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BMF-219: An Oral Menin Inhibitor in Clinical Development as a Short-Term Treatment to Address the Root Cause of Diabetes, Beta-Cell Dysfunction

December 7, 2023

Thomas Butler MS, MBA
Chief Executive Officer and Chairman of the Board
Biomea Fusion

Introduction to Biomea Fusion and the Discovery of the Covalent Menin Inhibitor, BMF-219

Priyanka Somanath PhD
Associate Director
Biomea Fusion

BMF-219 in Animal Models of Diabetes: Durable Improvement in Beta-cell Function and Glycemic Control

Rohit Kulkarni MD, PhD
Margaret A Congleton Professor Section Head; Professor of Medicine, Harvard Medical School

Menin Inhibition: What May Explain the Effects of BMF-219 on Beta-cell Function and Glycemic Control

Juan P Frias MD
Chief Medical Officer
Biomea Fusion

BMF-219 in People with T2D: Select Results of a Multiple Ascending Dose Study

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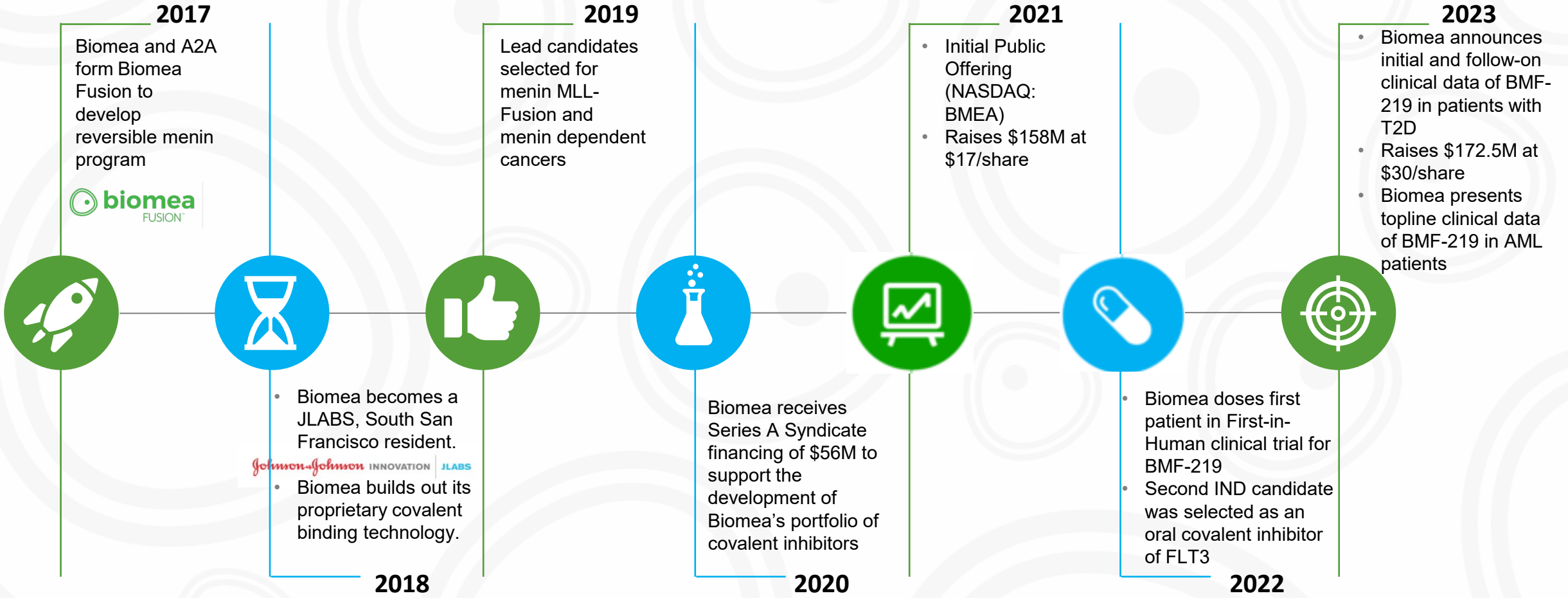
Agenda

- **Company Background**
- **Development Principles**
- **Benefit of Covalency**
- **BMF-219: Selectivity and Specificity of Covalent menin inhibition**
  - Target Engagement (Kd)
  - Peptide Mapping
  - Treatment Analysis – ZDF & STZ Animal Models
  - Gene Expression – Human Islets
  - Proliferation Data – Human Islets
- **Unique Profile: Why BMF-219 is uniquely positioned for targeting diabetes**

Biomea Fusion - A Biopharma Company Focused on Covalent Medicine since 2017



Aiming to Develop Some of the Most Impactful Medicines of Our Time

A Long History of Developing Successful Drugs - Together

Thomas Butler
Chairman & CEO

biomea FUSION
Co-Founder

The FUSION™ SYSTEM
BMF-219*
Co-Inventor

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

Veklury® remdesivir 100 MG FOR INJECTION
Co-Inventor

Ramses Erdtmann
President & COO

biomea FUSION
Co-Founder

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

Juan Frías, M.D.
Chief Medical Officer

once weekly mounjaro® (tirzepatide) injection 0.5 mL
2.5 mg | 5 mg | 7.5 mg

farxiga® (dapagliflozin) 5 mg & 10 mg tablets

Jardiance® (empagliflozin) tablets 10 mg/25 mg

once weekly trulicity® (dulaglutide) injection 0.5 mL
0.75 mg | 1.5 mg | 3.0 mg | 4.5 mg

ONCE-WEEKLY wegovy® semaglutide injection 2.4 mg

Byetta® (exenatide) injection

Invokana® (canagliflozin) tablets

OZEMPIC® semaglutide injection 0.5 mg, 1 mg, 2 mg

Januvia® sitagliptin

Naomi Cretcher
Chief of People

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

Heow Tan
Chief Technical & Quality Officer

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

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES II

ZADAXIN™

PLENAXIS®

HylatopicPlus® Cream

Steve Morris, M.D.
Chief Development Officer

XALKORI® 250 MG CAPSULES CRIZOTINIB

ZYKADIA® ceritinib 150 mg tablets

LORBRENA® LORLATINIB 100 mg tablets

ALECENSA® alectinib 150 mg capsules

ALUNBRIG™ BRIGATINIB 30mg TABLETS

Franco Valle
Chief Financial Officer

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

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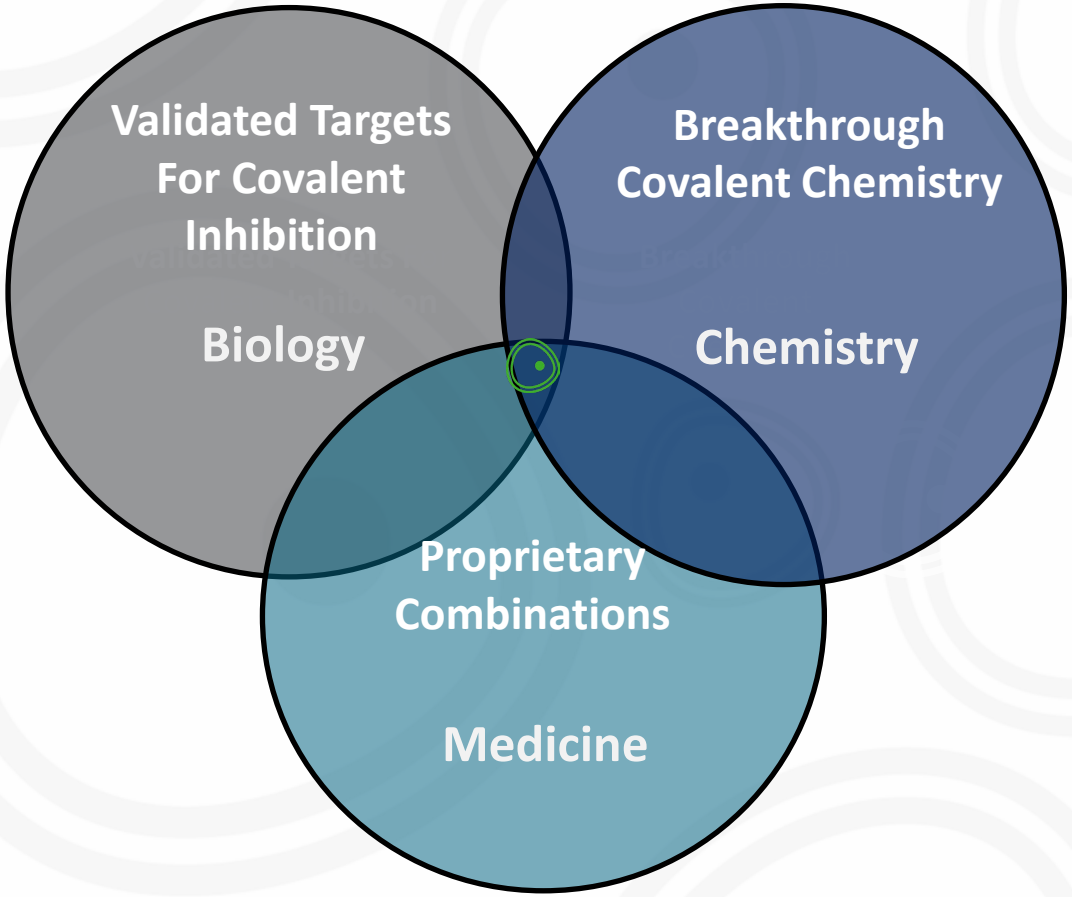
*Note: BMF-219 is an investigational new drug

