biomea FUSION™

JP Morgan 2023 Corporate Presentation

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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 **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 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

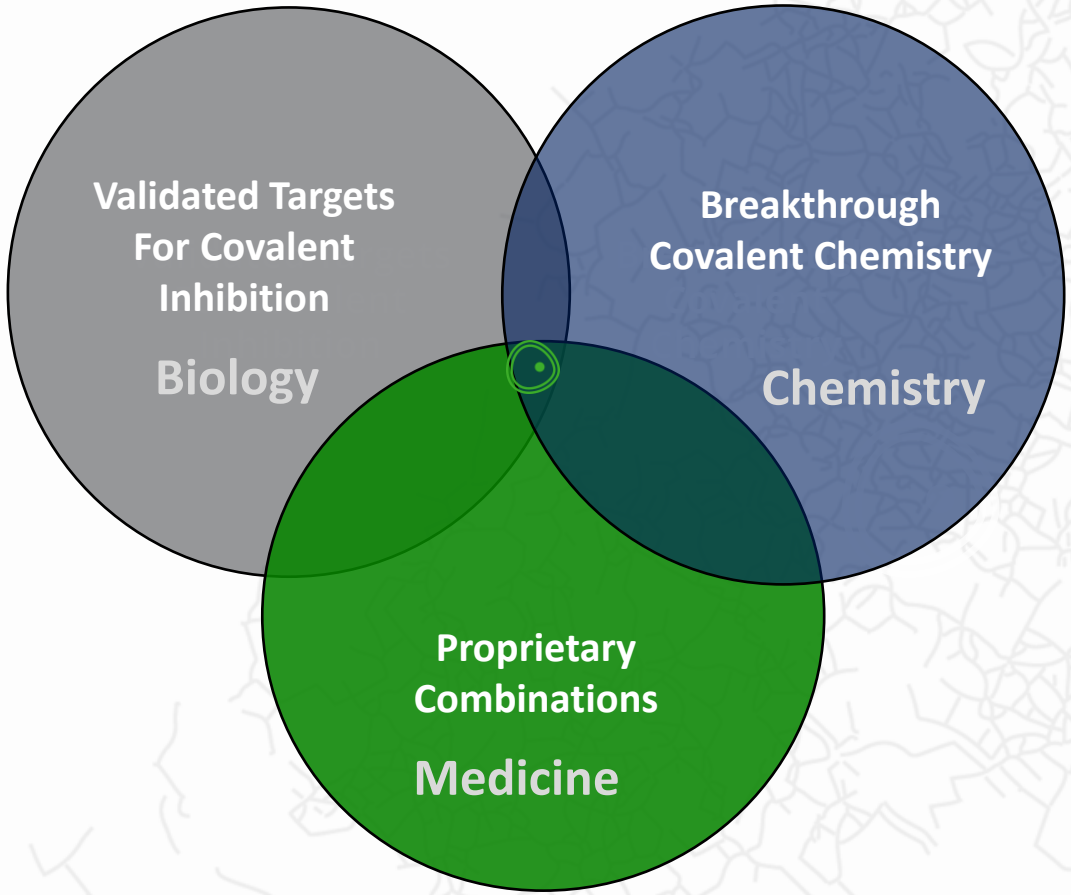
Jim Palmer
VP of Drug Discovery

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'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

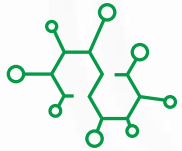
Utility:
Differentiated insights from X-ray crystal structures, identifying target cysteines

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

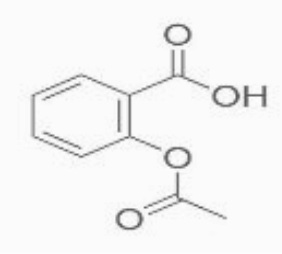
Utility:
Scaffolds are further refined with Mass spec, animal, and cell-based assays to two IND candidates

Covalent Chemistry creates very powerful results

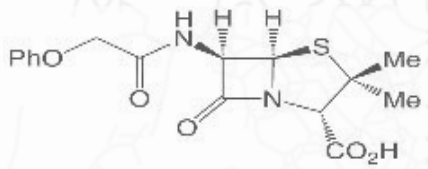
Covalent Inhibitors - a History of Medical & Commercial Success

Notable Covalent Inhibitors

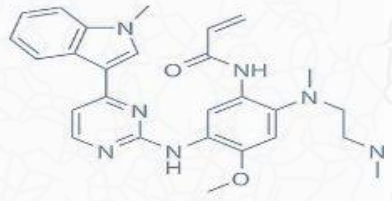
Aspirin

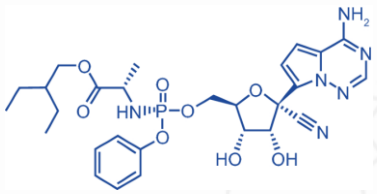


Penicillin

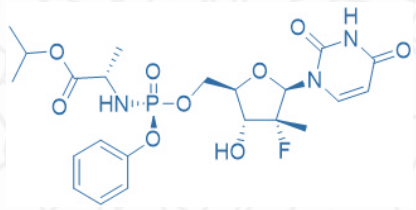


Osimertinib (TAGRISSO)

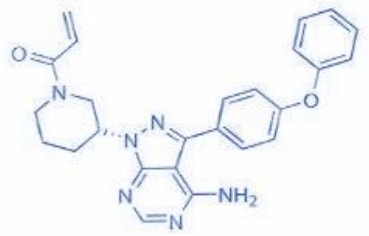




Remdesivir (VEKLURY)



Sofosbuvir (SOVALDI)

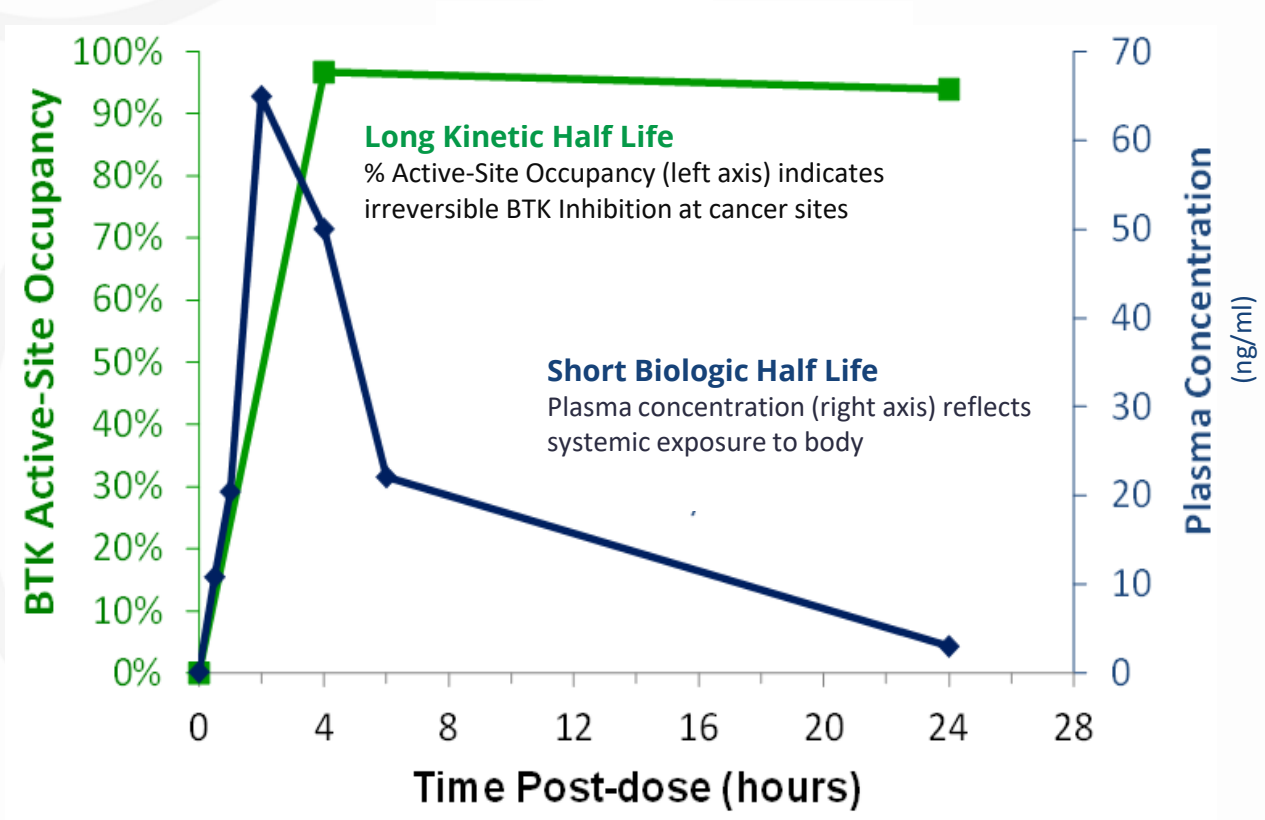


Ibrutinib (IMBRUVICA)

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 ✓

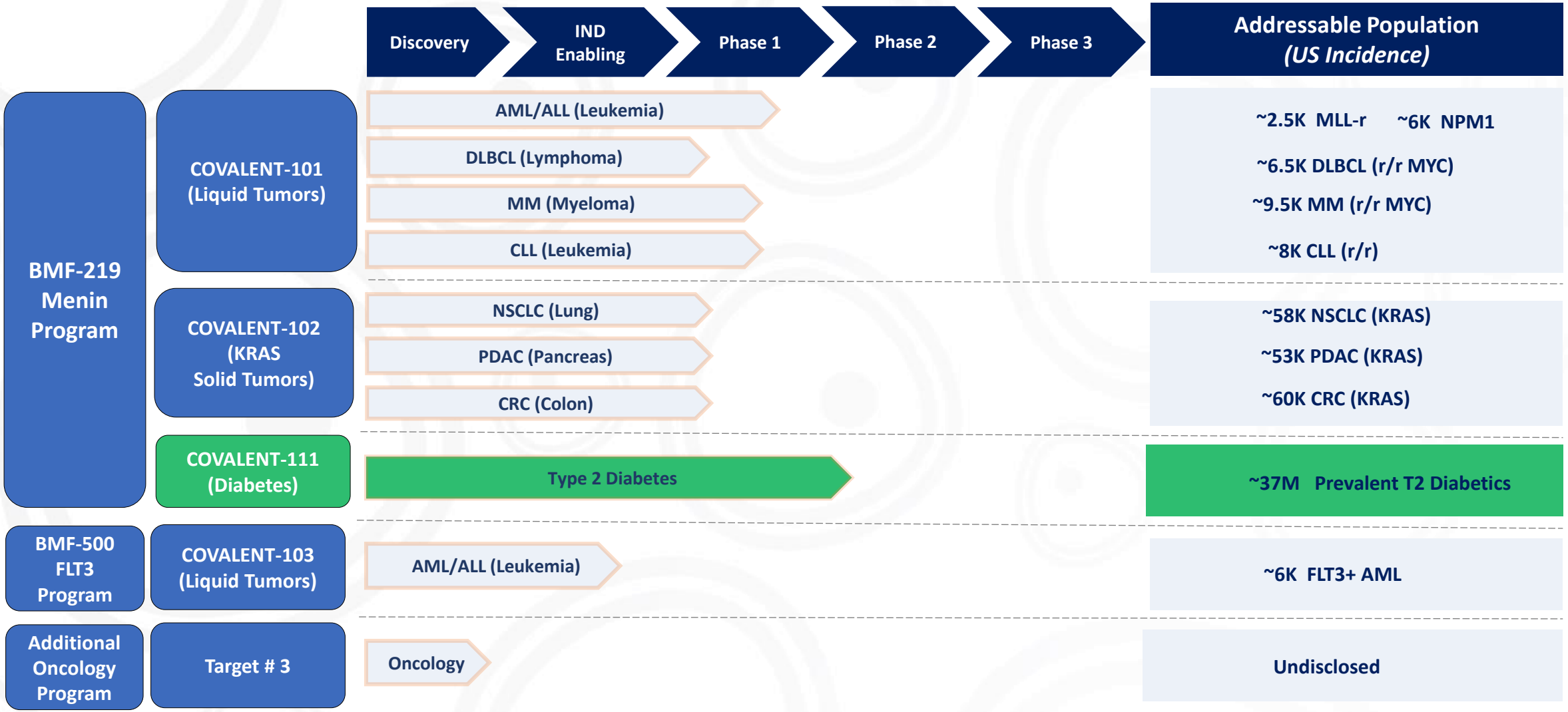
Completion of Healthy Volunteer Portion of Study	Completed ✓
Enrollment of First Diabetes Patient	Completed ✓

Additional Programs

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

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

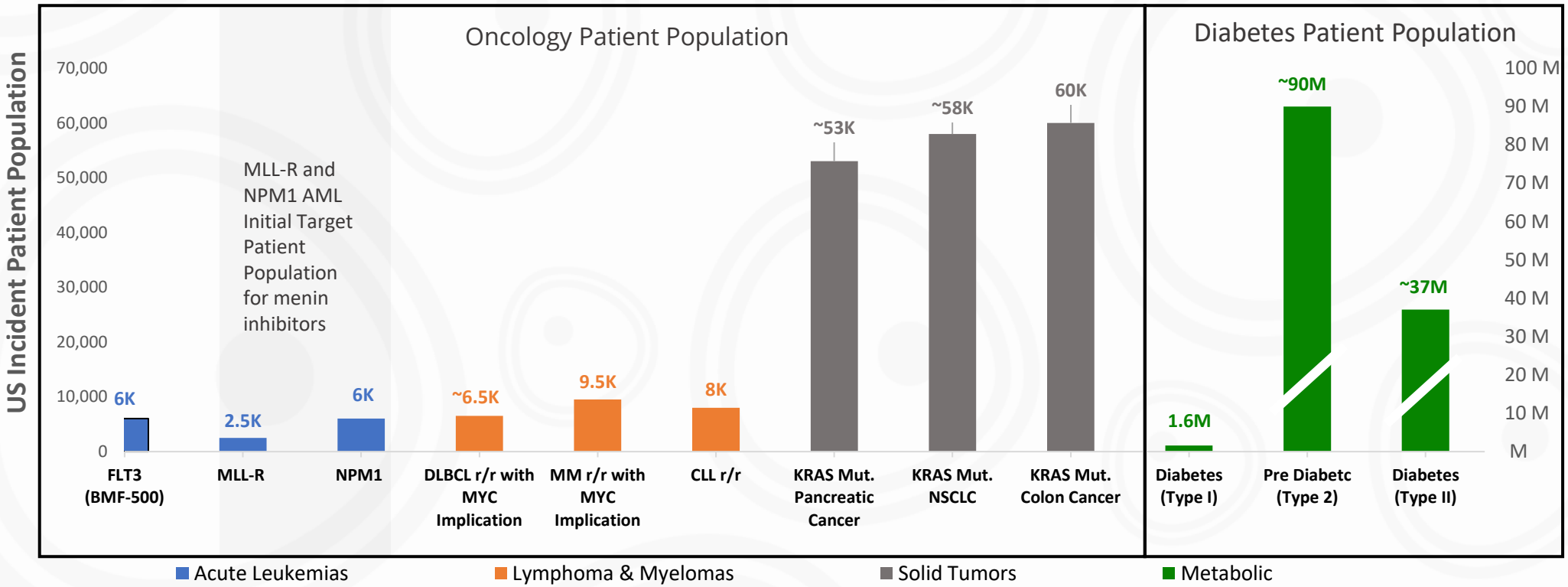
Biomea's Pipeline as of January 2023



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

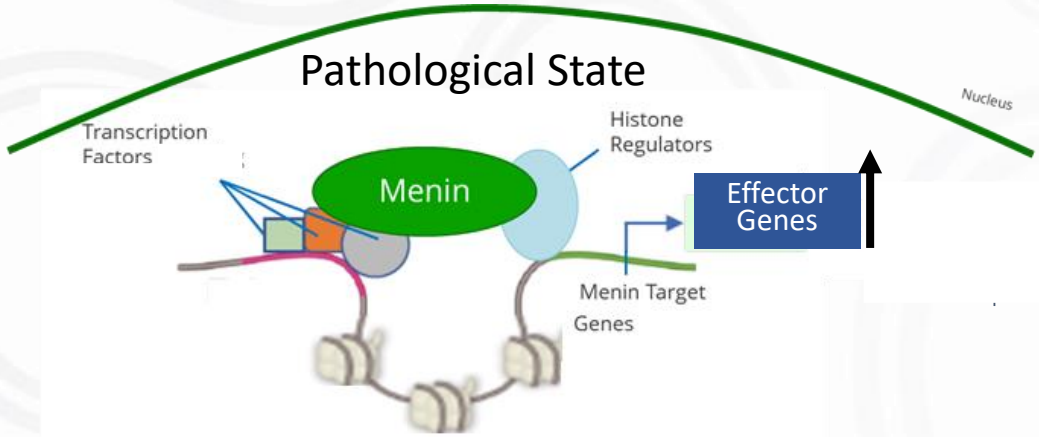
Cancer Indications: >200K and Diabetes: >125M

