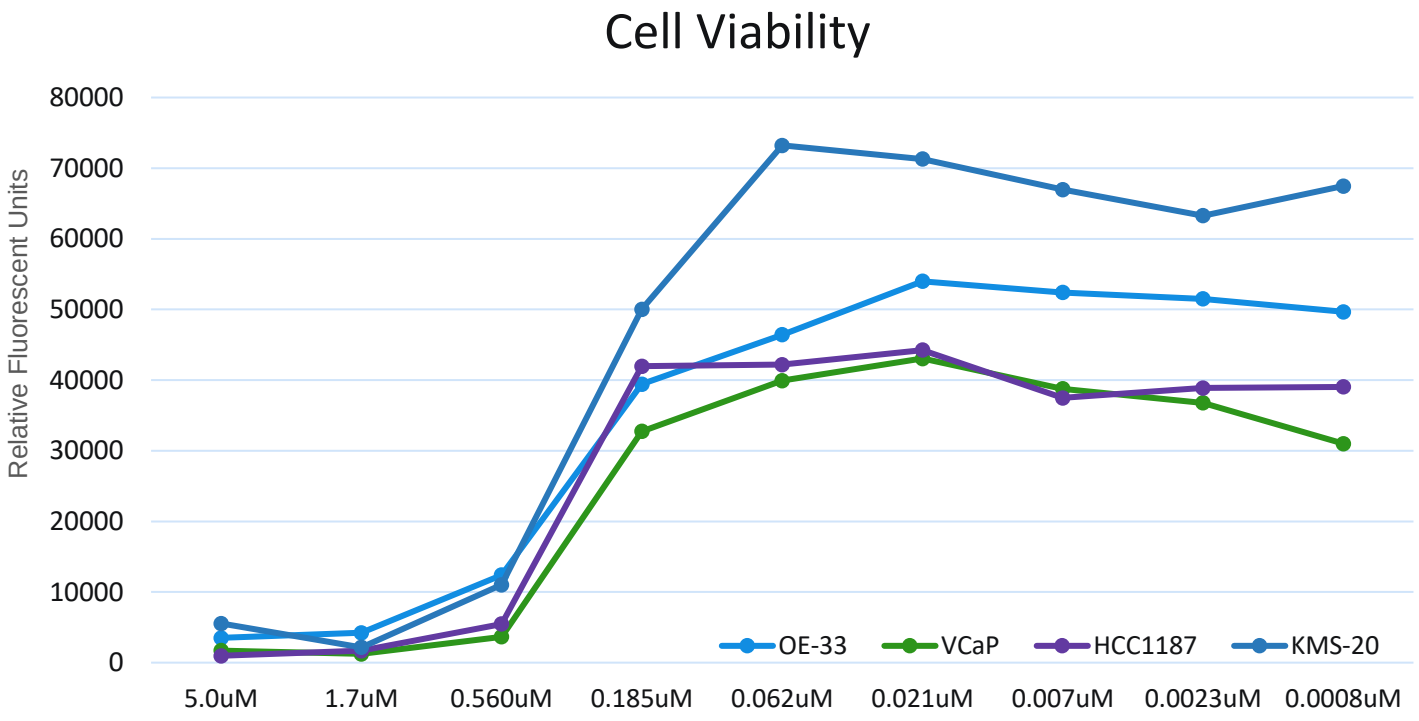
BMF-219 Administration has resulted in Reduction of Cell Survival at the lowest dose across all tested Cell Lines



- BMF-219 led to notable reduction in leukemic cell survival.
- BMF-219 responses were observable at the lowest tested doses across all cell lines.
- Reversible inhibitors (BMF-05, MI-503) showed minimal responses at the lowest dose and were unable to eliminate tumor cells at any tested dose.

BMF-219 demonstrated potent Growth Inhibition across a Range of menin-dependent Cancer Cell Lines



Day 7 – Long Term Proliferation Assay

Increasing Potency

Increasing Menin Dependency

Tumor Type	IC50 (nM)	Menin Dependency*
Triple negative Breast (HCC1187)	460	-0.71
B. Esophageal (OE-33)	300	-0.95
Prostate-met (VCaP)	290	-1.48
Multiple Myeloma (KMS-20)	260	-2.62

*Menin Dependency CERES Score from Depmap.org (Score ≤-1 defines an essential gene)

- Menin is a known dependency in a range of tumors, including multiple myeloma and multiple solid tumors.
- Observed menin Inhibitor potency was correlated to the level of menin dependency of each cell line. An indicator of the importance of menin in the underlying mechanism of proliferation in these cancer models.
- BMF-219 showed potent growth inhibition across multiple menin-dependent cancer cell lines.