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

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

Developing Some of the Most Impactful Covalent Inhibitors

Team Fusion has a History of Covalent Successes

Thomas Butler
Chairman & CEO

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

Veklury® remdesivir 100 MG FOR INJECTION

Jim Palmer
VP of Drug Discovery

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

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

Team Fusion developed the Biomea Fusion™ System and built R&D facilities to allow for efficient discovery and development of best-in-class covalent inhibitors. Target to IND candidate in hand has been produced on average in 18 mos.

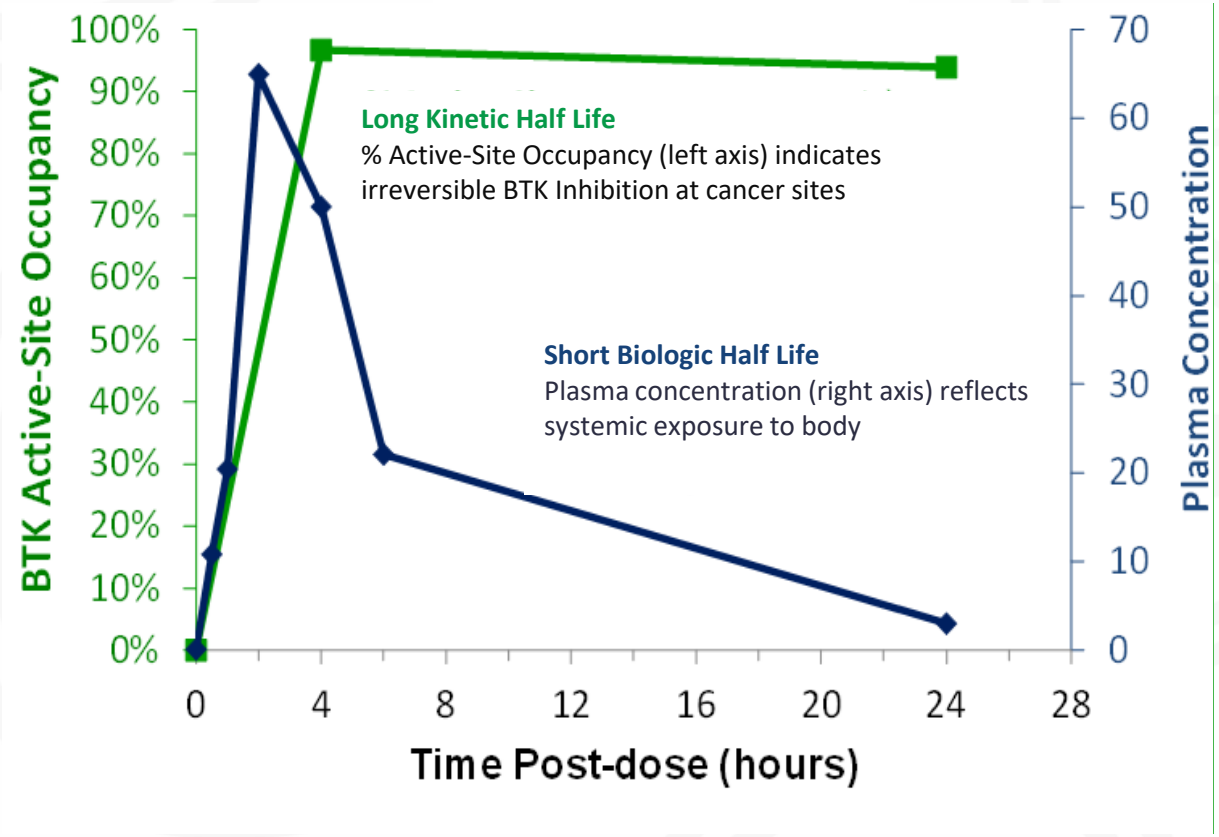
Thorsten Kirschberg
EVP of Chemistry

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

HARVONI® ledipasvir / sofosbuvir

Case Study PCI-32765 IMBRUVICA - Prolonged Target Occupancy Effect without Prolonged Systemic Exposure

Covalent Inhibitors Have Long Kinetic but Short Biological Half Life



*Pharmacyclics Corporate Deck 2012

High Selectivity

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

Deep Target Inactivation

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

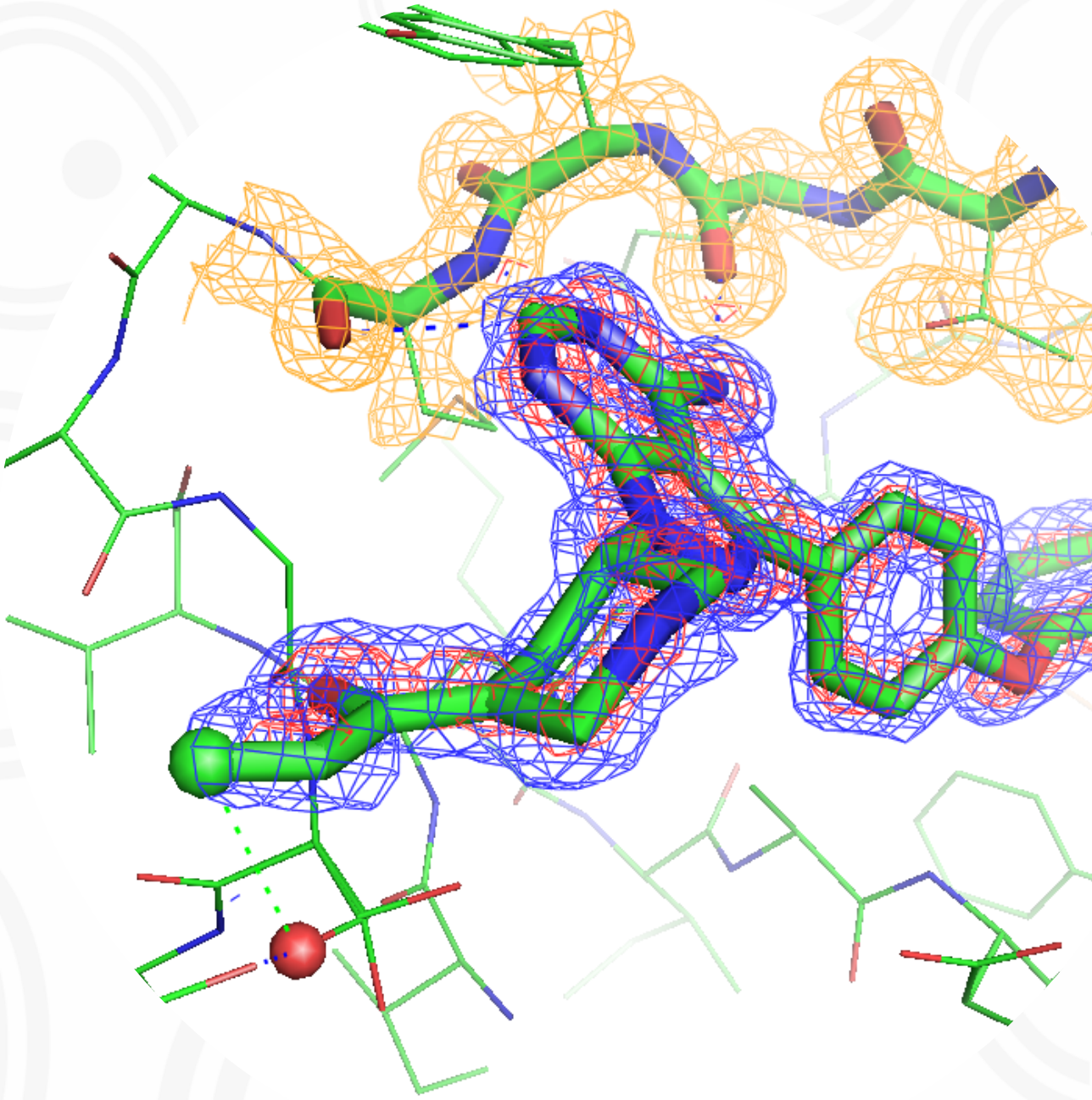
Greater Therapeutic Window

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

Our FUSION™ System

We leverage our FUSION System to discovery and develop Novel irreversible inhibitors against targets essential for many diseases.