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>

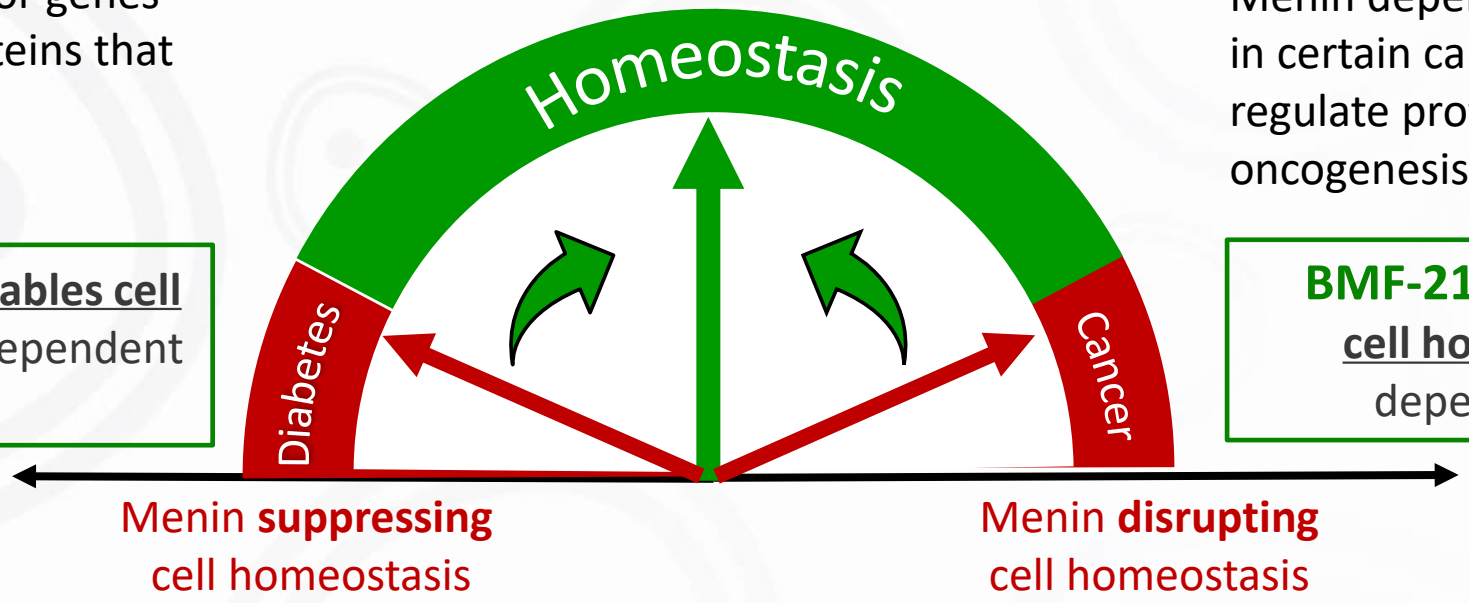
Restoring Balance in Menin Dependents Diseases is Context Specific



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

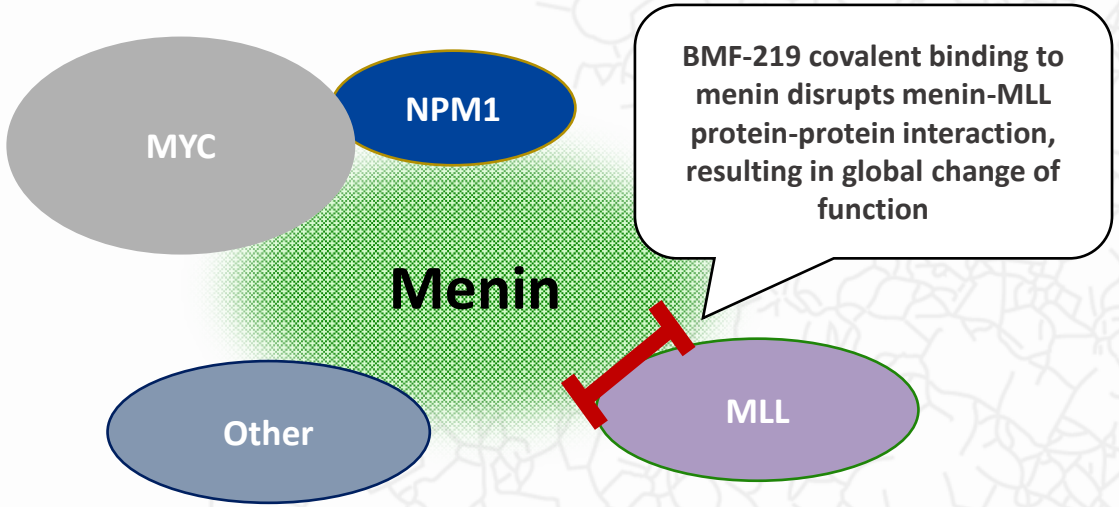
- Menin dependent effector genes in certain cancers express or regulate proteins that drive oncogenesis

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

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

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

MYC Addicted and MYC Driven Tumors

Expansion into r/r diffuse large b cell lymphoma, r/r multiple myeloma and r/r chronic lymphocytic leukemia

RAS/RAF Driven Solid Tumors

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

Diabetes

Pathway and clinical validation of covalent menin inhibition

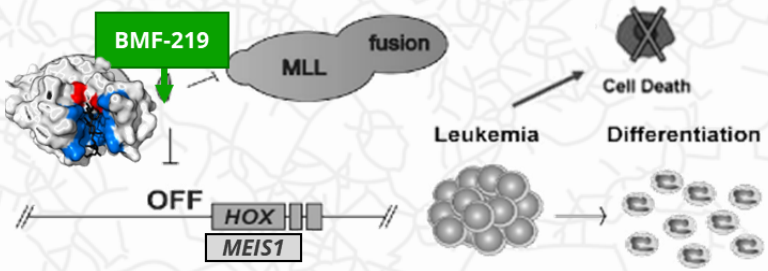
First Development Success with BMF-219 in MLL Fusion and NPM1 Driven Tumors

In Acute Leukemia

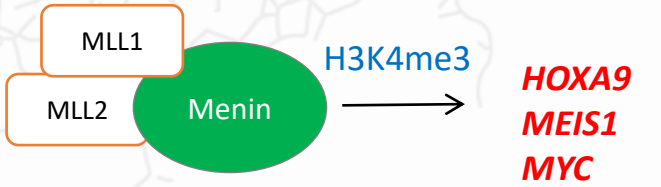
Development Stage:
Phase I Clinical Trial (COVALENT-101) enrolling patients with relapsed/refractory acute leukemia

Key Facts	MOA	Relevant Pathway
Estimated Addressable Population	BMF-219 covalently blocks menin / MLL interaction	Menin / MLL interaction can modify chromatin, activating key leukemic genes

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



- 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)



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

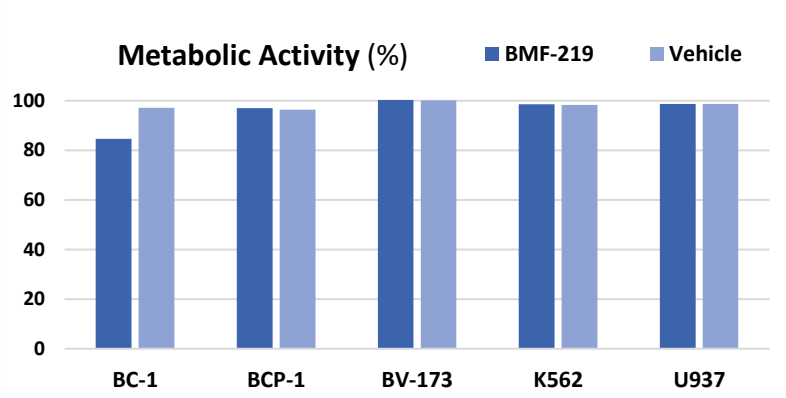
No Histopathology Findings Were Observed with BMF-219 in GLP and non-GLP IND-Enabling Toxicology Studies

✓ 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

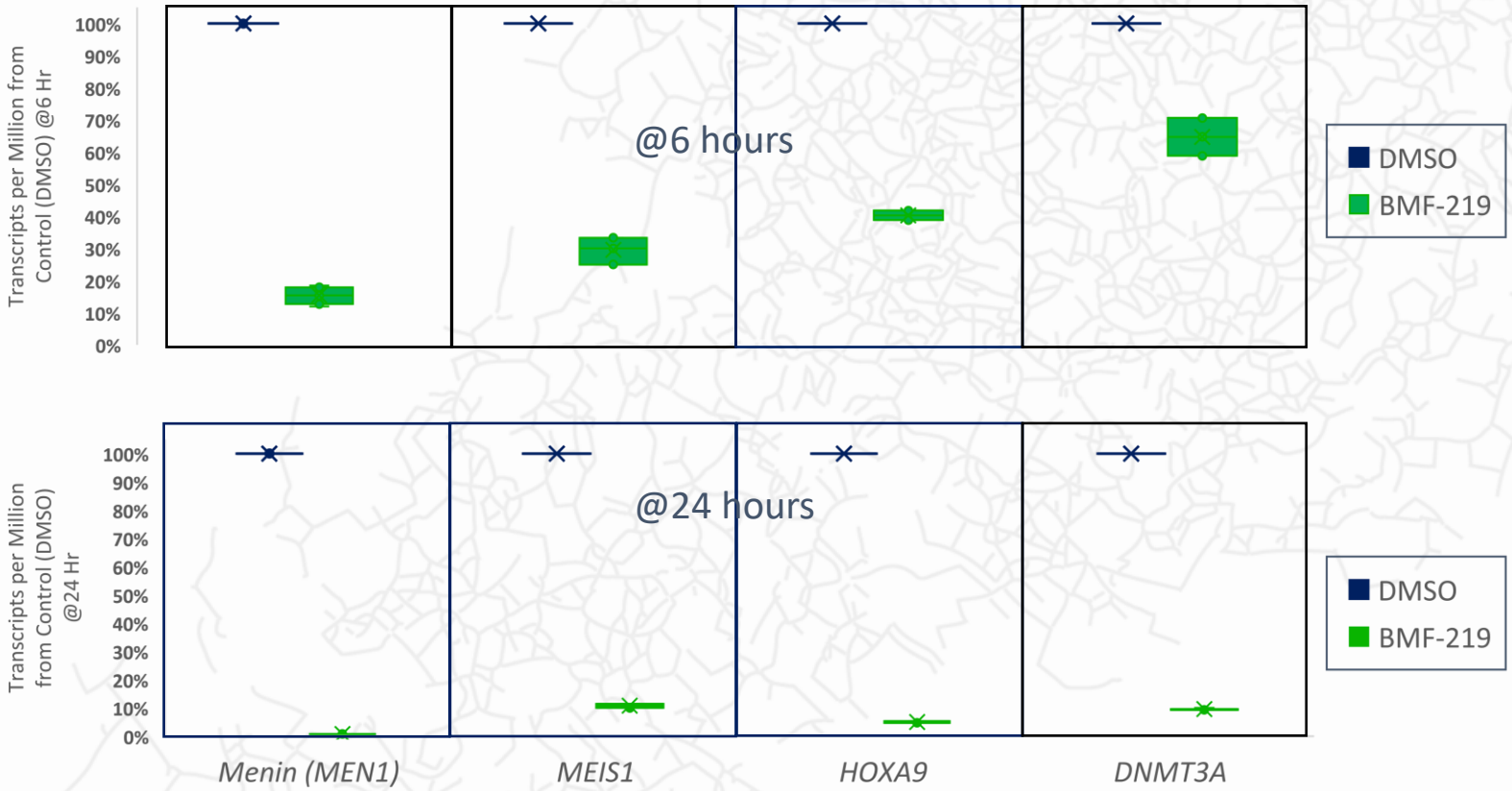
BMF-219 had **less reactivity than the approved covalent drugs omeprazole and neratinib**

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

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

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

Gene Expression Changes in AML cells following treatment w/ BMF-219 (0.500µM dose)

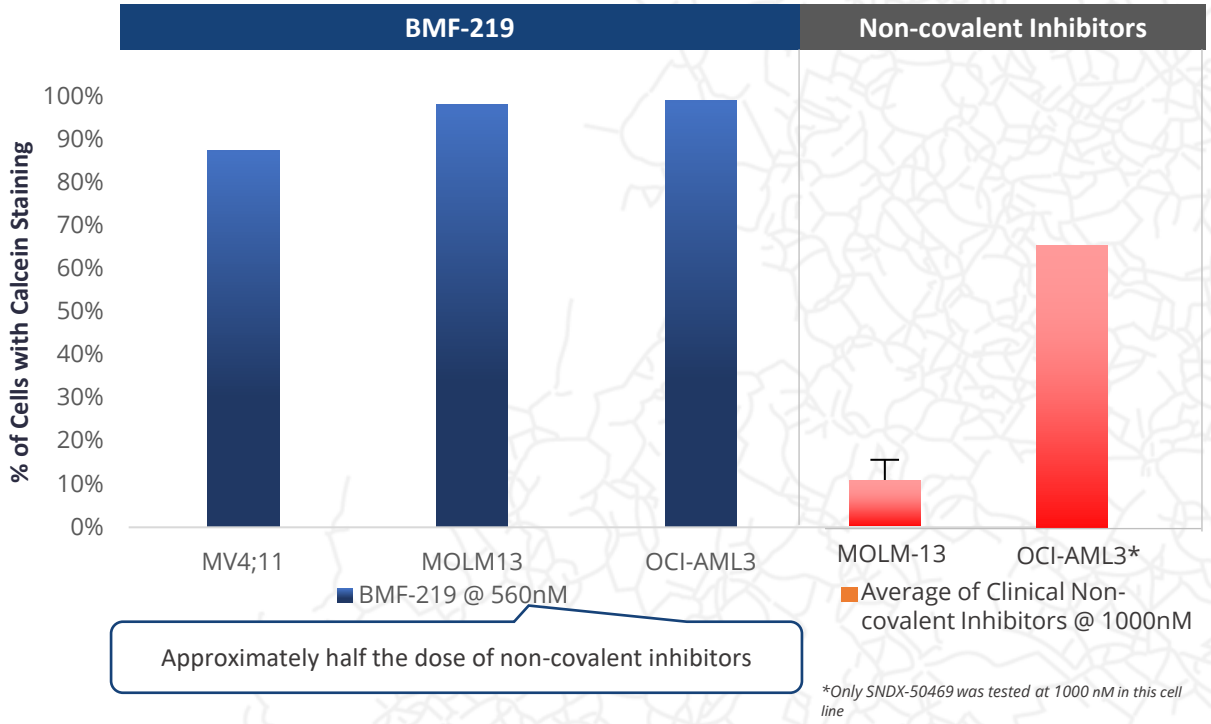


(Transcripts per Million is a measure of gene expression)