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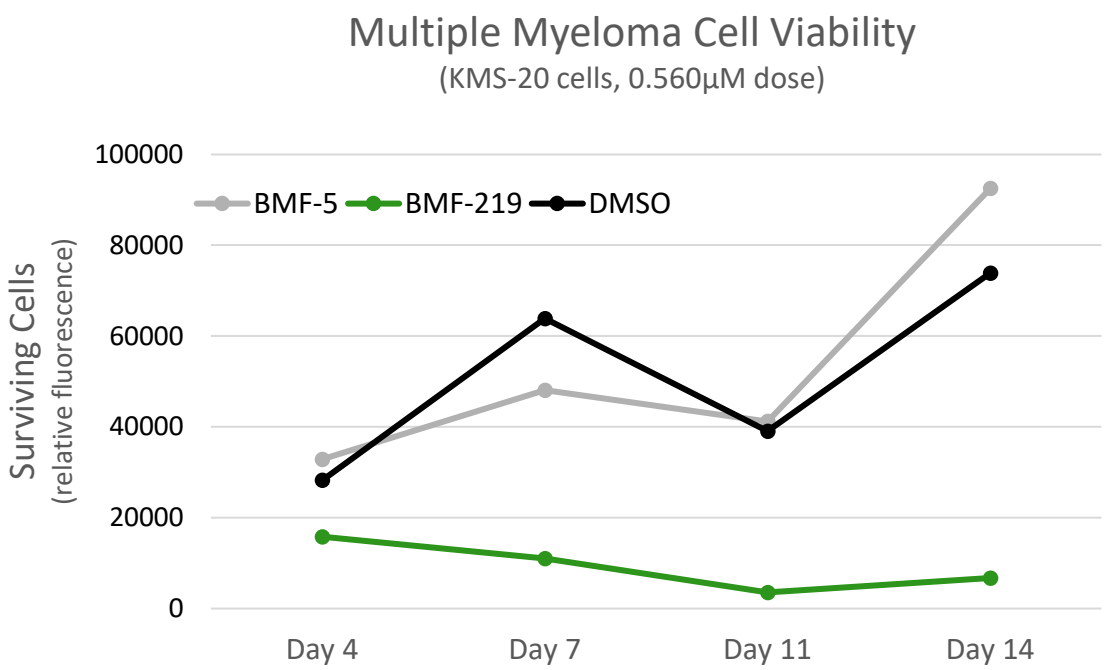
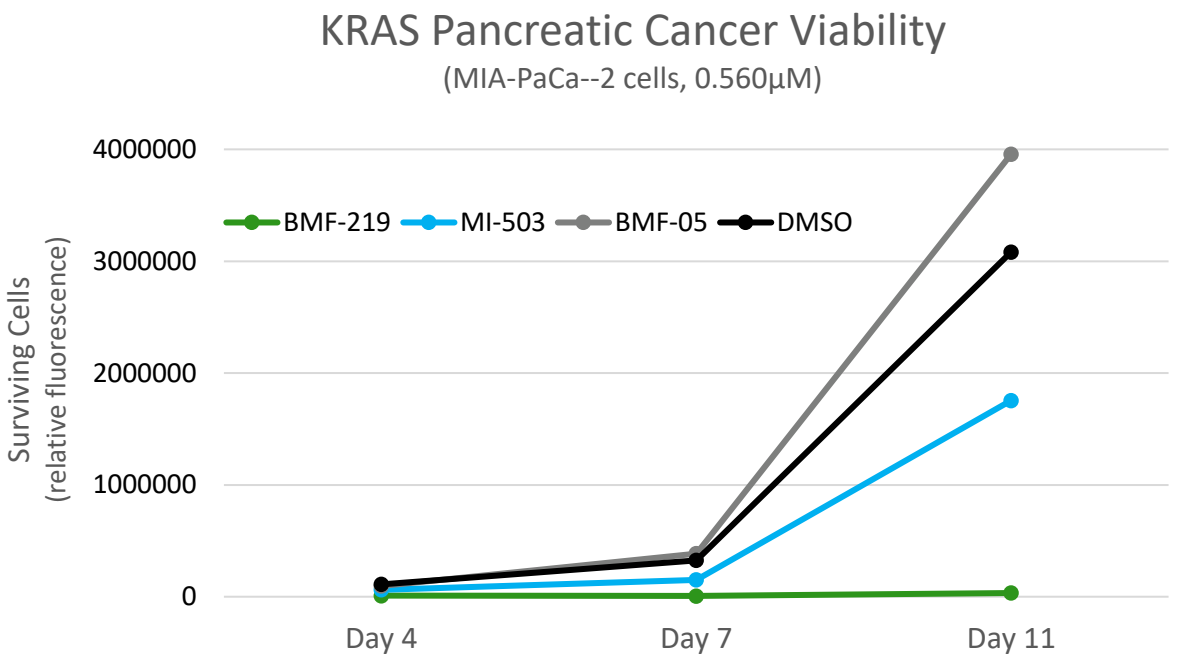
BMF-219 impaired Cell Survival in Multiple Myeloma and Pancreatic Cancer Models