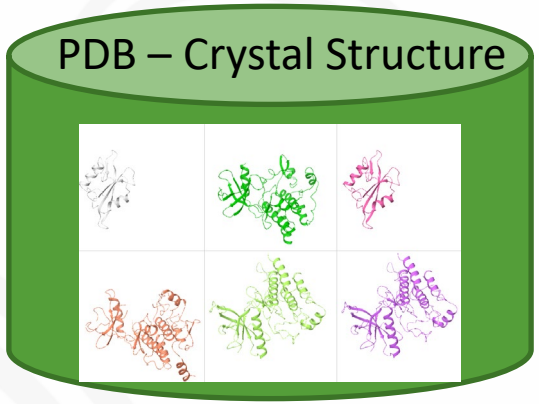
- Novel Target Selection Process
- Crystal Structure based Drug Design
- Proprietary Scaffold Construction

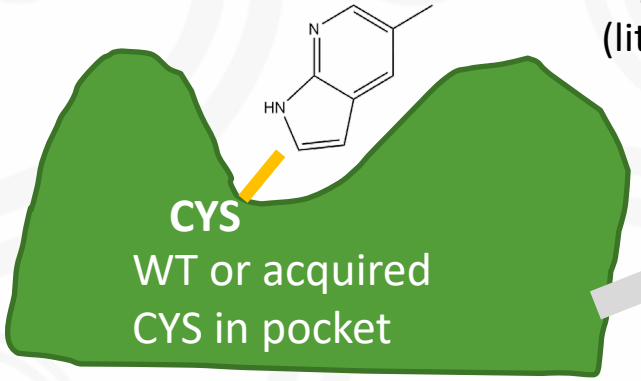


Covalent Target/Ligand Identification

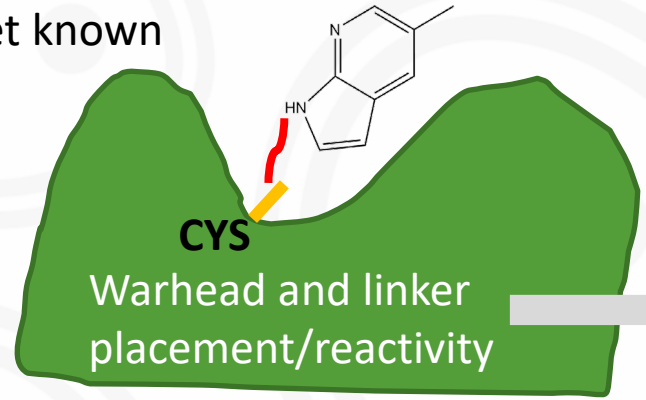
A) Target not known

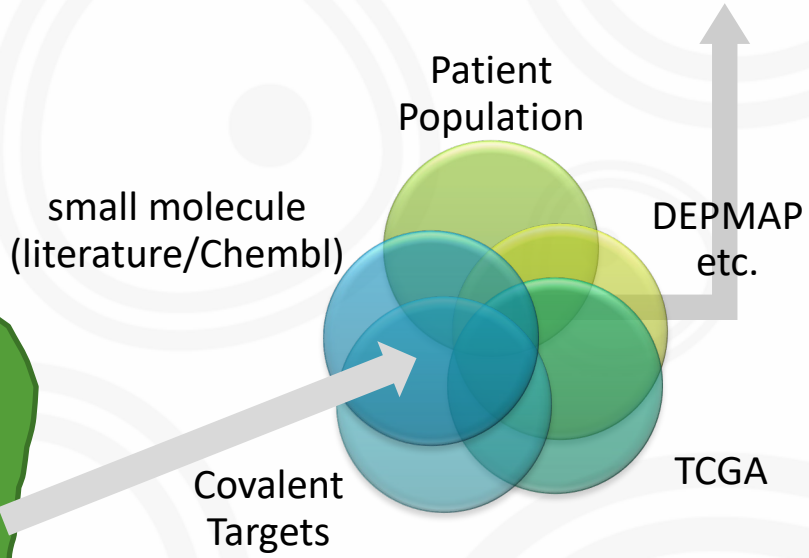
Survey Protein Data Bank for covalent targets