- 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

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

BMF-219 Superior Cell killing of the Target AML Cell Lines at Half the Dose vs Reversible Competitive Menin Inhibitors



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

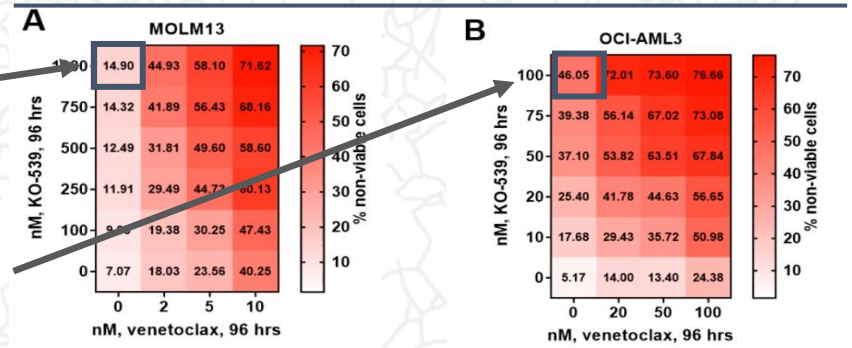
- BMF-219 **killed >90% of AML cells** in MLL-rearranged and NPM1 mutant cell lines at 4 days post-treatment
- Non-covalent menin inhibitors generally report significantly less cell killing of AML cell lines as a single agent

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

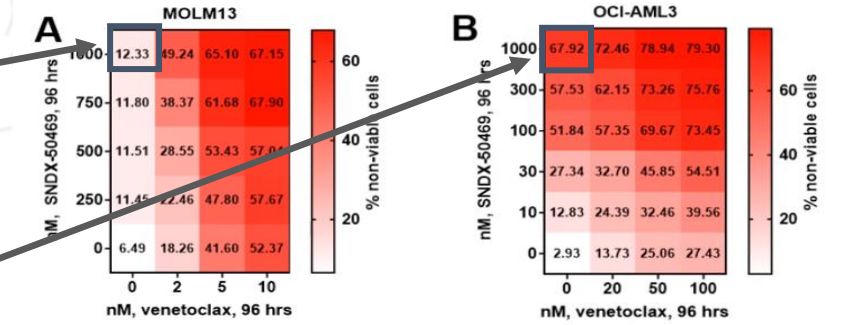
46% effective @ 100nM



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.

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

MYC Addicted and MYC Driven Tumors

Expansion into r/r diffuse large b cell lymphoma, r/r multiple myeloma and r/r chronic lymphocytic leukemia

RAS/RAF Driven Solid Tumors

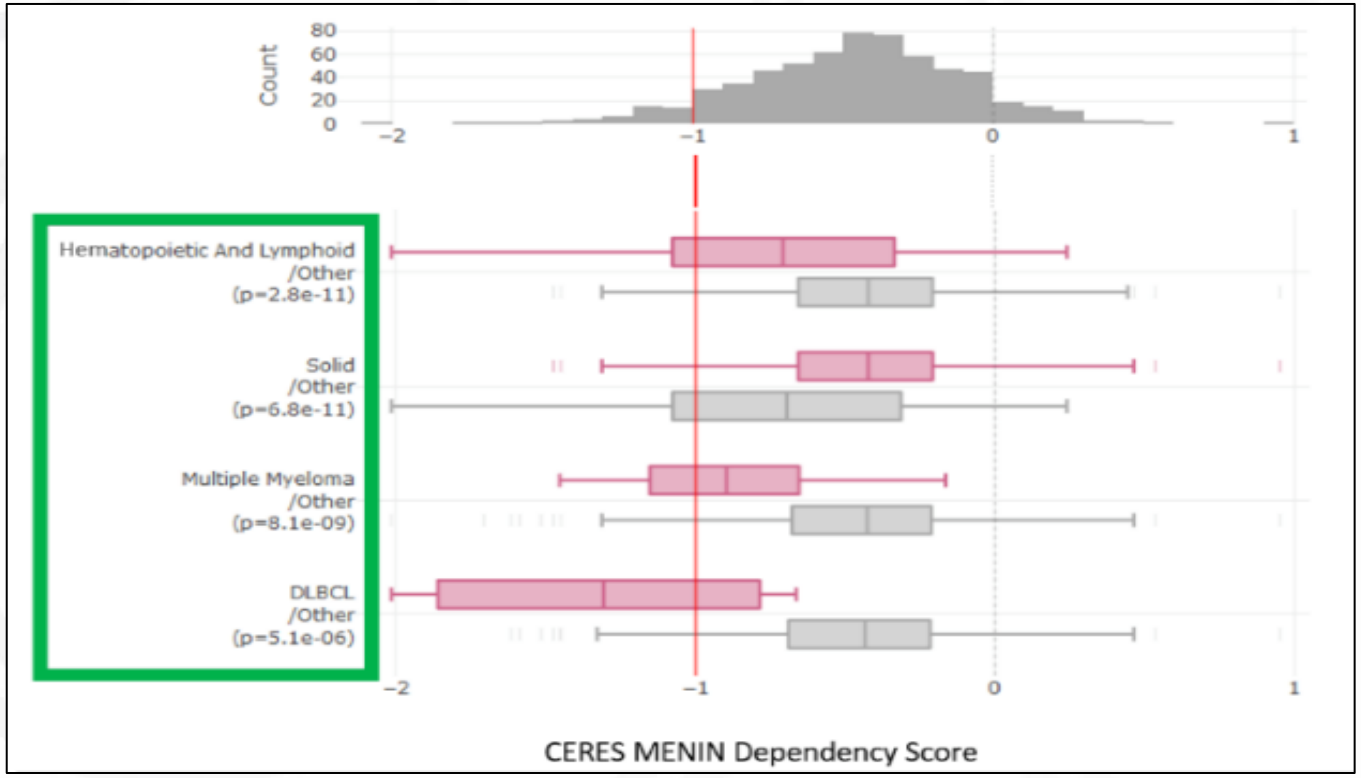
Further expansion into KRAS and RAS mutant colorectal, lung, and pancreatic cancer

Diabetes

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*)

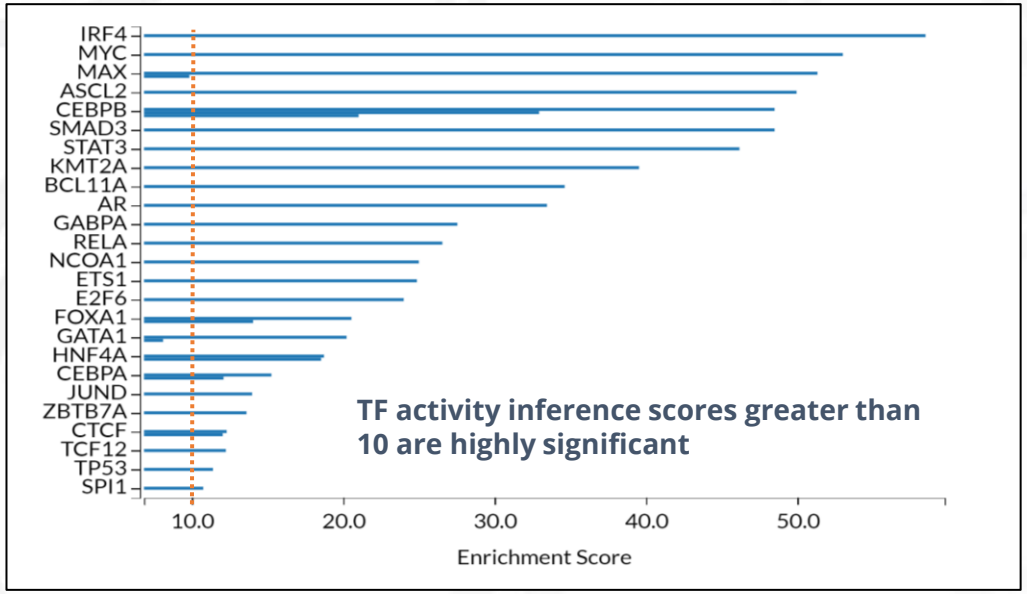


Note: CERES MENIN Dependency scores less than -1 in various tumor types imply that menin is considered essential for cell survival in those tumor types

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

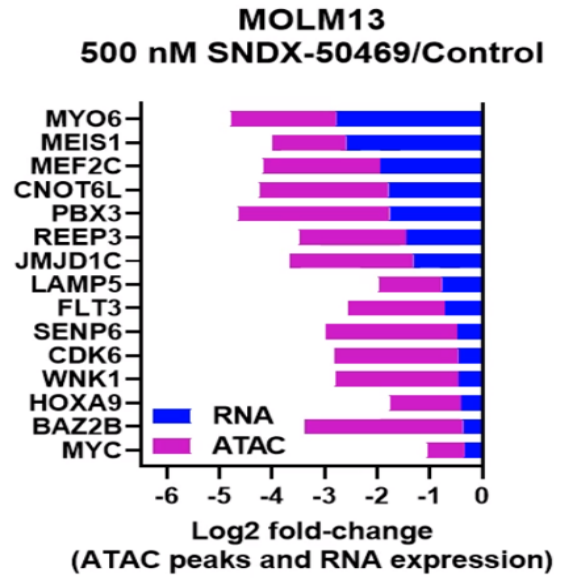
Covalent Menin Inhibitor – BMF-219



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

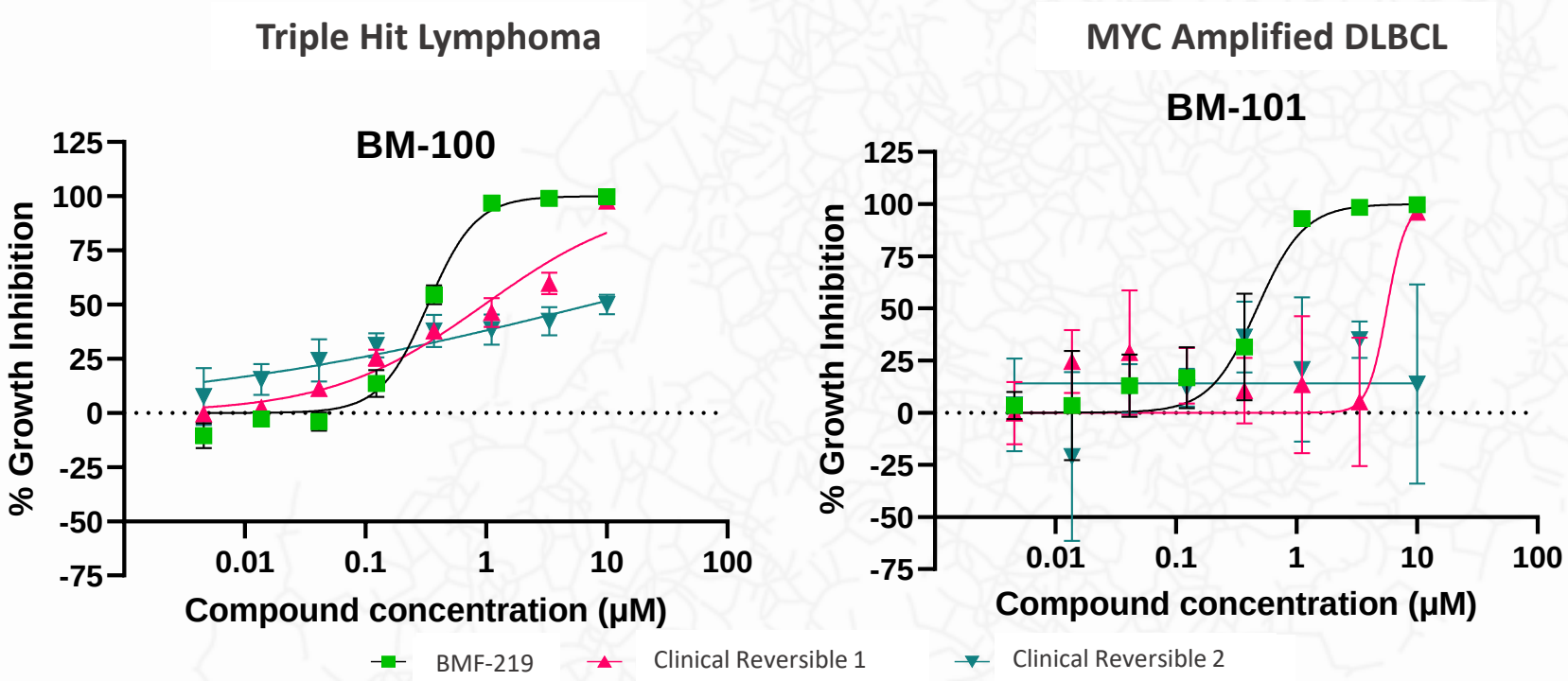
Non-Covalent Menin Inhibitor – SNDX-50469



***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



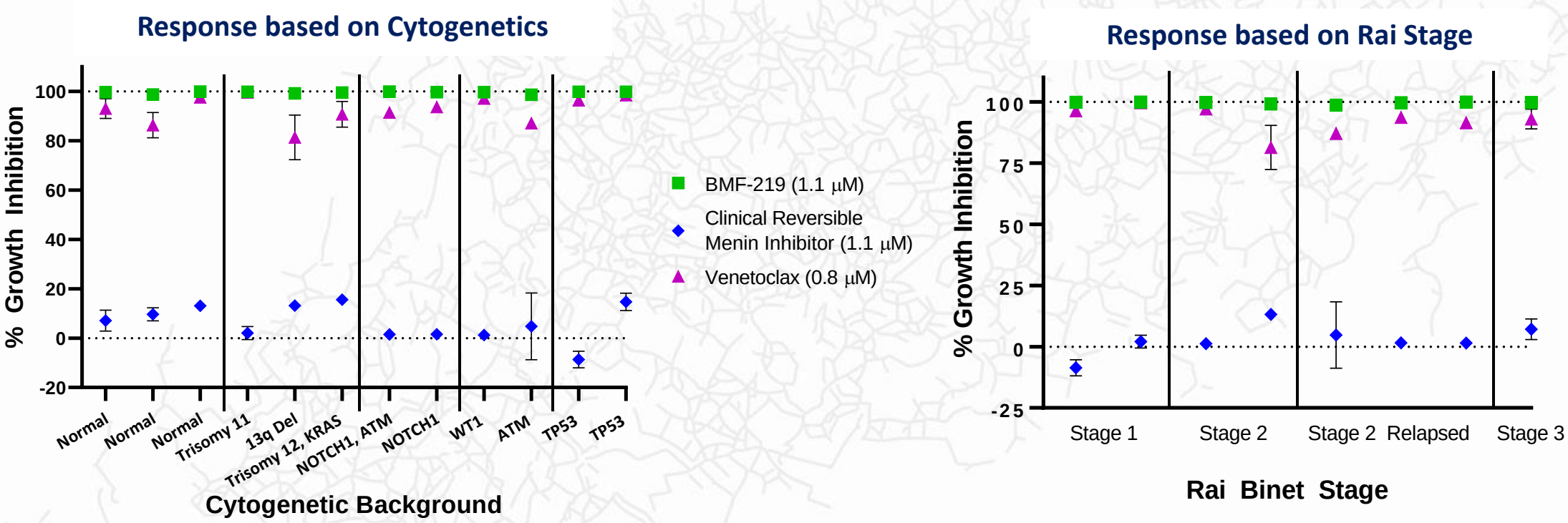
Treatment	Growth Inhibition IC_{50} (mM)	
	BM100	BM101
BMF-219	0.250	0.151
Clinical Reversible-1	0.969	5.63
Clinical Reversible-2	6.31	Max killing <30%