- Impairment of survival in multiple myeloma model (KMS-20 cell line, 0.56µM doses) by irreversible menin inhibitor BMF-219 versus a reversible inhibitor (BMF-05).

- Impairment of survival in G12C KRAS mutation driven pancreatic cancer line (MIA-PaCa-2, 0.56µM doses) shows the effects of irreversible menin inhibitor BMF-219 versus a reversible inhibitor (BMF-05) at far lower dose levels.

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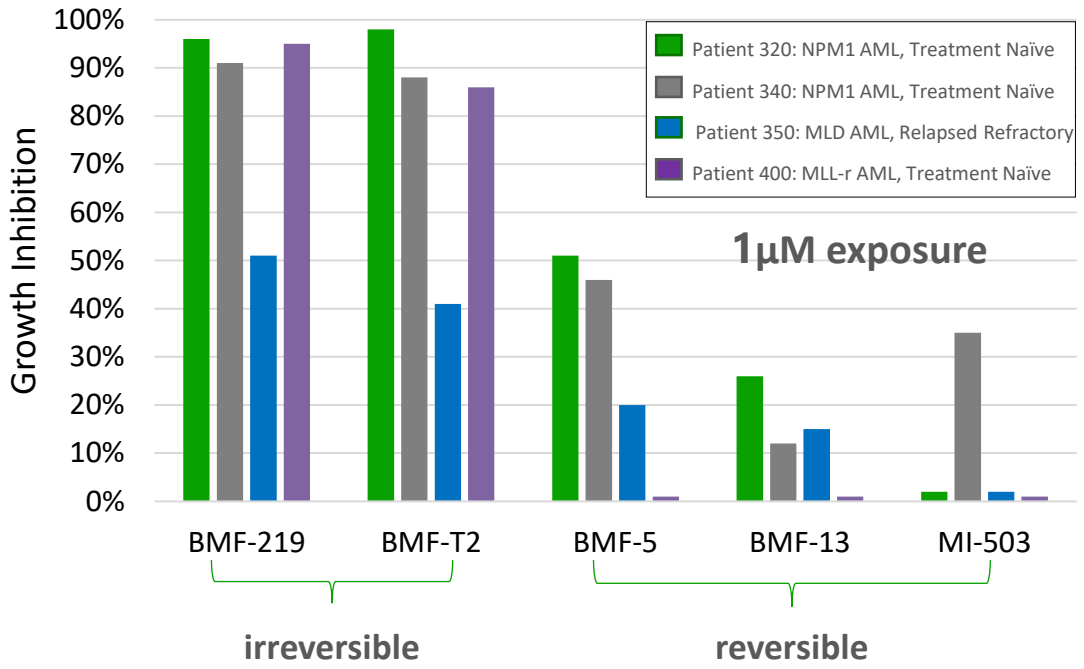
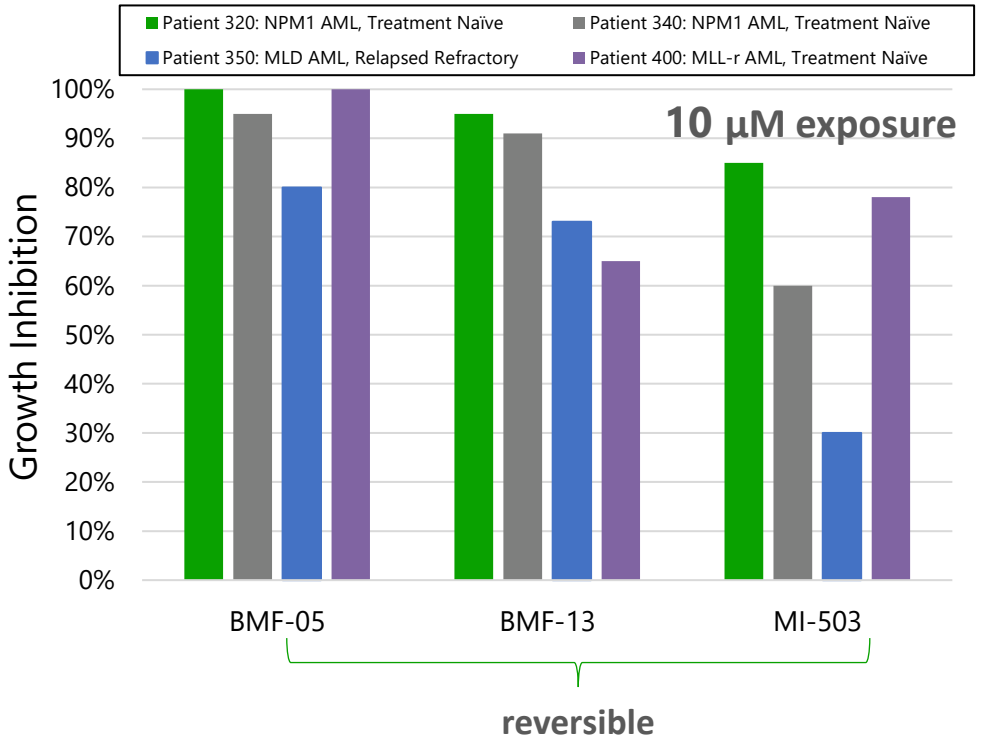
BMF-219 Inhibited Cell Survival in Multiple Cancer Cell Lines