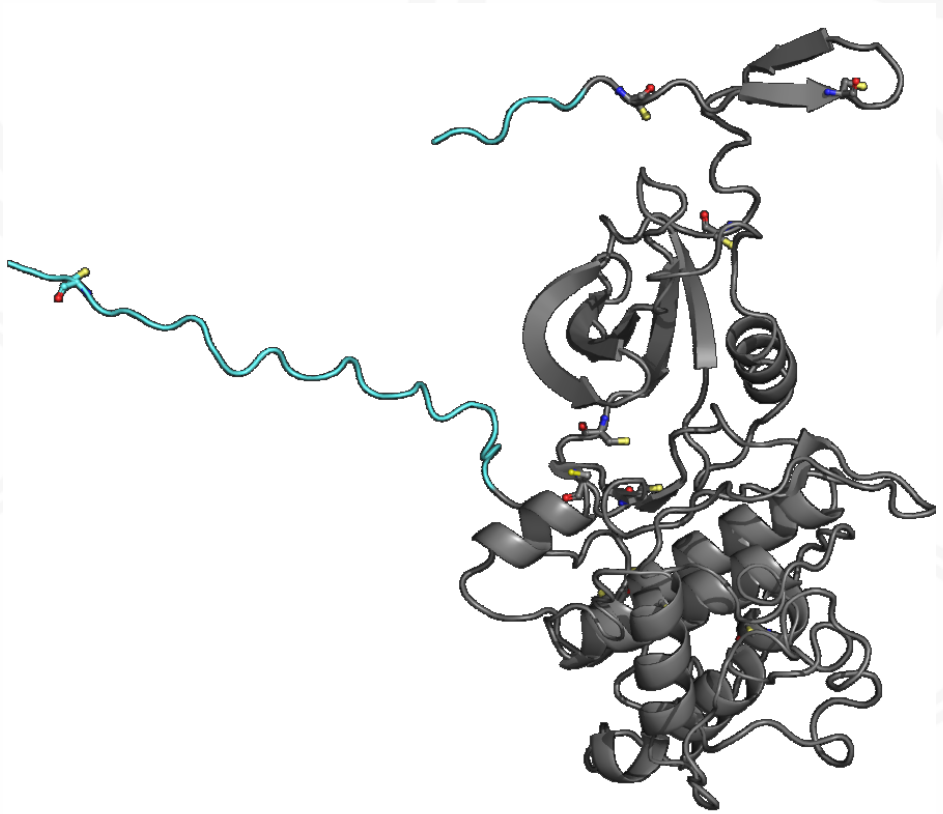
B) Target known

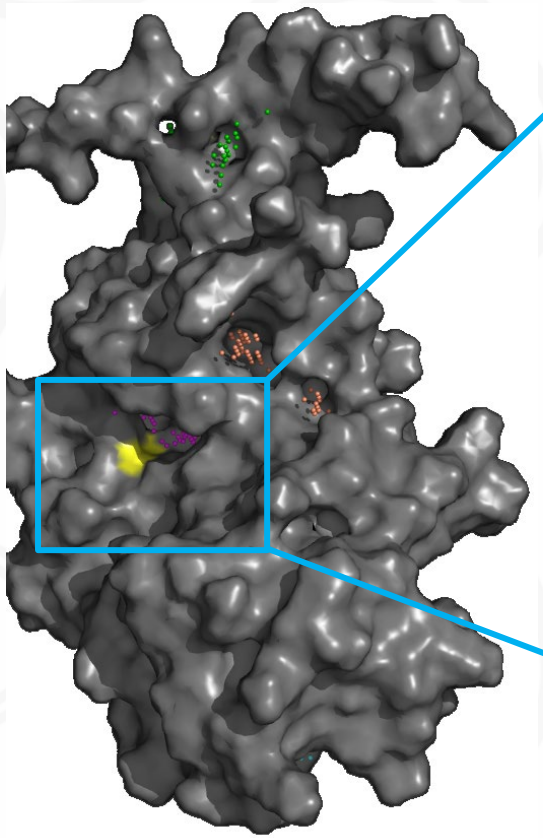


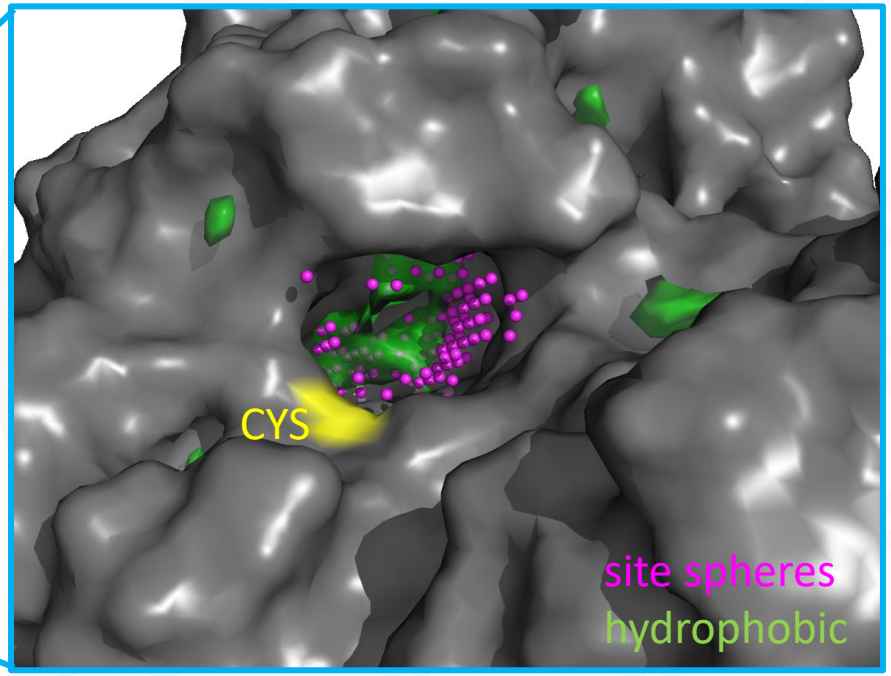


- Identify ligand
- Biomea Linker/Warhead Determination Protocol
- Optimize covalent ligand

Human Genome Wide Covalent Pocket Analysis







- 23,391 human genes as predicted structures; 14,159 novel vs PDB
- Remove spurious N- and C-termini (blue)
- Analyze individual domains if needed – potential artificial inter-domain pockets
- Manual curation for high interest targets

- Analyze Apo structures without ligands
- Pocket identification using established methods SiteMap → "bindability" ranking

- Top ranking pocket with sufficient hydrophobic character

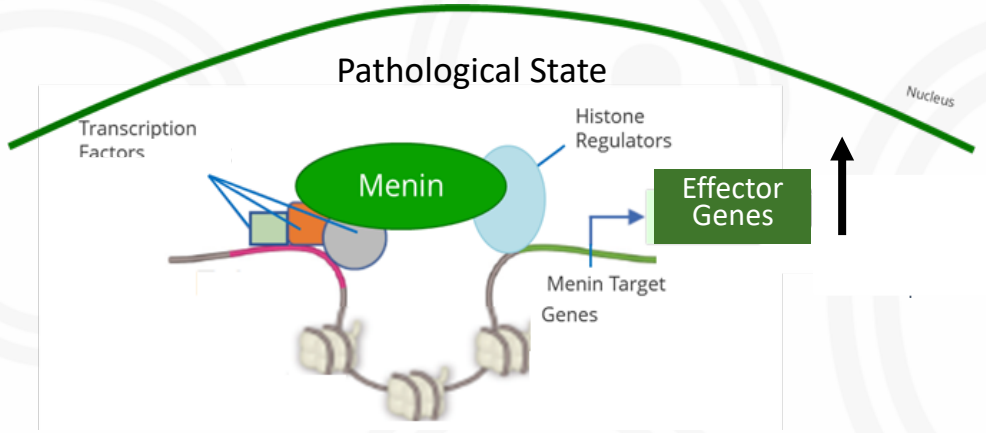
→ Virtual screening for ligands

→ Biomea Linker/Warhead Determination Protocol

→ Lead Molecule(s)

BMF-219 a covalent inhibitor of menin with unique properties

Restoring Balance in Menin Dependents Diseases is Context Specific



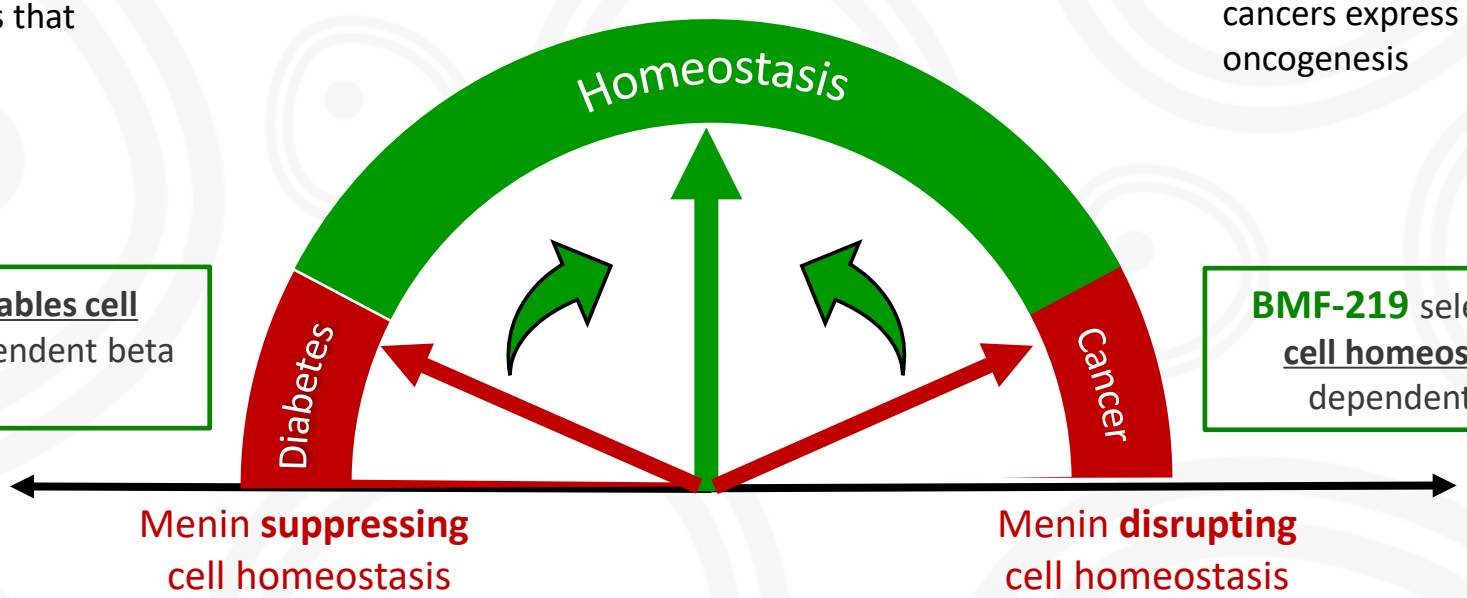
Treating Diabetes

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

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 beta cells



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

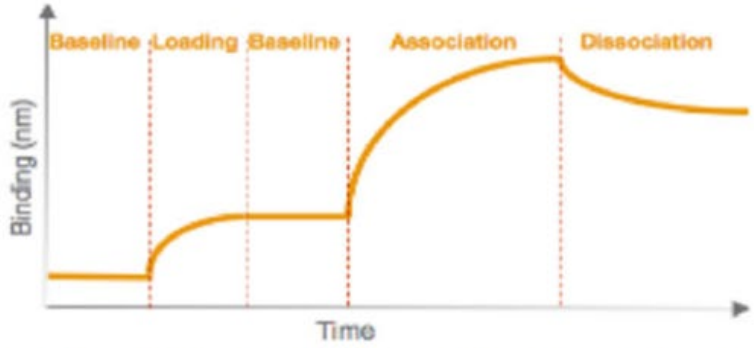
Target Engagement (Kd)