- 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

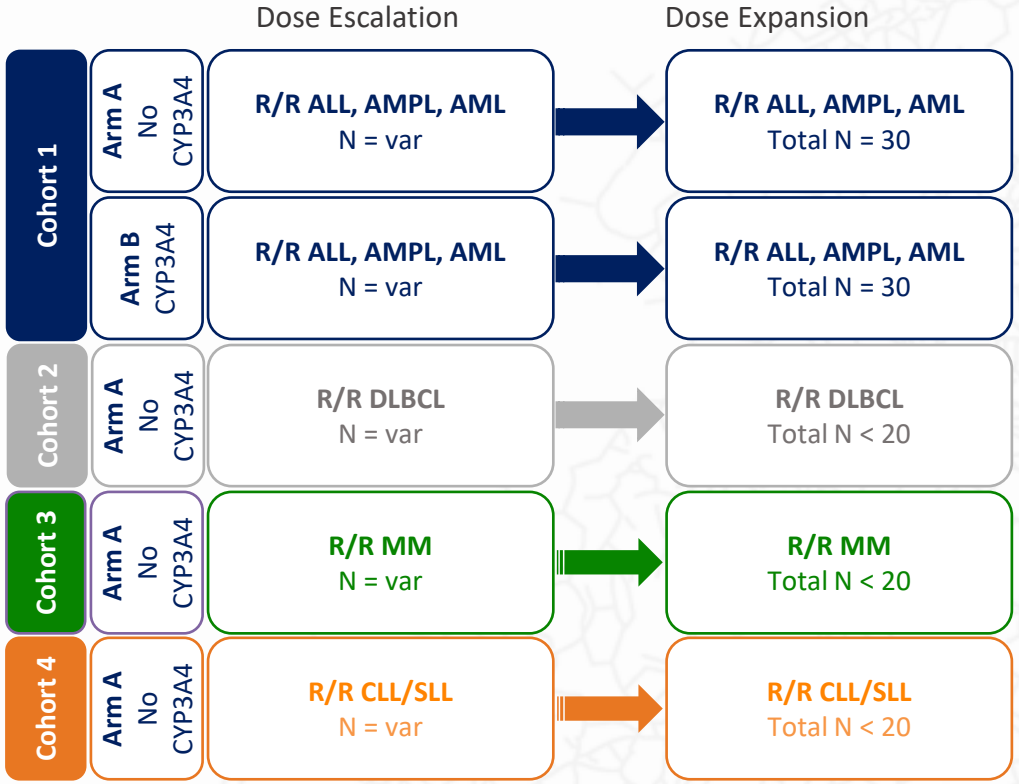
Growth inhibition of BMF-219 in CLL *ex vivo* models grouped by genetic background and Rai stage



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

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 MYC Driven Tumors

Expansion into r/r diffuse large b cell lymphoma, r/r multiple myeloma and r/r chronic lymphocytic leukemia

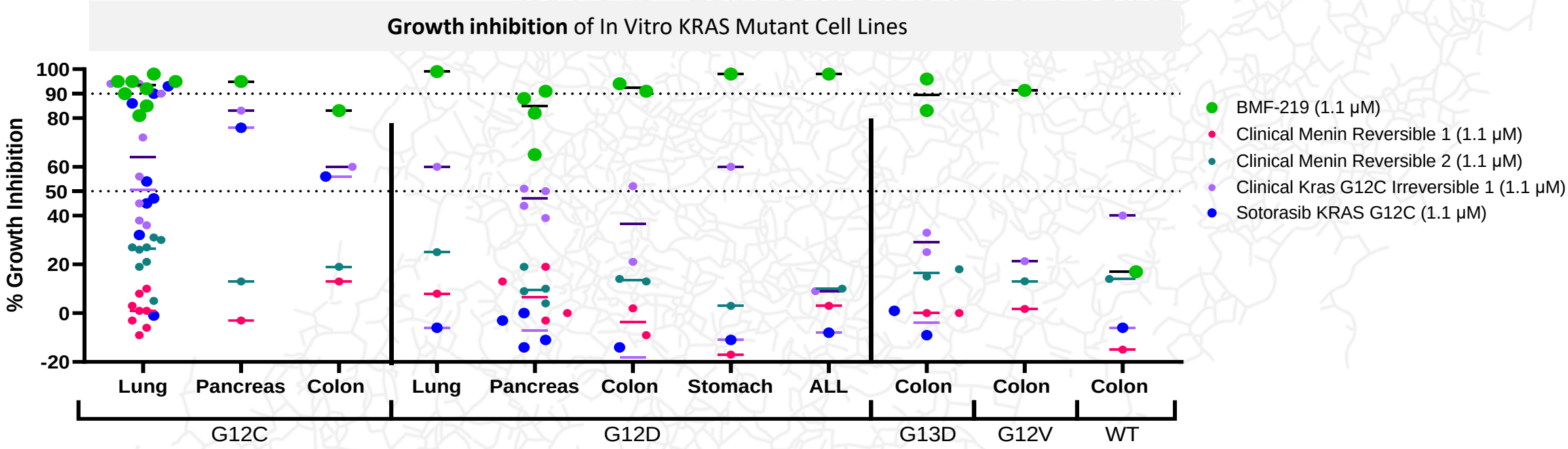
RAS/RAF Driven Solid Tumors

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

Diabetes

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

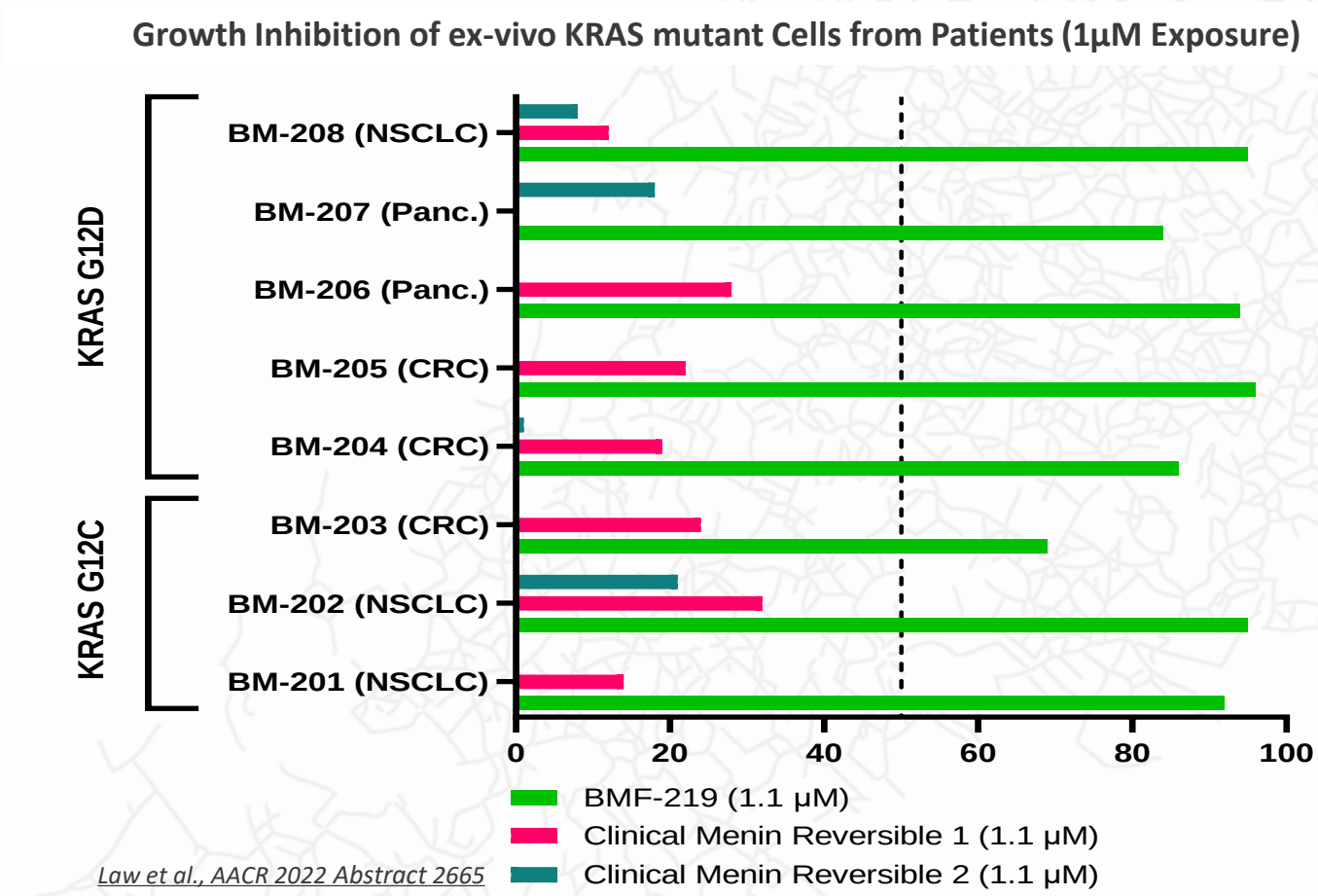


- Covalent menin inhibition by BMF-219 led to robust growth inhibition, comparable to clinical G12C inhibitors in G12C cell lines
- In non-G12C cell lines, BMF-219 achieved robust growth inhibition, higher than clinical KRAS G12C inhibitors
- Clinical reversible (non-covalent) inhibitors did not achieve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

Law et al., AACR 2022 Abstract 2665

First Development Success with BMF-219 in RAS/RAF Driven Solid Tumors

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

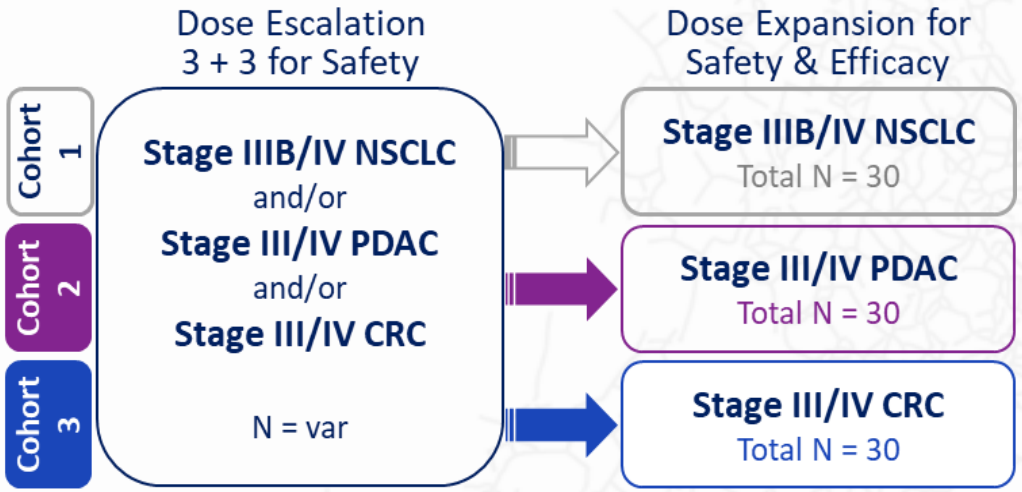


Law et al., AACR 2022 Abstract 2665

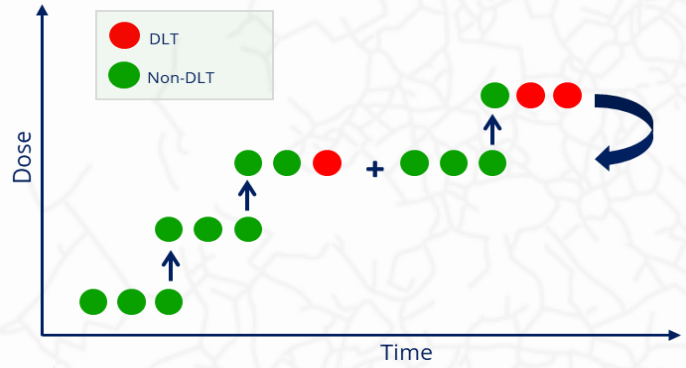
- 1.1µM exposure of BMF-219 produces robust growth inhibition in both G12C and G12D ex-vivo cell lines
- BMF-219 responses were superior to clinical reversible (non-covalent) inhibitors with respect to cell growth inhibition at the concentrations tested

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

- 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 / 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

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 MYC Driven Tumors

Expansion into r/r diffuse large b cell lymphoma, r/r multiple myeloma and r/r chronic lymphocytic leukemia

RAS/RAF Driven Solid Tumors

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

Diabetes

Pathway and clinical validation of covalent menin inhibition

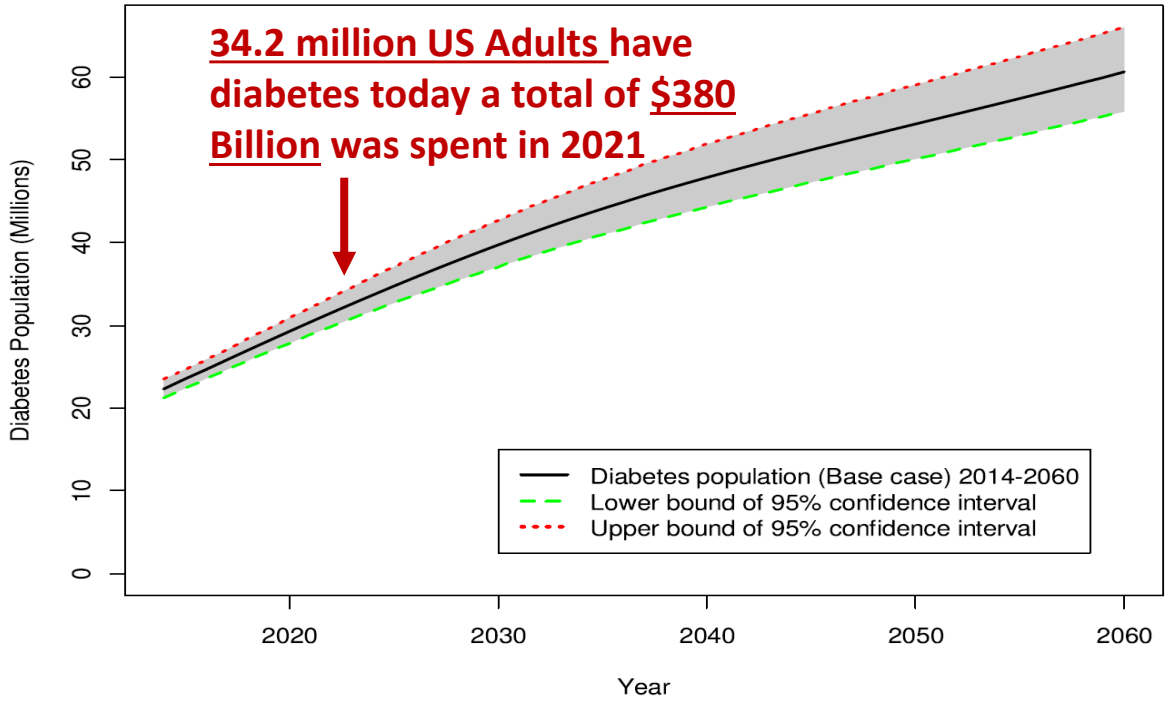
Diabetes – the biggest Epidemic of the 21st century

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.