- Responses to BMF-219 were screened across a range of cancer cell lines.
- Potent growth inhibition was observed across a range of cancer models including liquid and solid tumors.

	Cell Line/Tumor Type	IC50 (µM)
Fusion	MOLM-13/AML	0.05
	MV4;11/ALL-AML	0.07
NPM1 Mutation	OCI-AML3/AML	0.14
KRAS	MIA-PaCa-2/Pancreatic	0.23
	NCI-H23/Lung	0.26
Menin Dependent	KMS-20/Plasma Cell Myeloma	0.26
	VCaP/Prostate Adenocarcinoma (met)	0.29
	OE-33/Barrett Esophageal Adenocarcinoma	0.30
	KG-1/AML	0.33
	HC1187/Ductal Breast Carcinoma (TNBC)	0.46
KRAS	Panc 10.05/Pancreatic	0.49
	NCIH23/NSCLC	0.49
Menin Dependent	BT-474/invasive ductal carcinoma NOS	0.52
KRAS	SK-LU-1/Lung	0.59

BMF-219 inhibited Patient derived AML cells at very low Exposures vs Reversible Inhibitors





- Irreversible inhibition leads to dramatic growth inhibition at 1µM exposure while tested reversible inhibitors showed limited effect.
- At six days, reversible menin inhibitors show similar inhibition of growth at drug exposures 10-fold greater than their respective IC90 values (10µM).
- Findings support relevance of the mechanism in disease and our hypothesis that an irreversible inhibitor could potentially provide greater therapeutic benefit at lower exposure-levels versus reversible inhibitors.