Biomea Compounds Tested against Menin

BMF-219 Target Engagement (Kd) with Menin

Compound	Kd (nM)
BMF-203	250
BMF-219 (Compound D)	<0.001
BMF-222	1,250
BMF-224	1,804
BMF-5	3,191

*Compound D displays a K_{dis} rate that supports covalent engagement



Measuring the shift over time enables the determination of binding

Comments:
Samples A-F were tested by Octet BMIA for affinity to Menin-Biotin.
SA sensors were loaded with Menin-Biotin
Binding constants were calculated for association and dissociation of 7 dilutions of each compound.
1:1 Curve Fits were applied and Global Fits were calculated as:

Analyte ID	K_D	k_{on}	k_{dis}	R^2
Compound A	1.478E-06	8.101E+02	1.197E-03	0.718
Compound B	9.965E-05	7.179E+02	7.154E-02	0.977
Compound C	2.274E-07	1.698E+03	3.861E-04	0.568
Compound D	<1.0E-12	4.009E+02	<1.0E-07	0.713
Compound E	7.049E-06	3.367E+03	2.373E-02	0.636
Compound F	9.461E-05	4.085E+02	3.865E-02	0.987

Covalent Adduct Formation

Peptide Mapping with BMF-219

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BMF-219 Binding to Single Specific Cysteine in Menin

Overview: PROTEIN METRICS by Dotmatics (CRO) Identify attachment site(s) of BMF-219 to Human rMenin

Experimental Summary:

- Incubated rMenin and BMF-219
- After incubation, treat with solution to digest Tryp/Lys-C to split rMenin into singular cysteine fragments (potential binding sites) .
- Identify rMenin fragments that bound to BMF-219

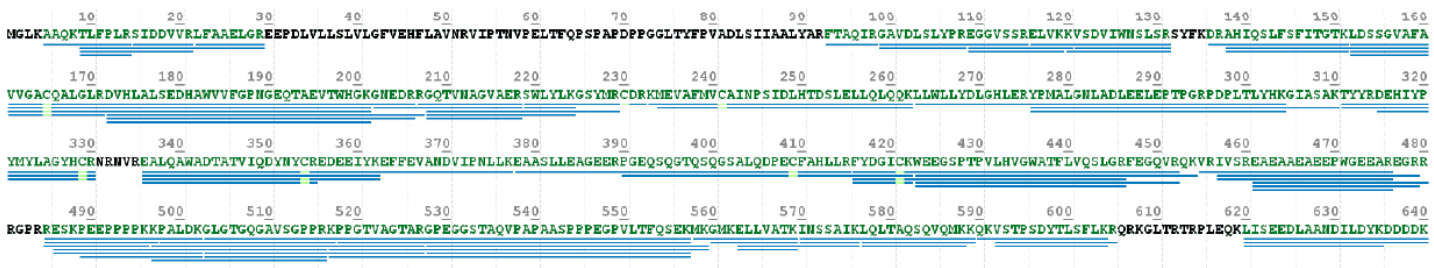
PROTEIN METRICS

Export of: C:\Users\wkittleman\Desktop\25Oct22 Biomea rMenin BMF219 rxns WK\25Oct22 Biomea rMenin BMF219 HEPES 2hr cntrl HEPES 2hr 1 to 50 two missed cleavages.blgc
Creation time: 2022.12.07 15:10:19
Created by: wkittleman
Protein sequence:

Origene_Human_rMenin_TP312368_with_CMycDDK_tag Coverage: (547 of 641) 85.34%

MGLKAAQKTLFPLRSIDDVVRLFAAELGREEPDLVLLSLVLGFVEHFLAVNRVIPTNVPELTFQPSPAPDPPGGLTYFPVADLSIIAALYARFTAQIRGAVDLSLYPREGGVSSRELVKKVSDVIWNSLSRSYFKDRAHIQSLFSFITGTKLDSSGVAFAVVGACQALGLRDVHLALSEDHAWVVFGPNGEQTAEVTWHGKGNEDRRGQTVNAGVAERSWLYLKGSYMRCDRK
MEVAFMVCAINPSIDLHTDSLELLQLQQKLLWLLYDLGHLERYPMALGNLADLEELEPTPGRPDPLTLYHKGIASAKTYYRDEHIYP
EAEEPWGEEAREGRRRGPRRESKPEEPPPPKKPALDKGLGTGQGAVSGPPRKPPGTVAGTARGPEGGSTAQVPAPAASPPPEGPVLTFQSEKMKGMKELLVATKINSSAIKLQLTAQSQVQMKKQKVSTPSDYTLSFLKRQRKGLTRTRPLEQKLISEEDLAANDILDYKDDDDKV

Protein coverage:
Origene_Human_rMenin_TP312368_with_CMycDDK_tag



- All cysteine fragments identified
- Overall sequence coverage of 85.34%

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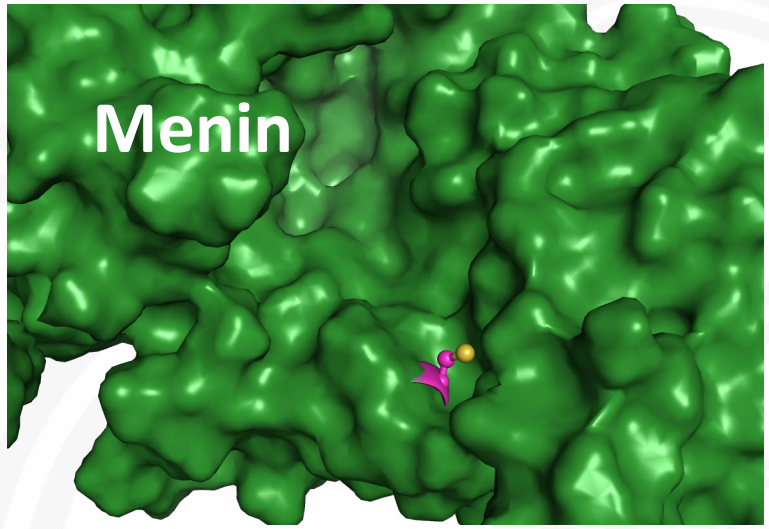
BMF-219 Binding to Specific Cysteine in Menin



Targetable Cysteine	Binding Selectivity
CYS1	100.0%
CYS2	0.0%
CYS3	0.0%
CYS4	0.0%
CYS5	0.0%
CYS6	0.0%

Peptide Mapping Data

BMF-219 binds only to single, desired target cysteine

Peptide Mapping Results Summary

- Analyzed all reactions through Freestyle
- Only observed BMF-219 attached to Cys1 (Biomea numbering)
- Did not observe BMF-219 attached to any other cysteine