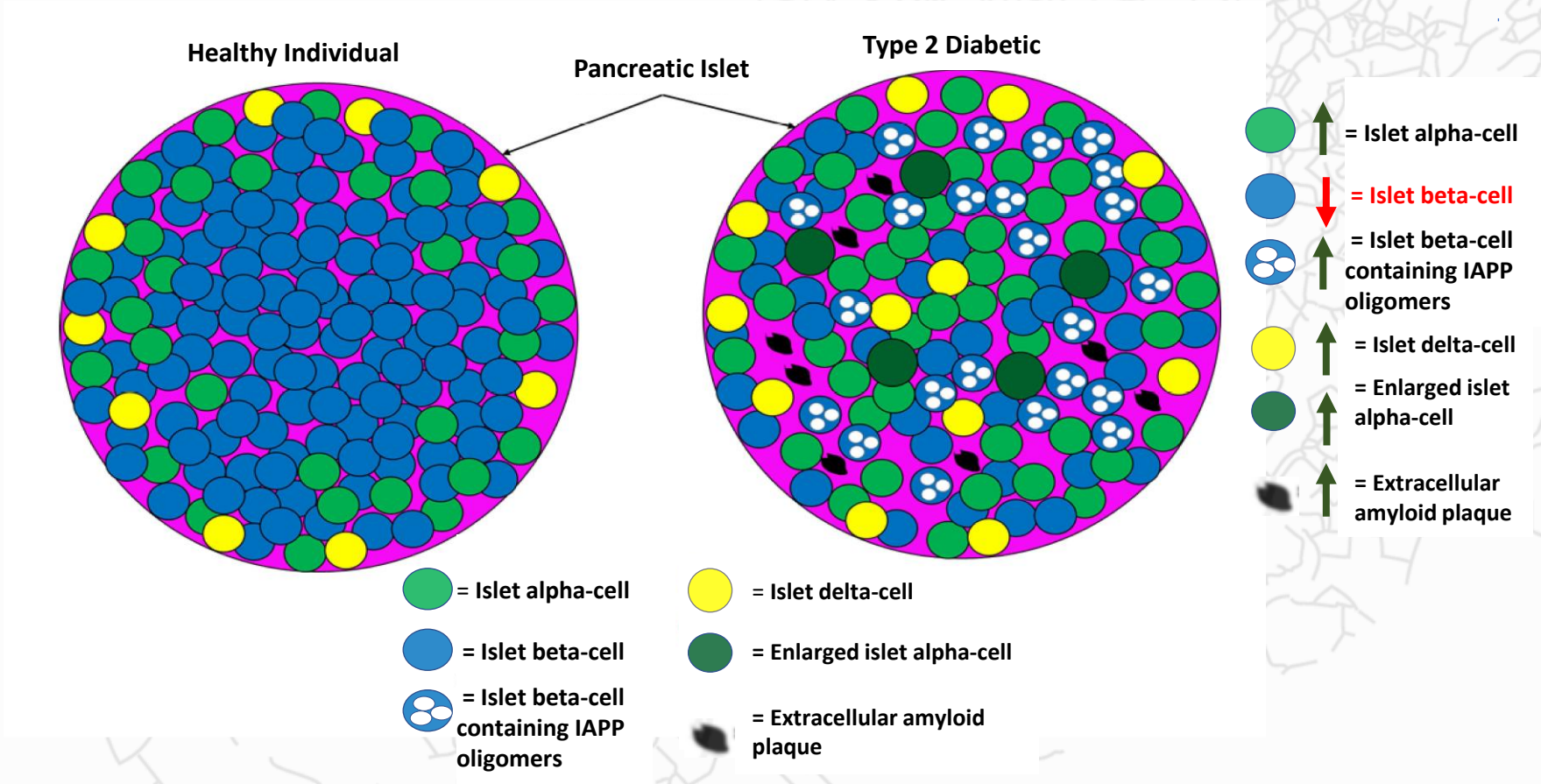


- According to the CDC, worldwide 463 million adults have diabetes. In the United States alone, 34.2 million adults have diabetes, 10.5% of the population. 96 million adults (more than 1 in 3) in the US have pre-diabetes.

= ***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

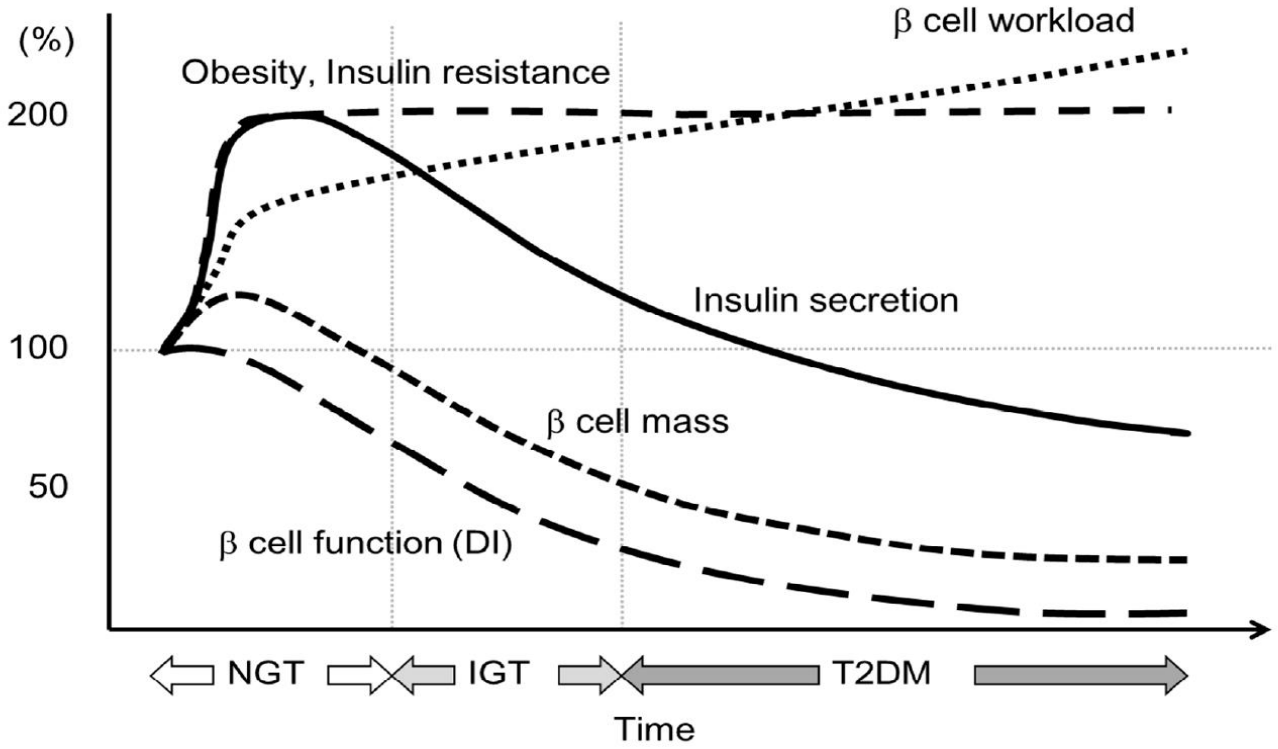
Types 2 Diabetes Progression: Beta Cell Loss



- 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.

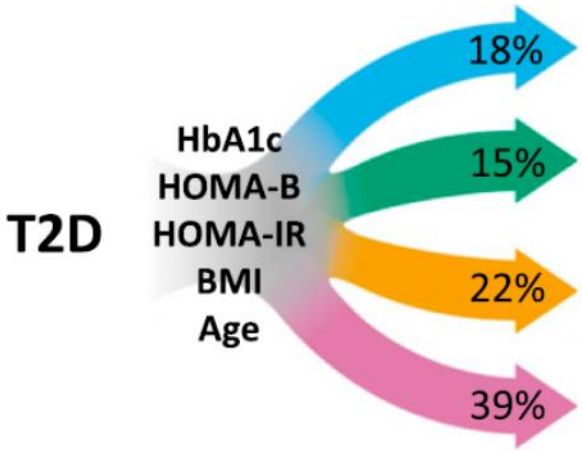
Type 1 and Type 2 Diabetes results in Beta Cell Loss and Reduction in Beta Cell Mass

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

Diabetes – the biggest Epidemic of the 21st century

Diabetes Patient Segments

Pre-Diabetes



	Patient Population	Proposed BMF-219 MOA
Initial Decline in Glycemic Control Increasing HbA1c, Increasing Insulin Resistance Decreasing beta cell numbers and function	90M	Beta Cell Preservation Beta Cell Growth
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

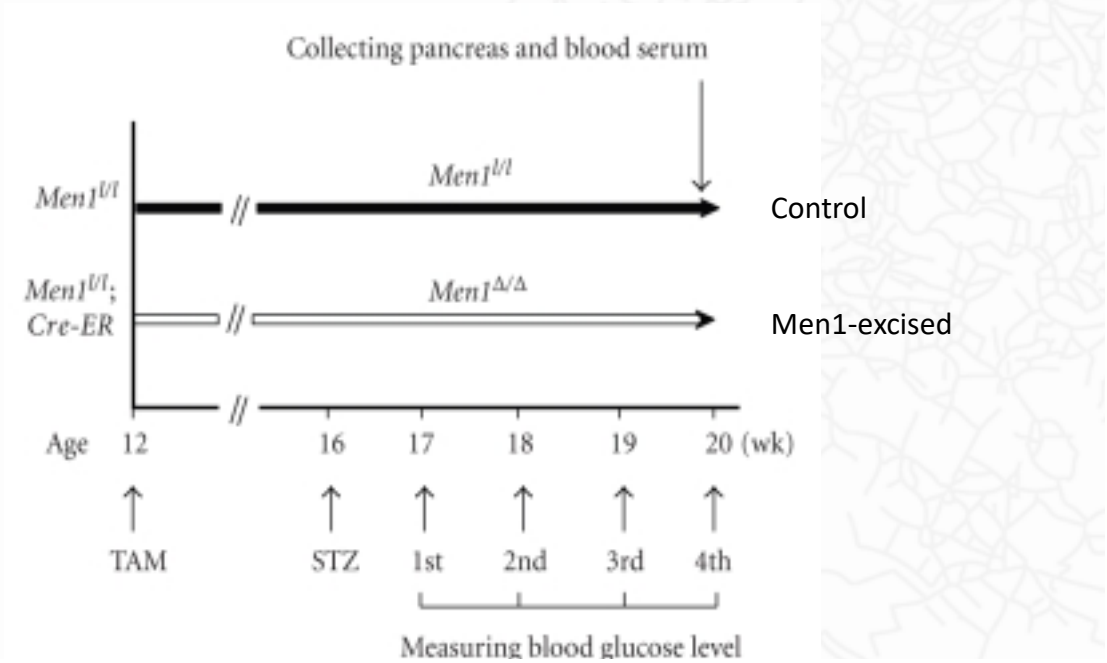
Oral Treatment for the Regeneration, Preservation, and Reactivation of Beta Cells

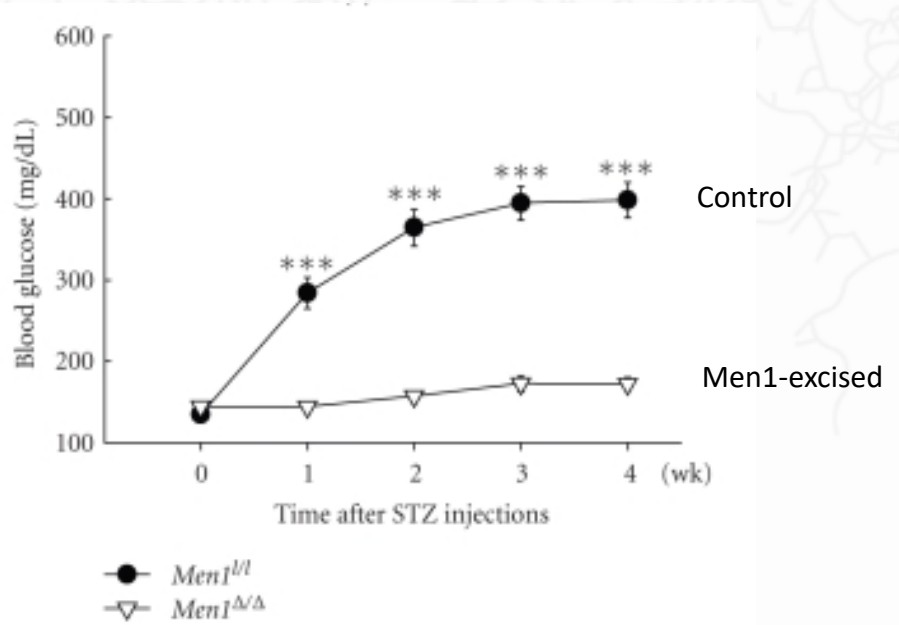
- **Disease modification** as the first treatment to potentially provide a functional cure of diabetes via restoration of beta cell homeostasis
- **Synergistic with GLP-1** based treatments while potentially insulin sparing. Potential utility in:
  - Prevention of T2D (90M prediabetic patients in the 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

First Development Success with BMF-219 in Type II Diabetes

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**

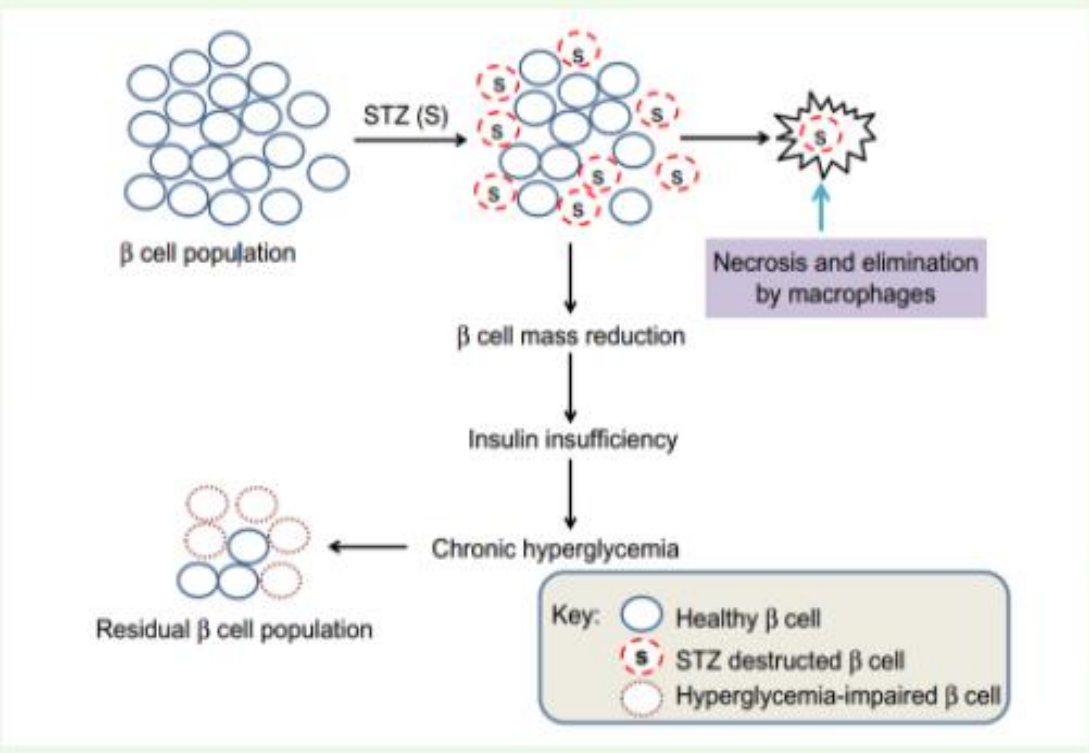
Sources: Yang et al. (2010) Deletion of theMen1Gene Prevents Streptozotocin-Induced Hyperglycemia in Mice. Experimental Diabetes Research, 2010, 1–11. doi:10.1155/2010/876701