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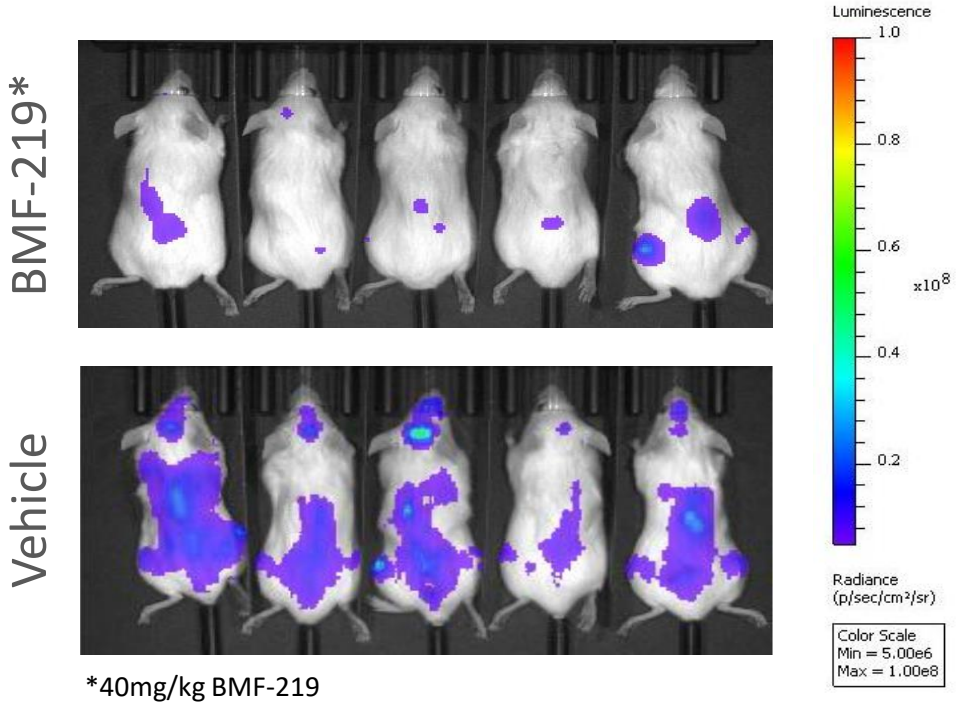
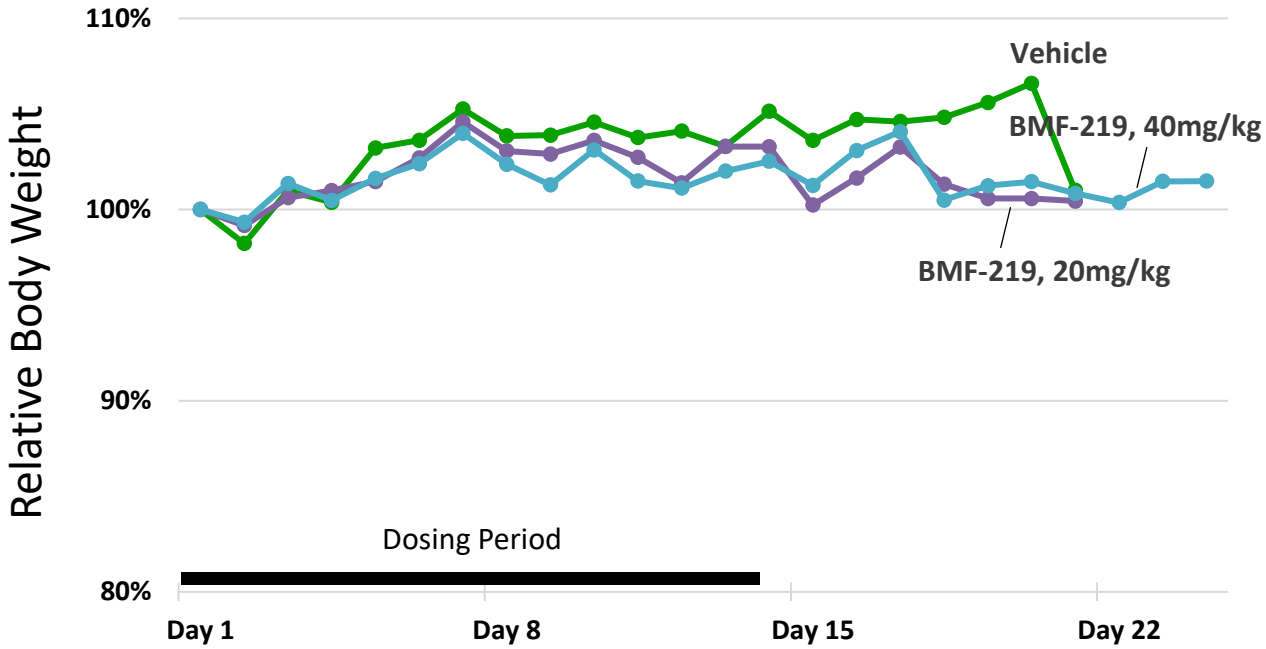
BMF-219 showed significant Survival Benefit in a Disseminated Leukemia Xenograft Model vs Standard of Care



*40mg/kg BMF-219



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

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Selectivity Profiling of BMF-219 in multiple Safety Models

Kinase screening

- In-house analysis of menin revealed limited structural similarity between targeted binding pocket and tyrosine kinases with known involvement in hematological cancers.
- 169 kinases screened; only two wild type kinases showed greater than 50% inhibition upon treatment with BMF-219.