Gene Expression – Human Islets

BMF-219 Impact on Menin Gene Signatures

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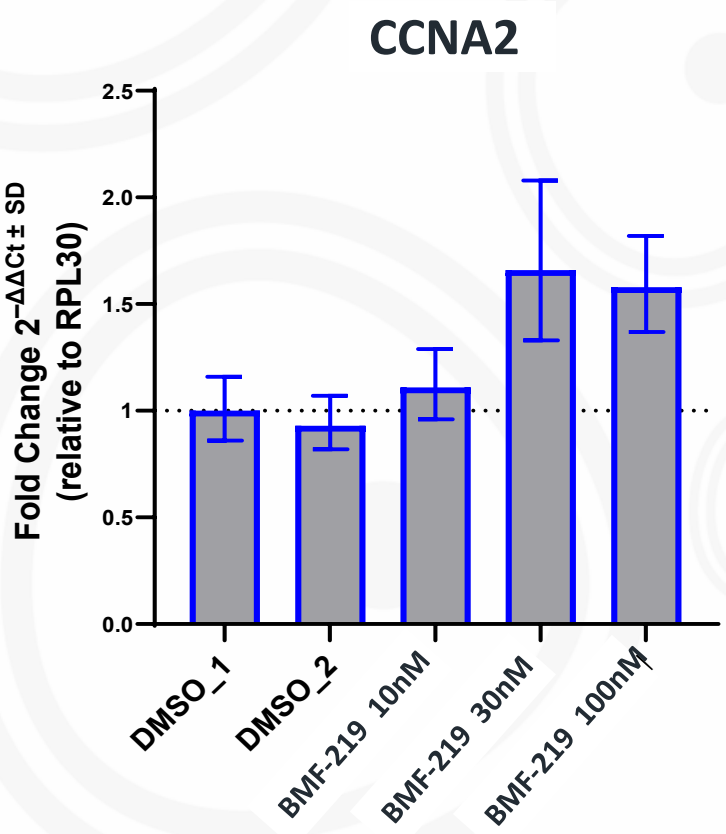
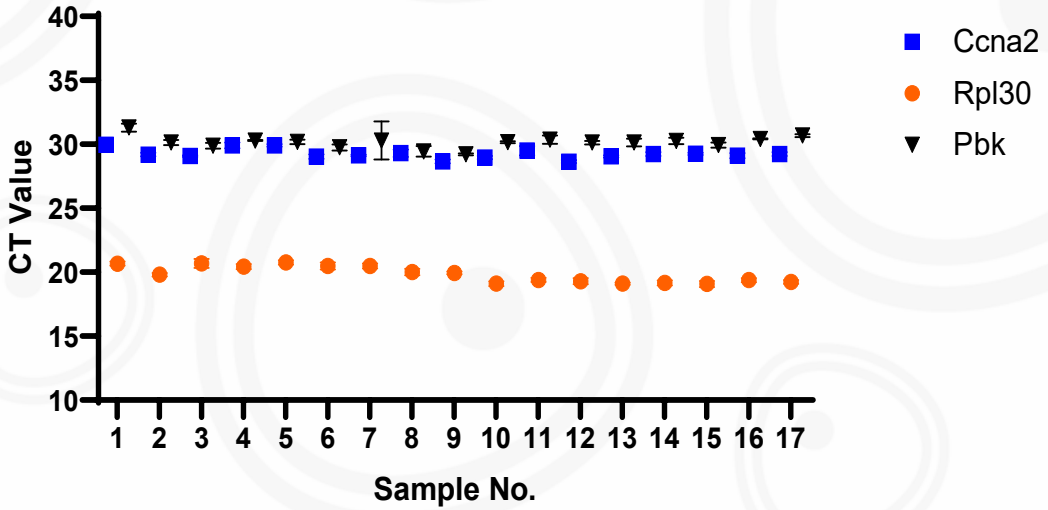
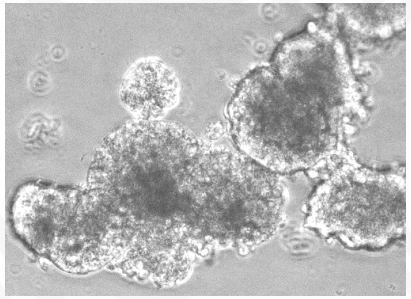
Ex-Vivo Experiments – Human Islets (CCNA2 encodes Cyclin A2)







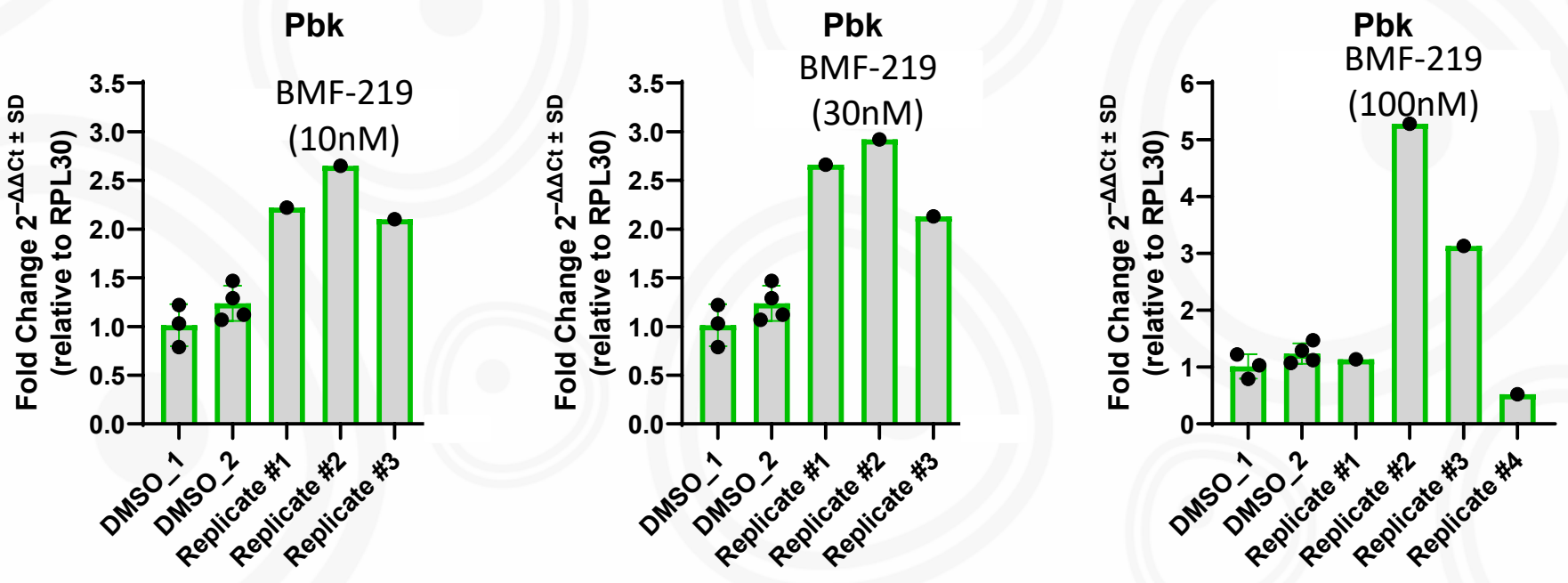
Human pancreatic islet

Treatment for 5 days

Examine gene expression by Q-PCR

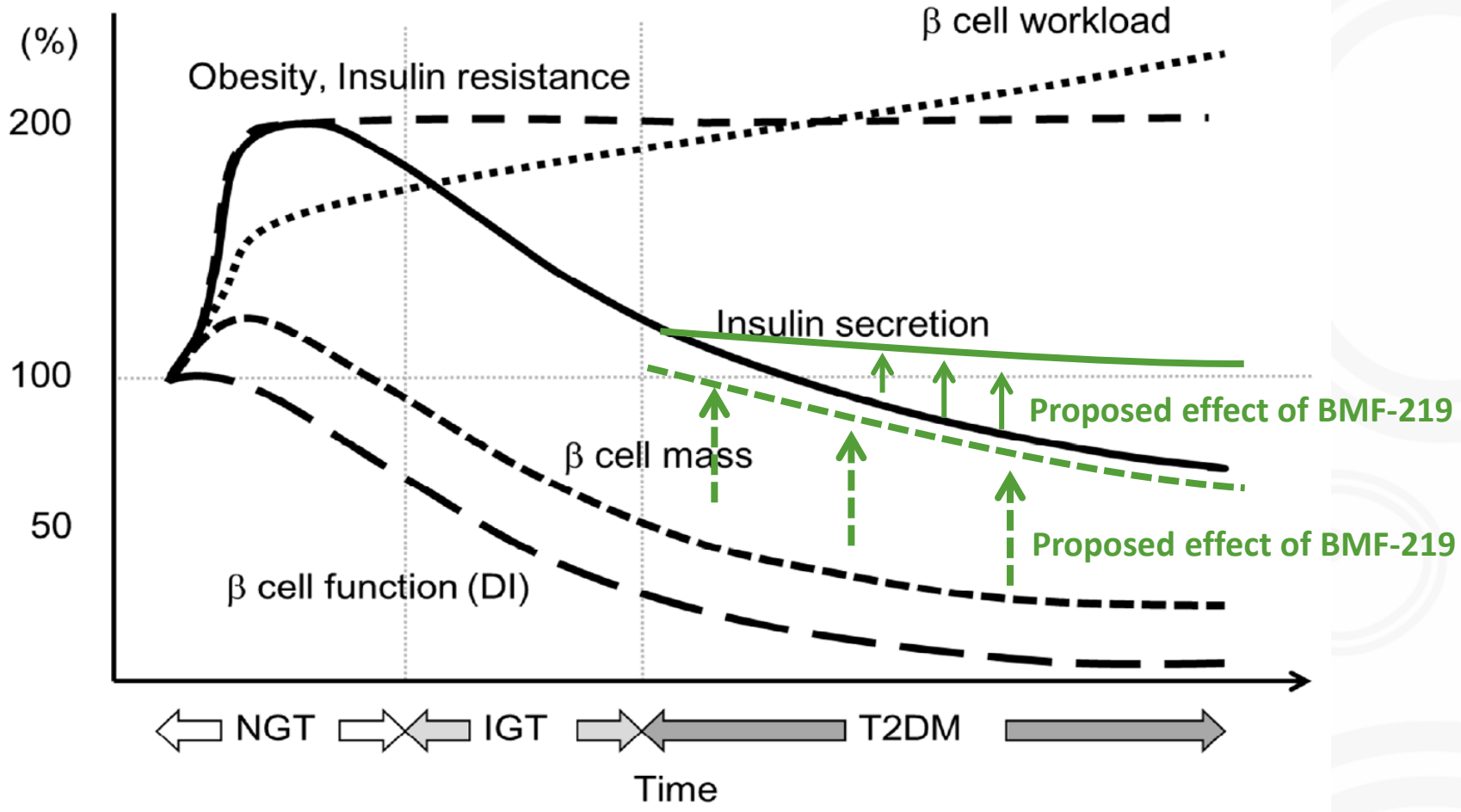
BMF-219 treatment results in an increase in CCNA2 expression, similar data in published literature results of Menin knockdown experiments. CCNA2 expression has been shown to support proliferation of beta cells, resulting in an increase in beta cell mass. CCNA2, the gene for Cyclin A2, is known to be regulated by the menin binding pathway Pbk/JunD, which are glucose controlled.