First Development Success with BMF-219 in Type II Diabetes

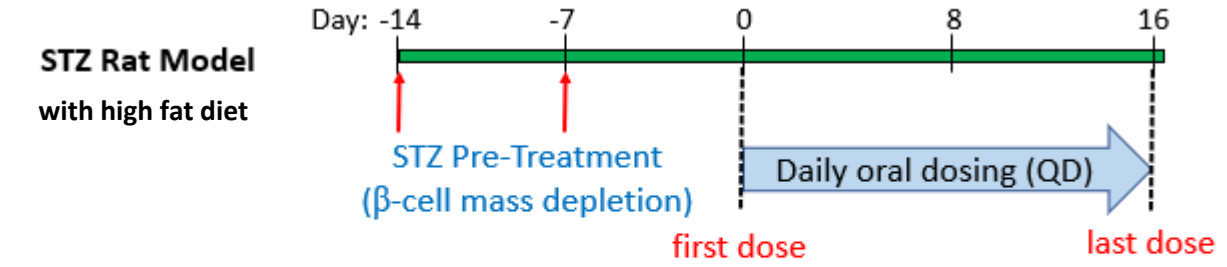
STZ Rat Model Study Design

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

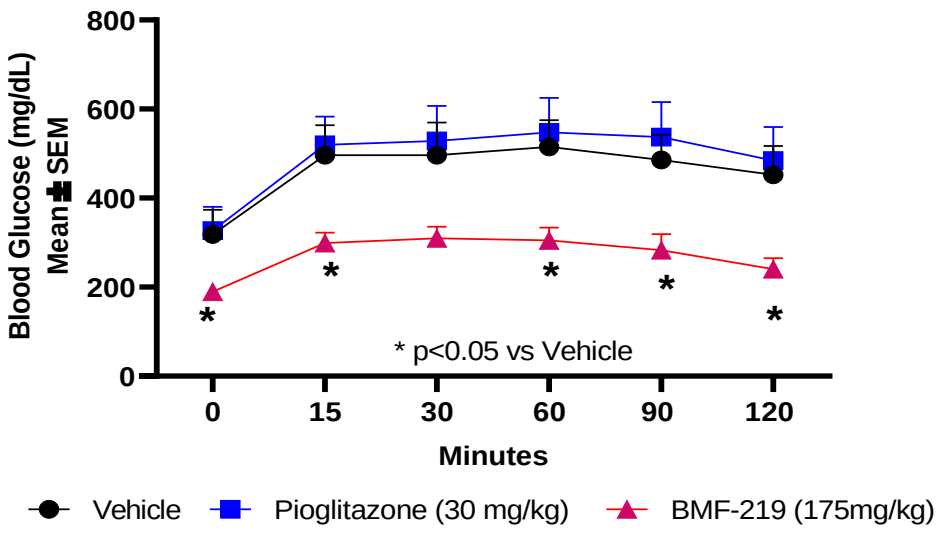
STZ treatment typically results in ~50% Beta Cell Loss

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

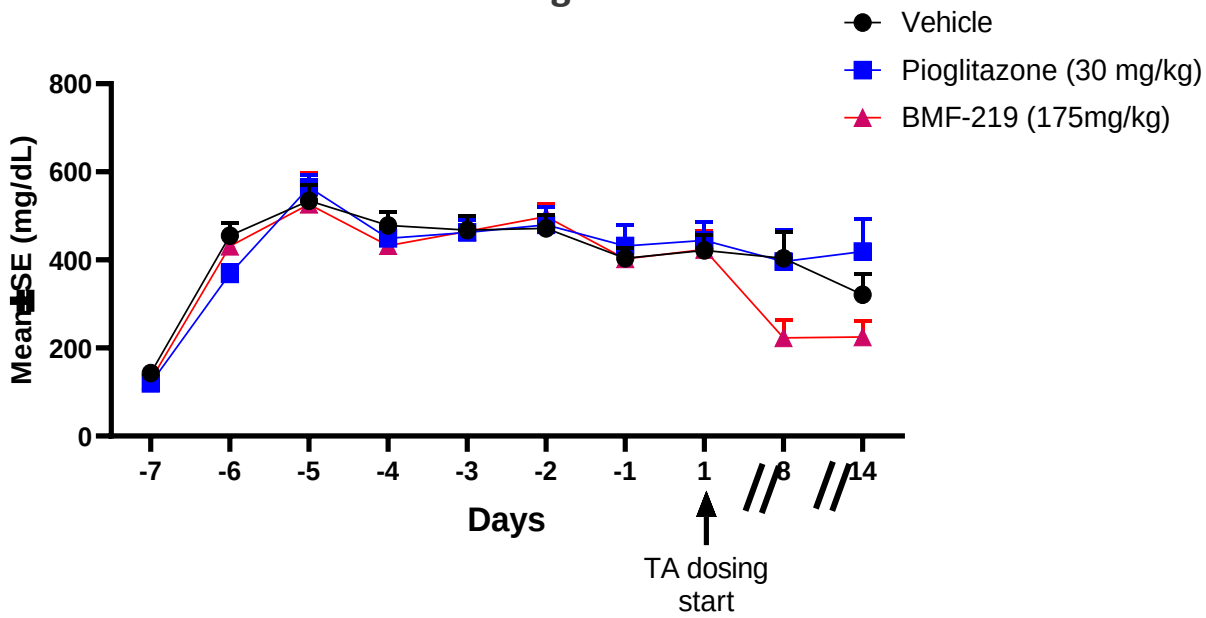
Oral Glucose Tolerance Test (Day 17)



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

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

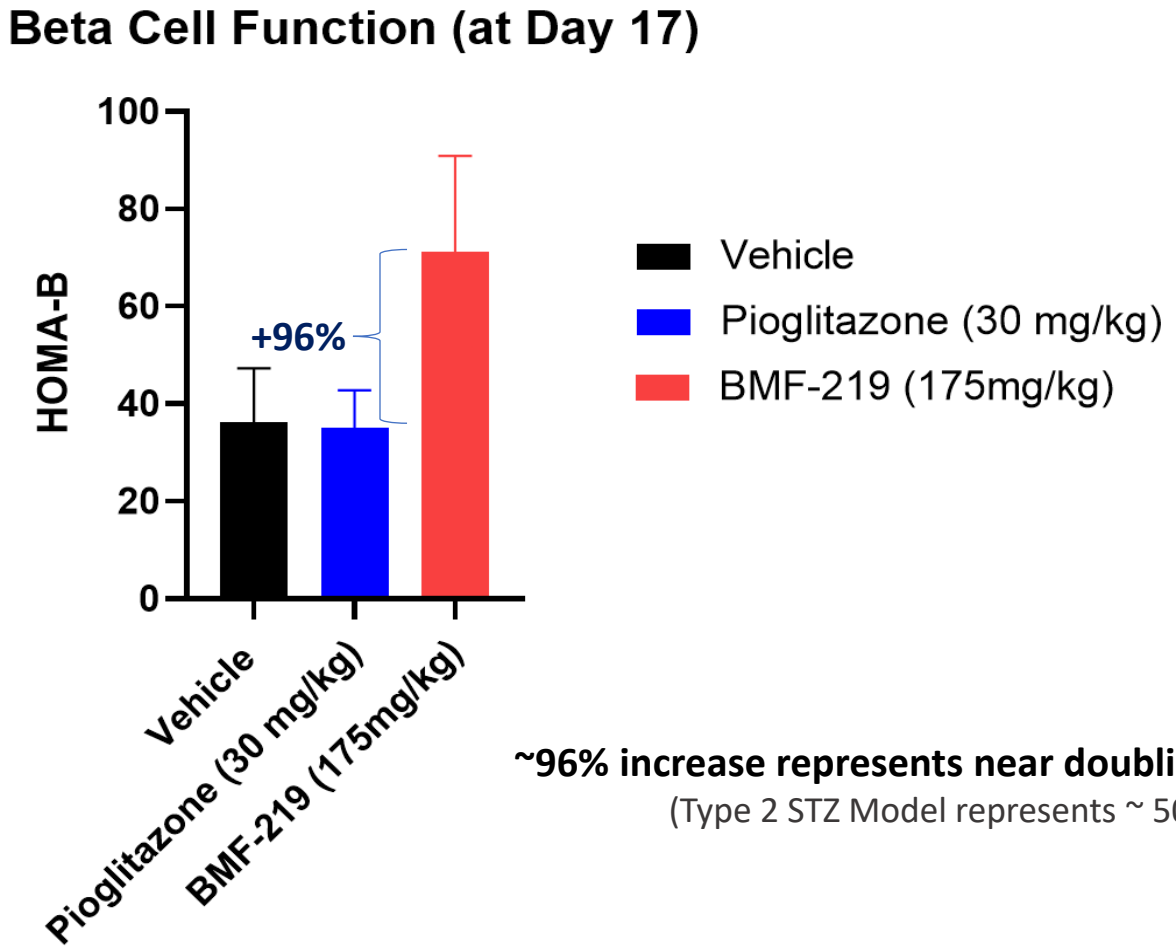
Non-Fasting Glucose



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

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.

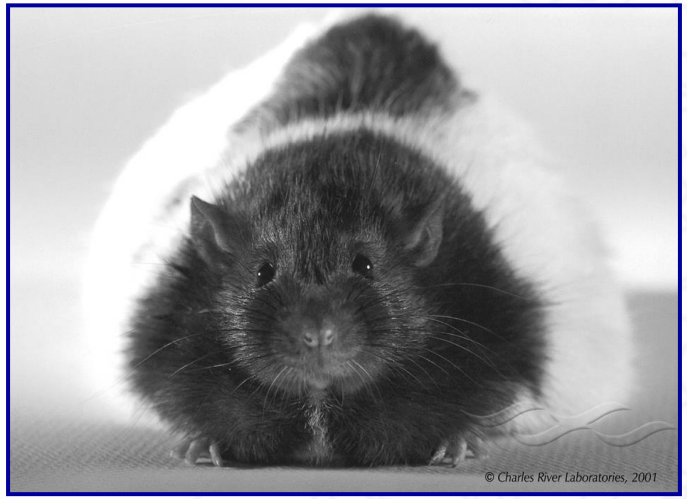
~96% increase represents near doubling of beta cell function

(Type 2 STZ Model represents ~ 50% Beta Cell Destruction)

First Development Success with BMF-219 in Type II Diabetes

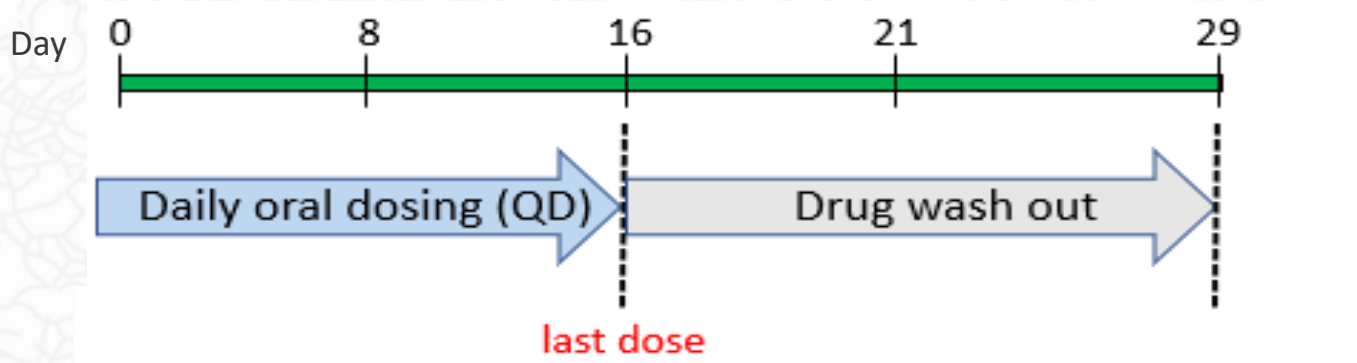
Zucker Diabetic Fatty Rat - a Model of Insulin Resistance

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

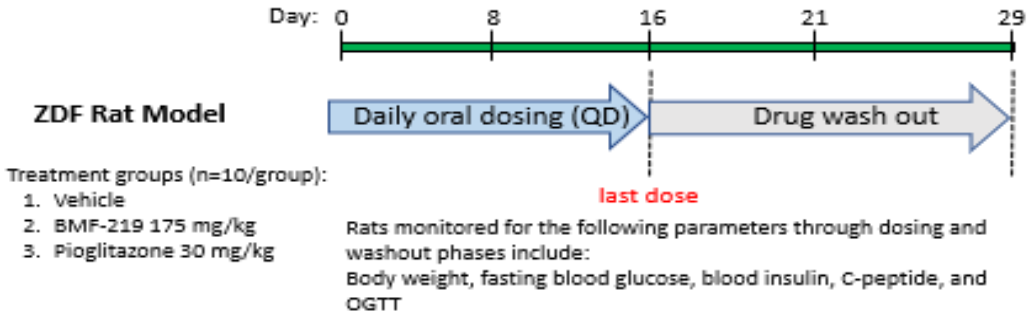
Treatment groups (n = 10/group):

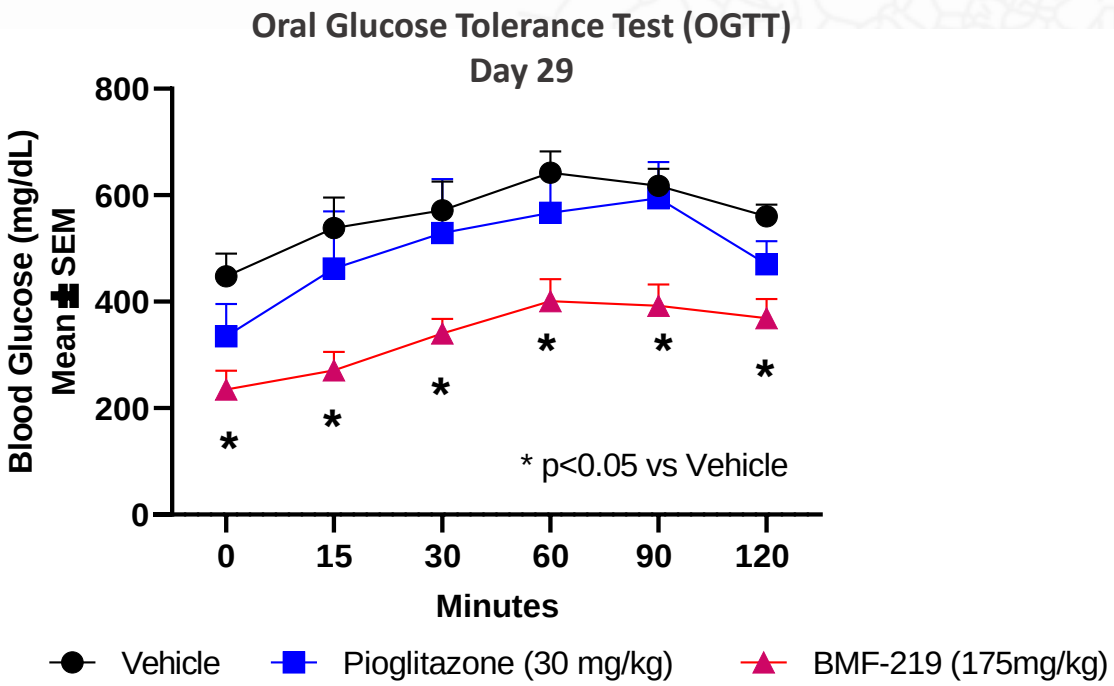
1. Vehicle
2. BMF-219 175 mg/kg
3. Pioglitazone 30 m g/kg