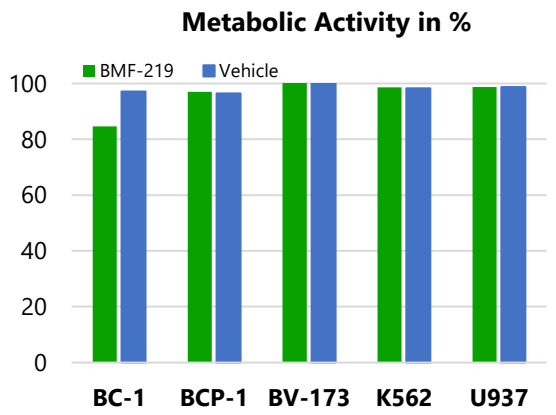
Glutathione reactivity

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

- Drugs with limited non-specific interactions have long half-lives as the drug does not get consumed in a reaction with wildly-used glutathione (GSH).
- BMF-219 showed negligible interaction with the strong nucleophile GSH and showed less reactivity than the approved irreversible drugs omeprazole and neratinib.

Oncopanel screening

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



Safety screen

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

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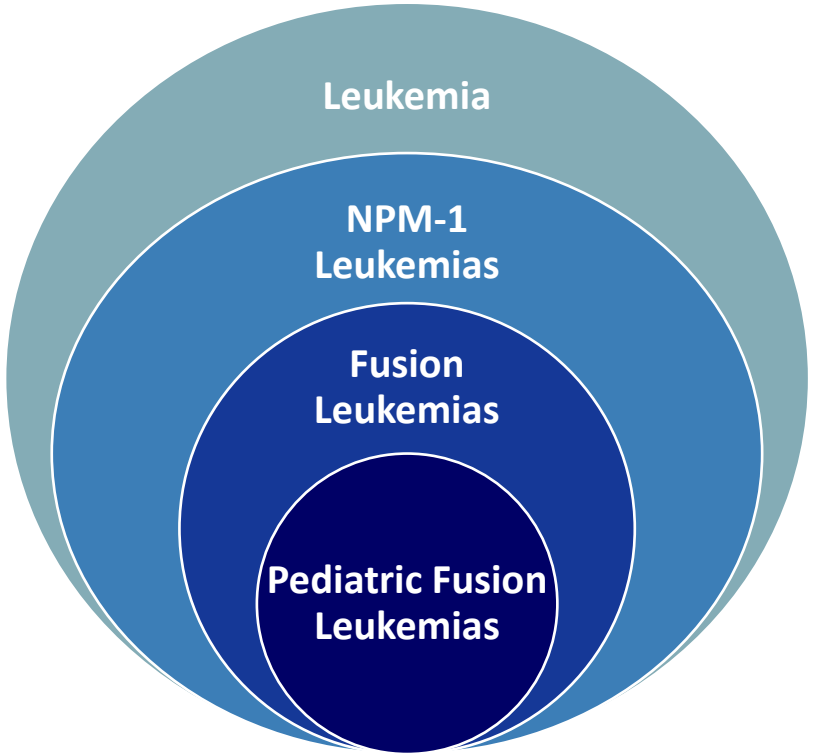
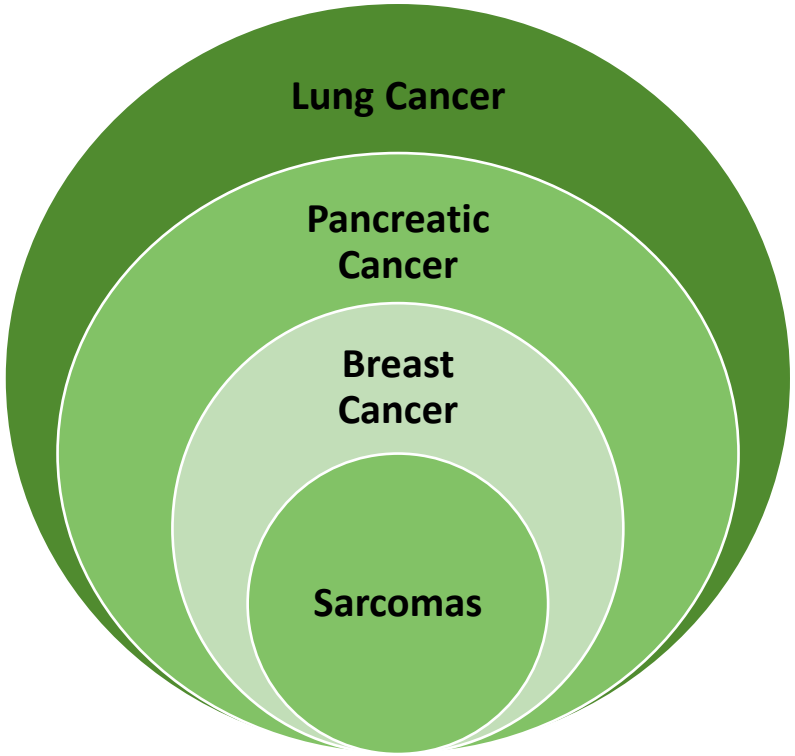
Estimated Target Population for irreversible Menin Inhibitor BMF-219