Ex-Vivo Experiments – Human Islets



BMF-219 treatment results in an increase in PbK (PDZ-binding kinase) expression, similar to results seen in literature describing Menin knockdown experiments. PbK expression has been shown to help drive proliferation of beta cells, resulting in an increase in beta cell mass and function. PbK expression is regulated by menin binding partner JunD, in a glucose dependent manner.

The Goal for BMF-219 is to Improve Glycemic Control without Continuous Medication



BMF-219 is aimed to increase beta cell mass and function, thereby increase insulin production in order to achieve glycemic control - without the need of continuous medication.

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

Investigational BMF-219 - Focusing on Beta Cell Health

BMF-219: 1st in Class Agent with a Differentiated Profile

- Oral Small Molecule
- Complementary Agent to Available Diabetes Therapies
- Short-Treatment Duration
- Well-Tolerated Profile To-Date
- Disease Modifying Potential Addressing the Root Cause of Diabetes
- Durable Glycemic Control
- Broad Application to Diabetic Patients

BMF-219 in Animal Models of Diabetes

Durable Improvement in Beta-cell Function and Glycemic Control

Priyanka Somanath, PhD
Associate Director, Translational Drug Discovery & Development
Biomea Fusion

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Study Design: Zucker Diabetic Fatty (ZDF) Rat Model of T2D

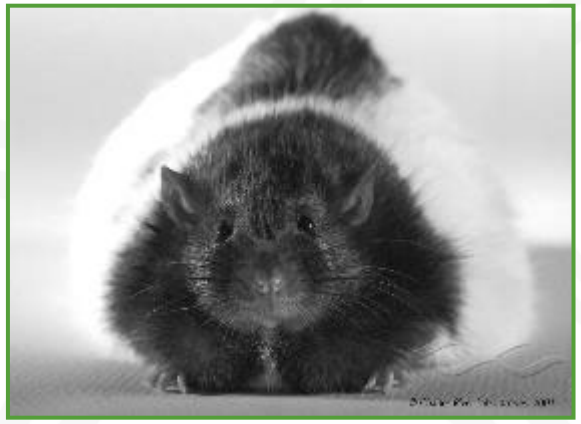


Image Source: Charles River Laboratories, 2001

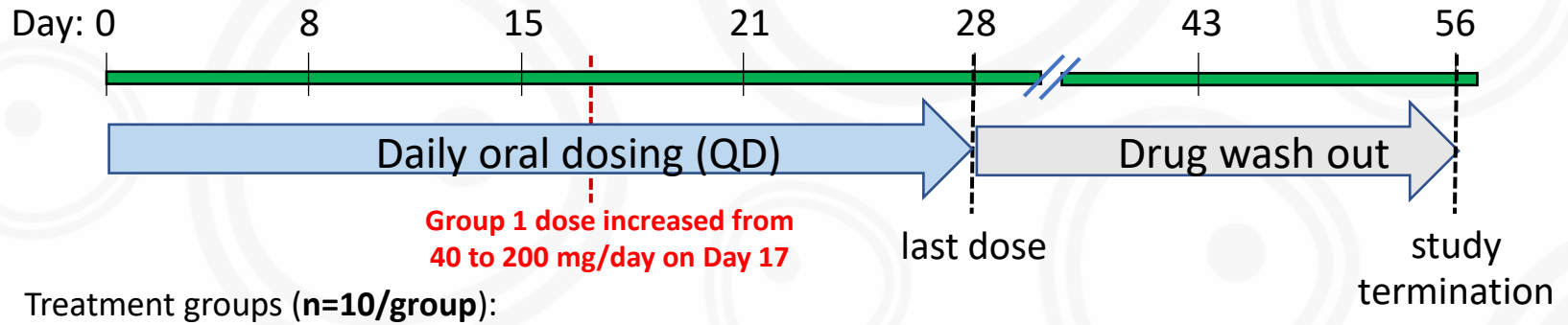
- The ZDF rat is a model of pancreatic exhaustion and insulin resistance, thus mimicking some aspects of human diabetes.
- The ZDF rat is a translatable model for studying the development of T2D.

Age: 11-12 weeks old male rats

Study Objective

Measure the ability of BMF-219 to restoring glycemic control in Zucker Diabetic Fatty (ZDF) Rat over a 4-week dosing study.

Treatment Scheme of ZDF Rat Model



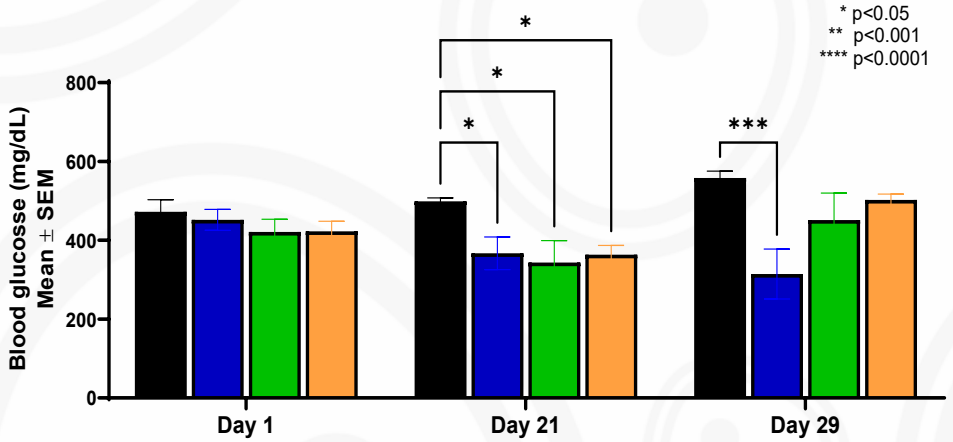
Treatment groups (**n=10/group**):

1. Vehicle
2. BMF-219 40 mg/kg days 1-16, 200 mg/kg days 17-28 (QD, PO)
3. BMF-219 85 mg/kg (QD, PO)
4. BMF-219 170 mg/kg (QD, PO)
5. Liraglutide 0.2 mg/kg (BID, SC)

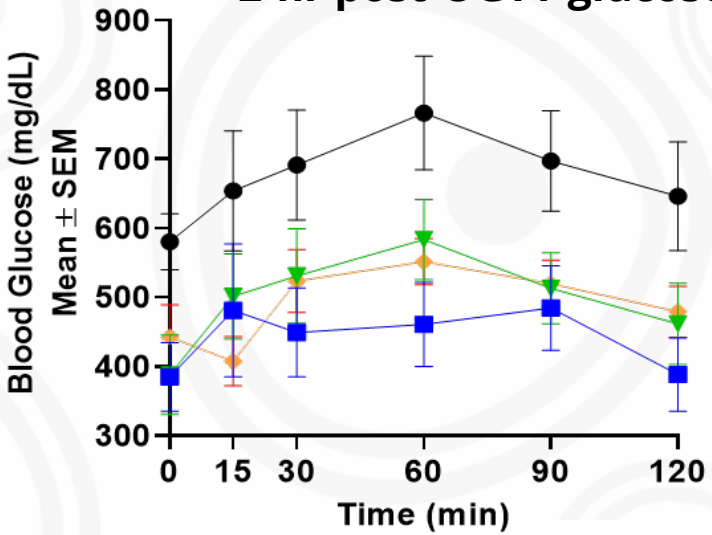
Rats monitored through dosing and washout phases: Fasting blood glucose, insulin, OGTT, HbA1c, body weight, blood lipemic levels