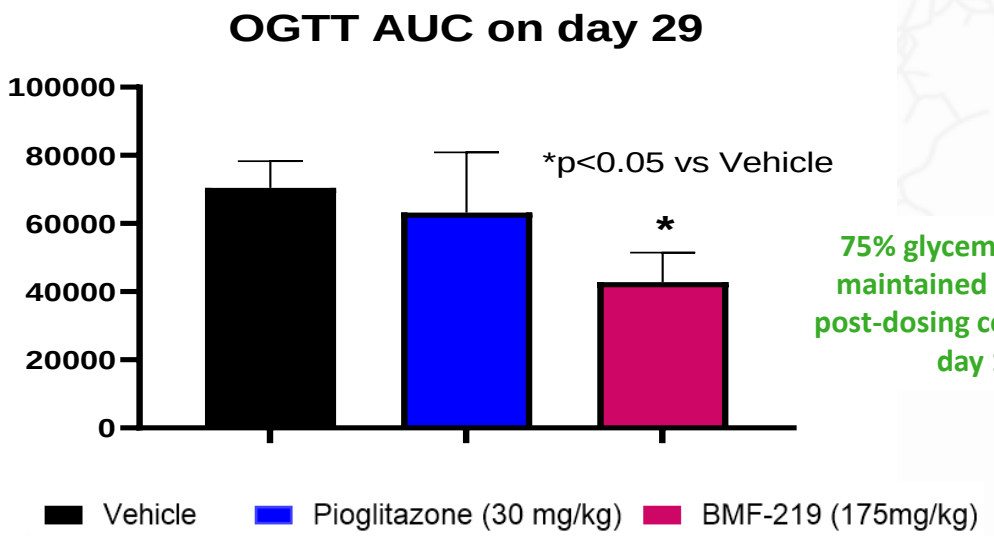
First Development Success with BMF-219 in Type II Diabetes

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

After 2-week Drug Washout





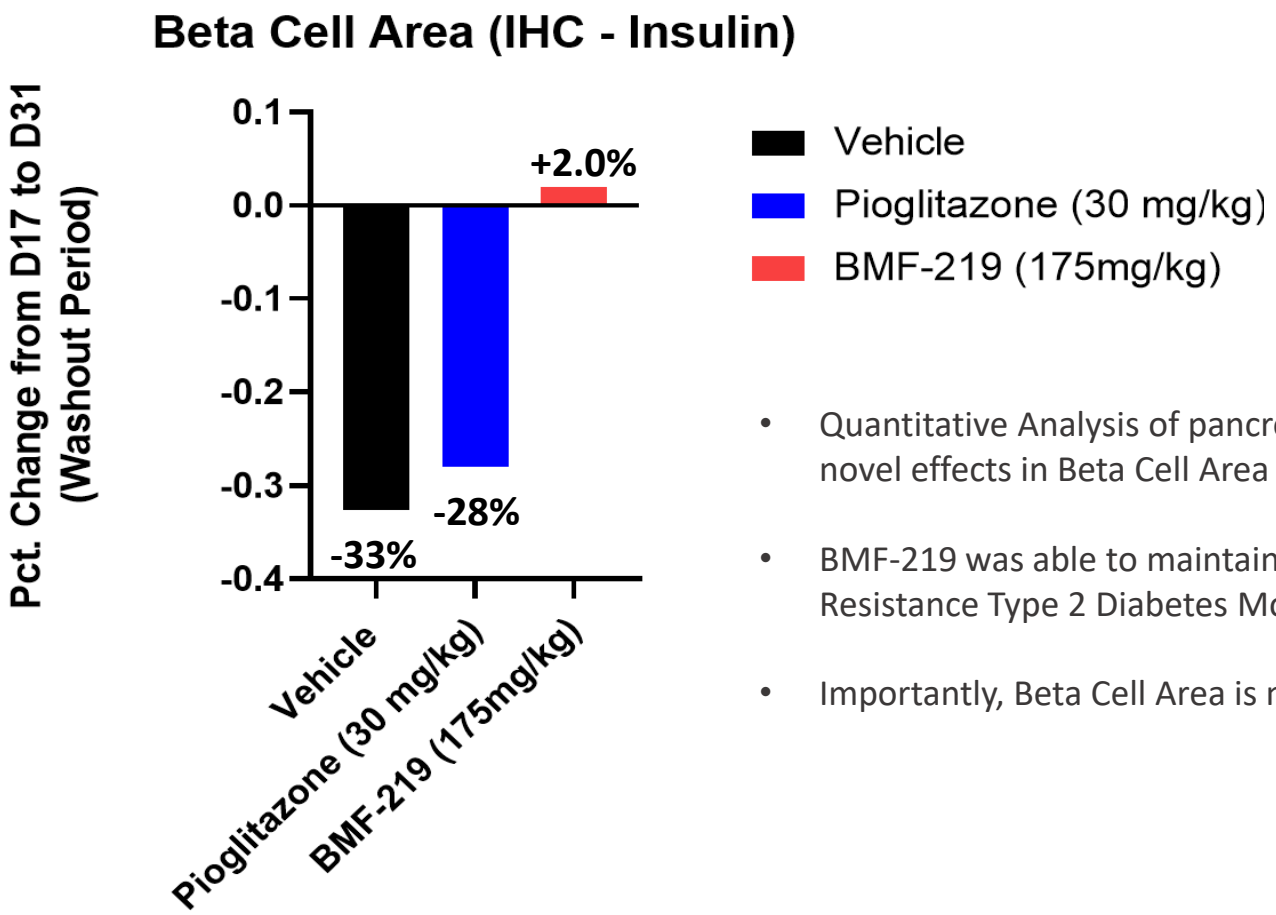


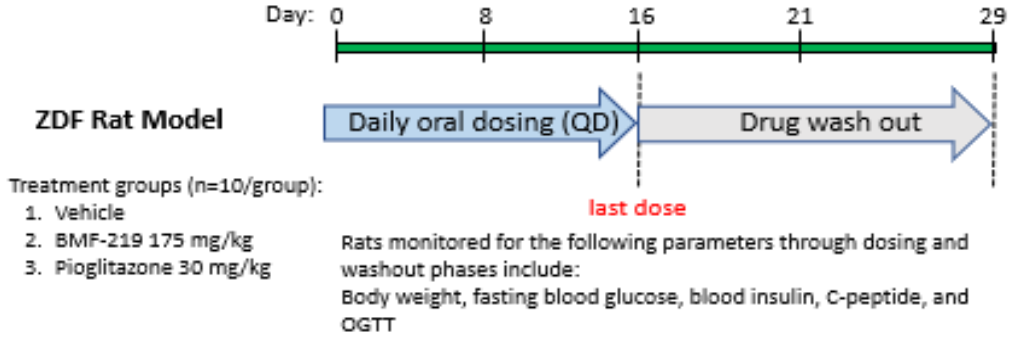
75% glycemic control maintained on day 29 post-dosing compared to day 15

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

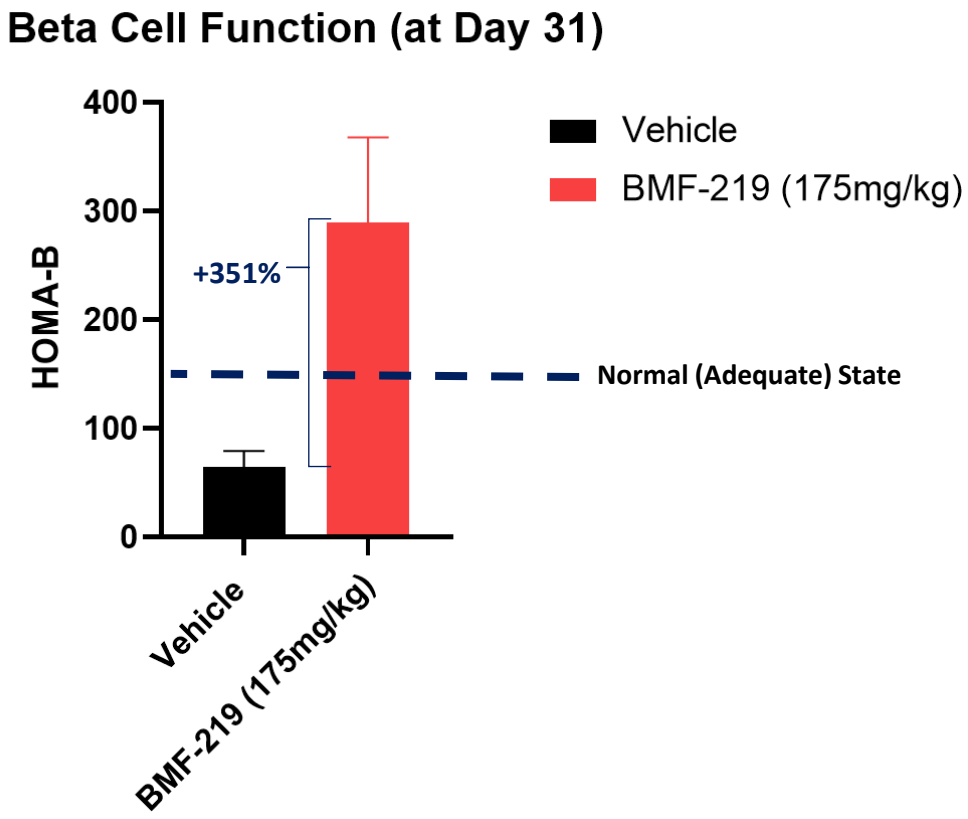




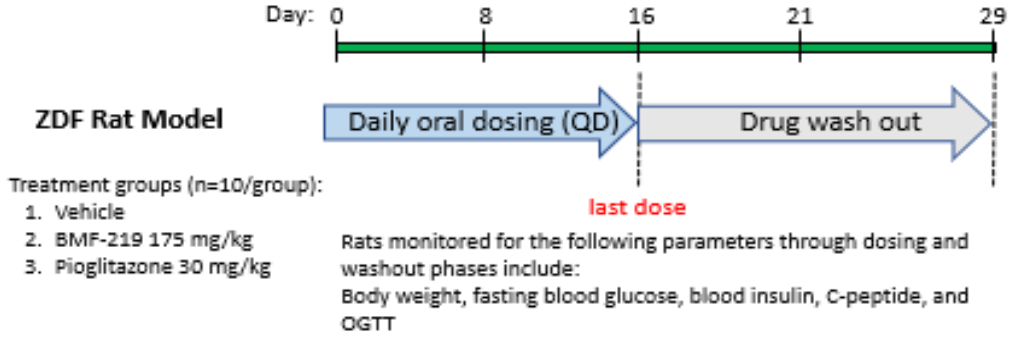
- Quantitative Analysis of pancreatic islet tissue cross sections shows BMF-219 treated animals show novel effects in Beta Cell Area growth and maintenance.
- BMF-219 was able to maintain Beta Cell function and prevent Beta Cell Area Loss in an Insulin Resistance Type 2 Diabetes Model.
- Importantly,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

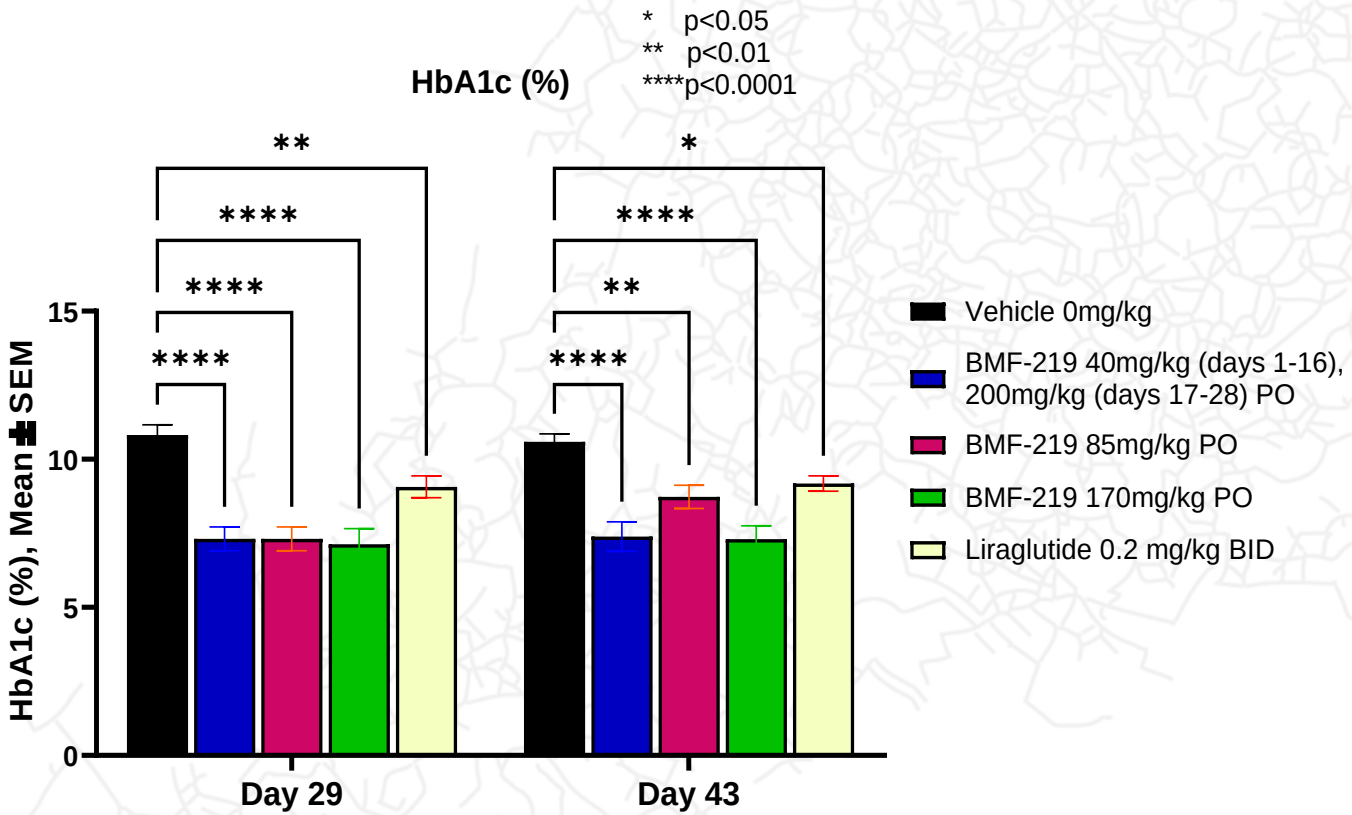


- HOMA-Beta, a measurement of Beta Cell Function, was analyzed using 4-hr fasting glucose and insulin levels in animal plasma.
- BMF-219 displayed a significant level of Beta Cell function compared to vehicle at Day 31 in an Insulin Resistance Type 2 Diabetes Model.
- This data supports the observed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

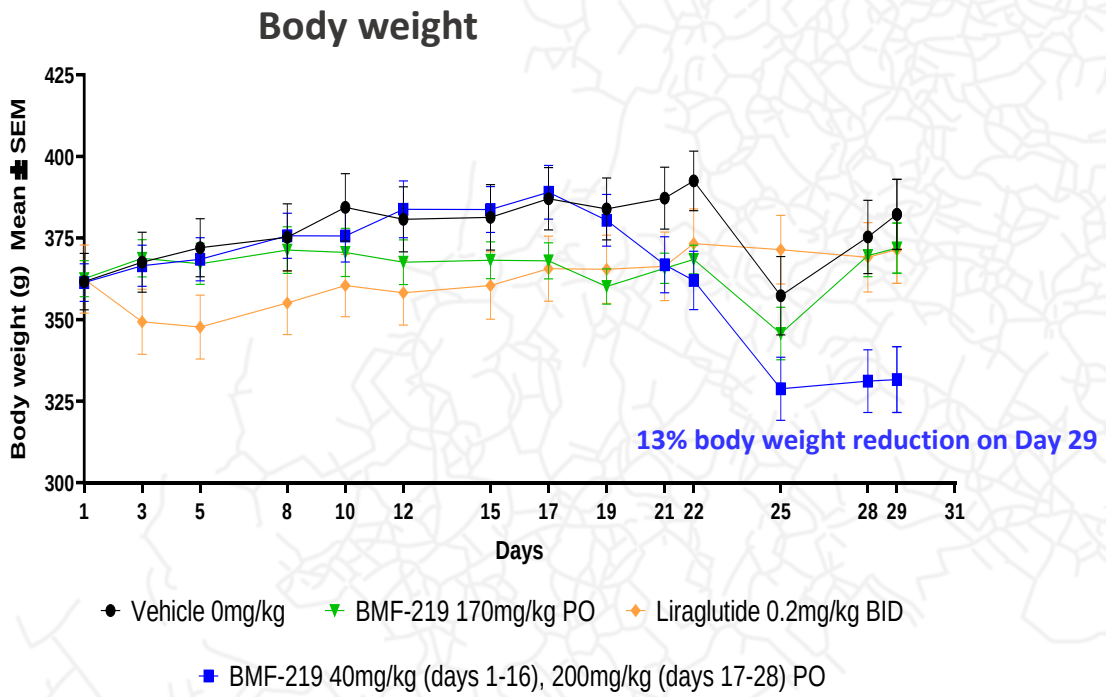
BMF-219 treated group demonstrated significant weight reduction starting at day 25