LIQUID TUMORS

Liquid Tumors	
Disease	Est. US Patient Population (Annual Incidence)
AML/ALL (MLL-R)	2,500
AML/ALL (NPM1)	7,000
DLBCL*	18,000
MM*	32,000

Solid Tumors	
Disease	Est. US Patient Population (Annual Incidence)
EWS	1,000
KRAS-Lung	34,000
KRAS-Pancreatic	26,000
KRAS-CRC	17,000



SOLID TUMORS

*** Investigation ongoing to further define menin dependent subset**

Patient Numbers see:

AML/ALL/DLBCL/MM/Lung/Pancreatic/Colorectal: https://seer.cancer.gov

EWS: pubmed.ncbi.nlm.nih.gov/18525458/

Mutation Status see:

AML/ALL MLL-R & NPM1 www.ncbi.nlm.nih.gov/pmc/articles/PMC5299633/ and www.ncbi.nlm.nih.gov/pmc/articles/PMC3069851

KRAS NSCLC G12C&D https://err.ersjournals.com/content/25/139/71#

KRAS PDAC G12C&D www.cell.com/trends/biochemical-sciences/pdf/S0968-0004(13)00203-X.pdf

KRAS CRC G12C&D www.ncbi.nlm.nih.gov/pmc/articles/PMC6945179/#!po=15.9091

biomea FUSION

Biomea Fusion Intellectual Property

We believe our Patent Portfolio with novel irreversible Scaffolds is strong and growing

We have seven patent applications (2 international (PCT) and five US (PTO))*:
PCT/US2019/69155, PCT/US2019/69157, and US PTO 16/732226, US PTO 16/732228 and 62/956,099; 63/105,839, 63/105,839, 63/126,505.
All seven patents are composition of matter patents. For the two non-provisional patent applications, one covers the reversible inhibitor series and the other covers the irreversible inhibitor series. Both of these PCT filings have a priority date of 12/31/2018. The third, fourth, and fifth filing, provisional patent applications, cover the back-up series for the irreversible inhibitor program. These patent applications have priority dates of 10/7/2020, 10/26/2020, 12/7/2020.
Regarding exclusivity, we expect standard extensions to be granted for clinical development time of 3-4 years (Actual granted extensions can vary in time and are not guaranteed).
Once granted, this would put expiry of the patents out to approximately 2042 for the PCT and 2044 for the provisional patent applications.

* As of 12/31/2020

Looking Ahead - 2021 and beyond

Developing BMF-219 for multiple tumor types and building out a platform of irreversible inhibitors

2017- 2020

- ✓ FUSION™ System Discovery Platform built, created early differentiated profiles for multiple irreversible inhibitors.
- ✓ Established menin is a key signaling intermediate in multiple tumor types (liquid and solid).
- ✓ BMF-219 has shown improved preclinical results versus the other two reversible, early-stage, menin programs.
- ✓ Series A ~$56 million financing round in Dec 2020 is expected to allow Biomea to bring lead product candidate into the clinic and further develop its potential in multiple indications

2021 and beyond

- Completion of IND-enabling studies with irreversibly bound menin inhibitor BMF-219.
- Initiation of first in human clinical trial with BMF-219 expected to produce data for a variety of tumor types in Phase I and Phase II Basket-Study.
- Advancement of irreversible platform to generate one additional IND candidate expected in 1H of 2022.


Thank You
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FUSION