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

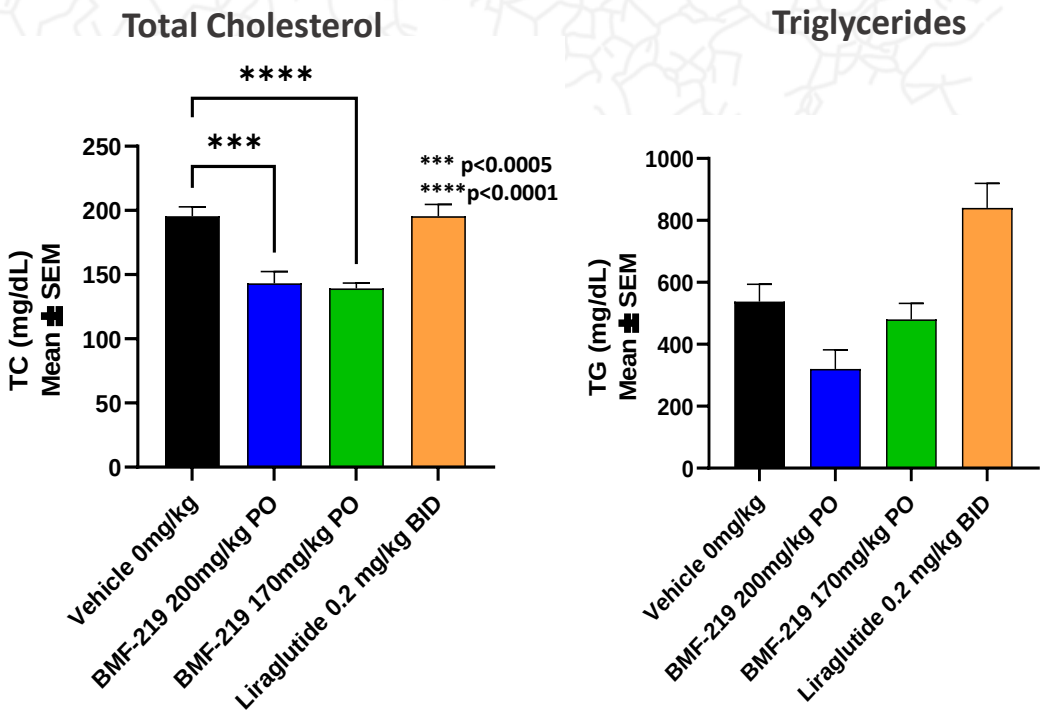
First Development Success with BMF-219 in Type II Diabetes

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:

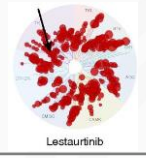
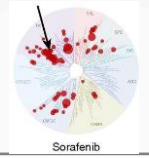
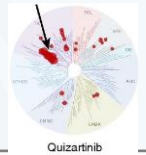
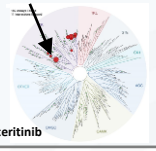
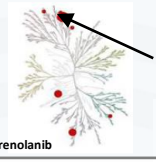
- Evaluate PK of BMF-219
- Evaluate the effect on BMF-219 on glycemic parameters (HbA1C, PG) and few additional parameters using OGTT, 7-day CGM
- Evaluate the changes in beta cell function
- Evaluate impact on lipid parameters, body weight etc.

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	 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

BMF-500 Highly Effective FLT3 Inhibitor Against Resistance Mutations

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

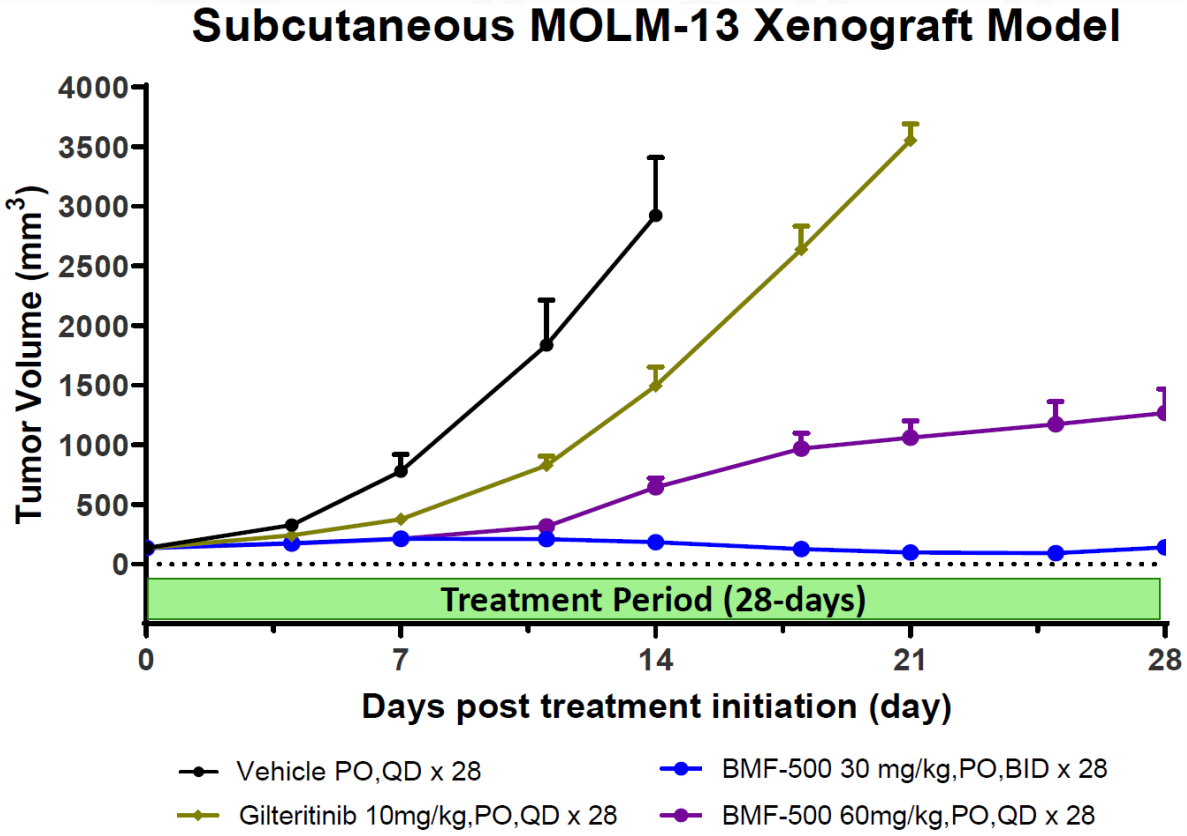
Cmpd ID	FLT3 WT	FLT3 (D835H)	FLT3 (D835V)	FLT3 (D835Y)
BMF-500	0.31	0.18	0.22	0.25
Gilteritinib	23.4	1.45	1.1	1.4

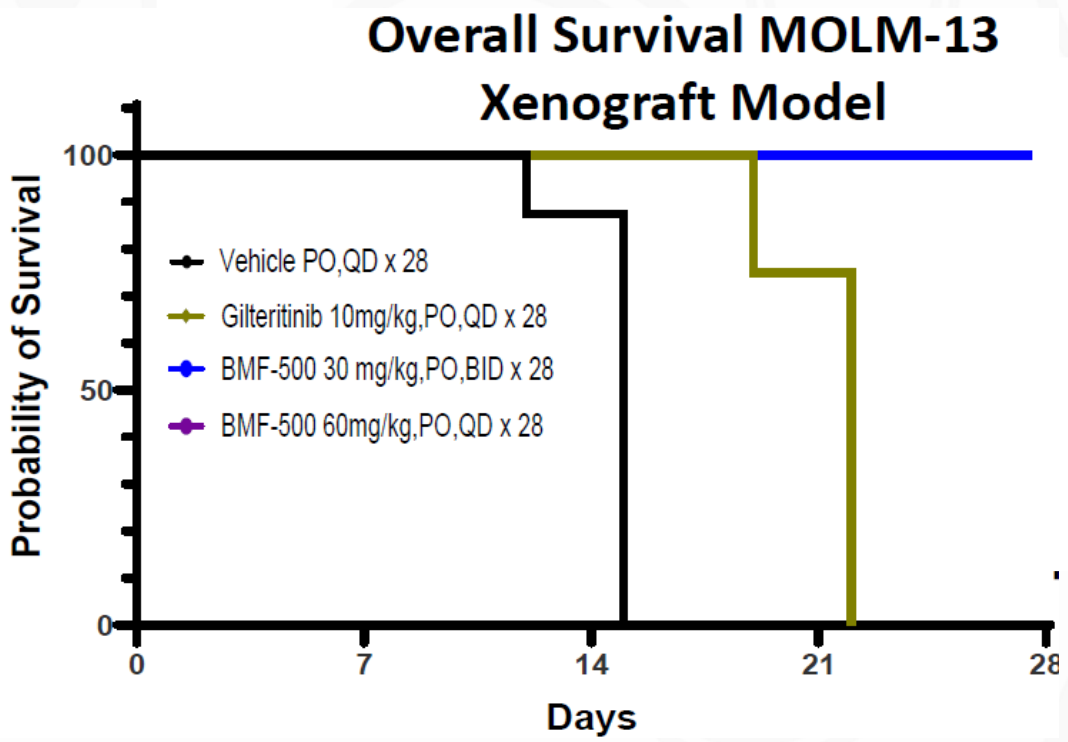
FLT3 Inhibitor Resistance Mutations Coverage, IC_{50} (nM)

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

Second Development Success with BMF-500

BMF-500 Highly Potent and Durable FLT3 Inhibitor

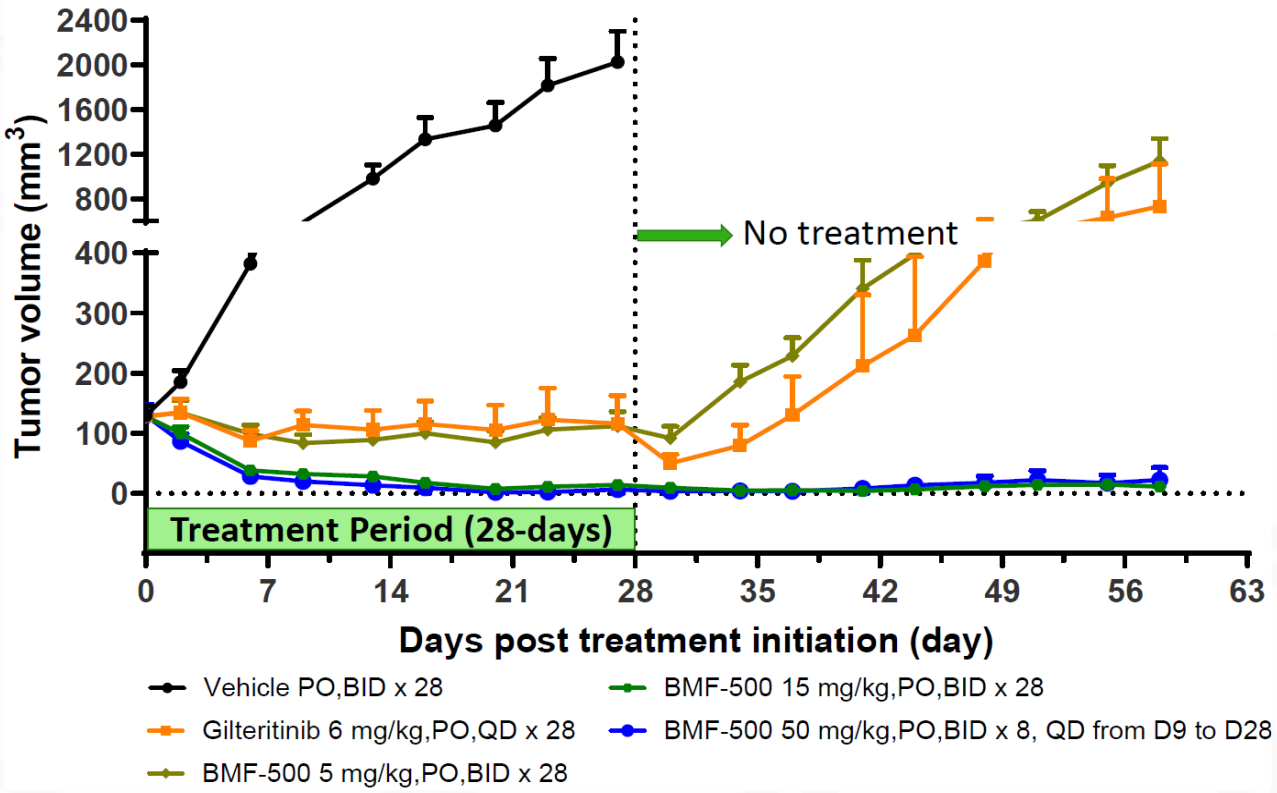




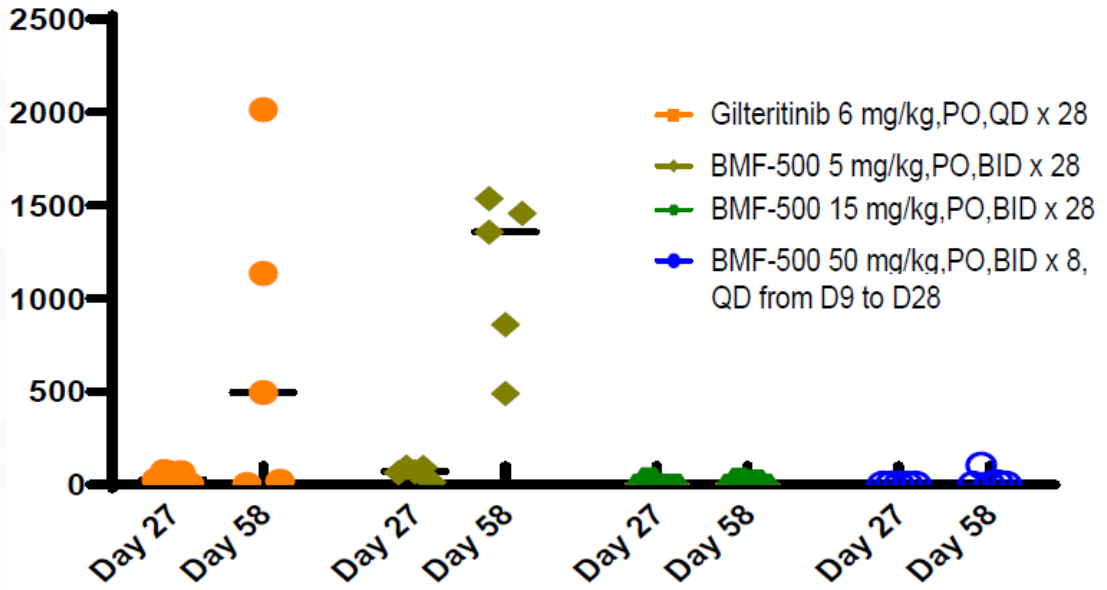
Second Development Success with BMF-500

BMF-500: Highly Potent and Durable FLT3 Inhibitor

Subcutaneous MV-4-11 Xenograft Model



Individual Tumor Volume MV-4-11 Xenograft Model



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

- ☑ 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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