BMF-219 Substantially Controlled Blood Glucose Levels in a 4-Week Dosing Study

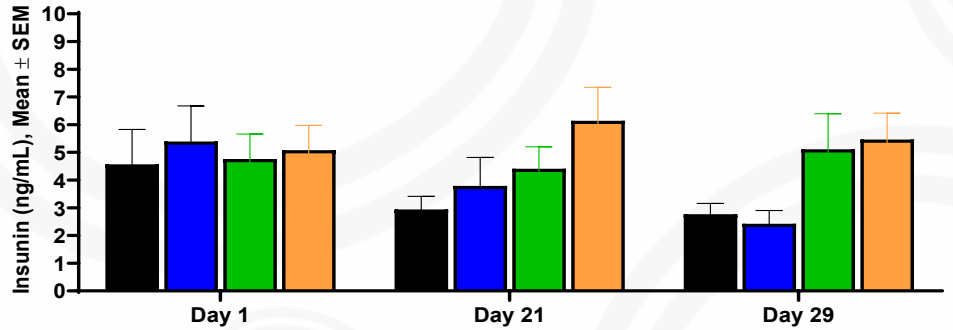
4-hr Fasting Blood Glucose



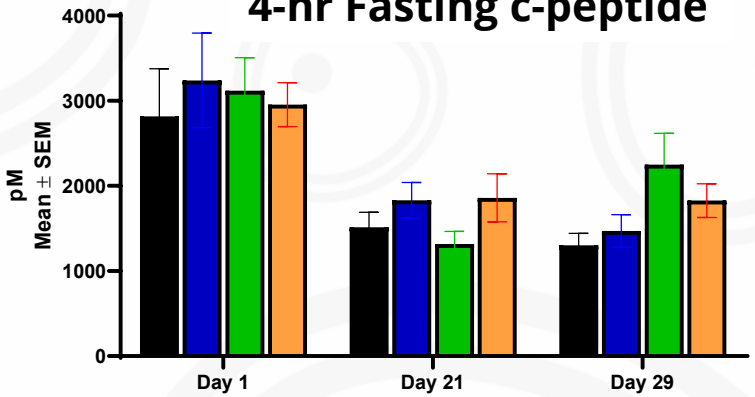
2-hr post-OGTT glucose



4-hr Fasting Insulin



4-hr Fasting c-peptide



Vehicle 0mg/kg
BMF-219 40 mg/kg PO (days 1-16), 200 mg/kg PO (day 17-28)
BMF-219 170mg/kg PO
Liraglutide 0.2 mg/kg BID

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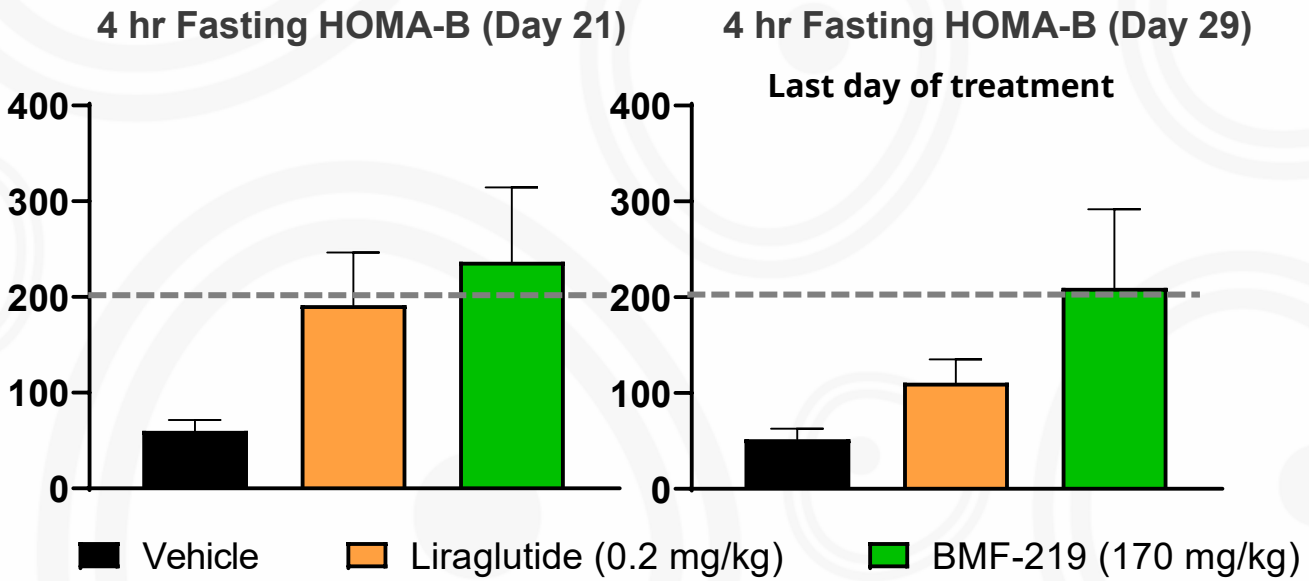
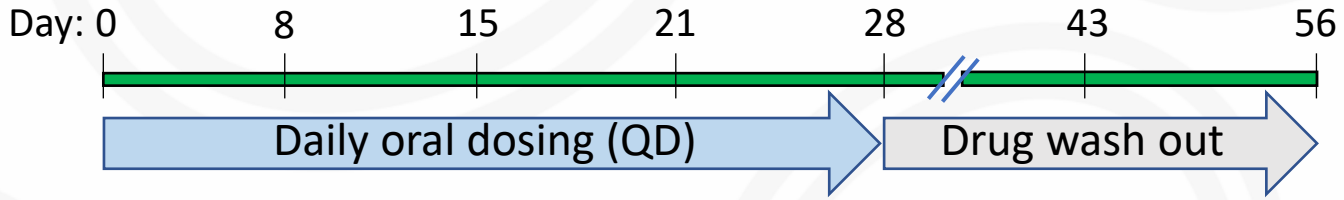
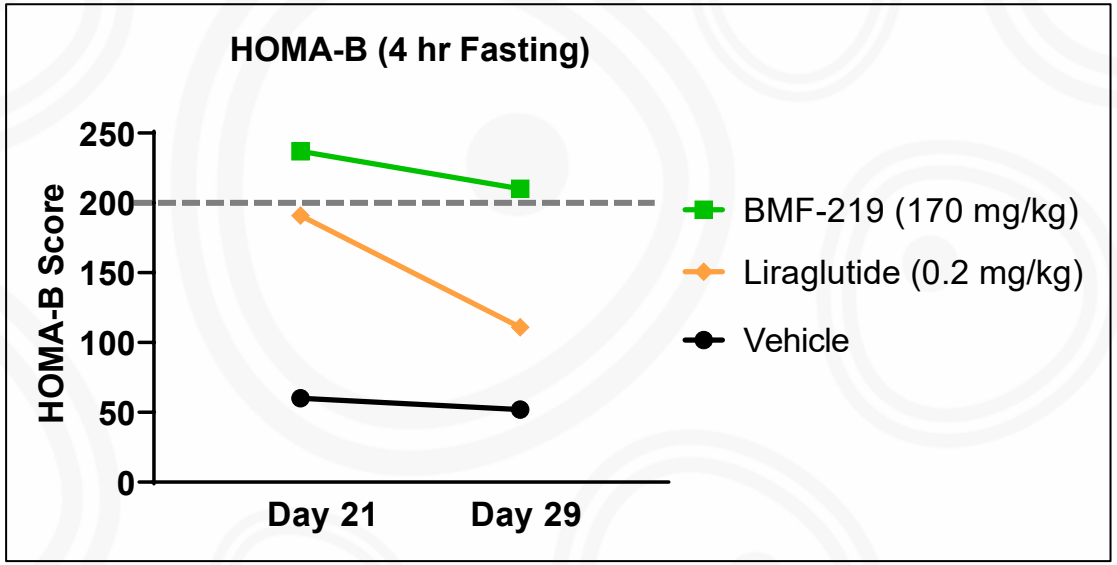
BMF-219 Restores Beta-Cell Function over 4 Weeks of Treatment





Group 1 dose increased from 40 to 200 mg/kg day on Day 17

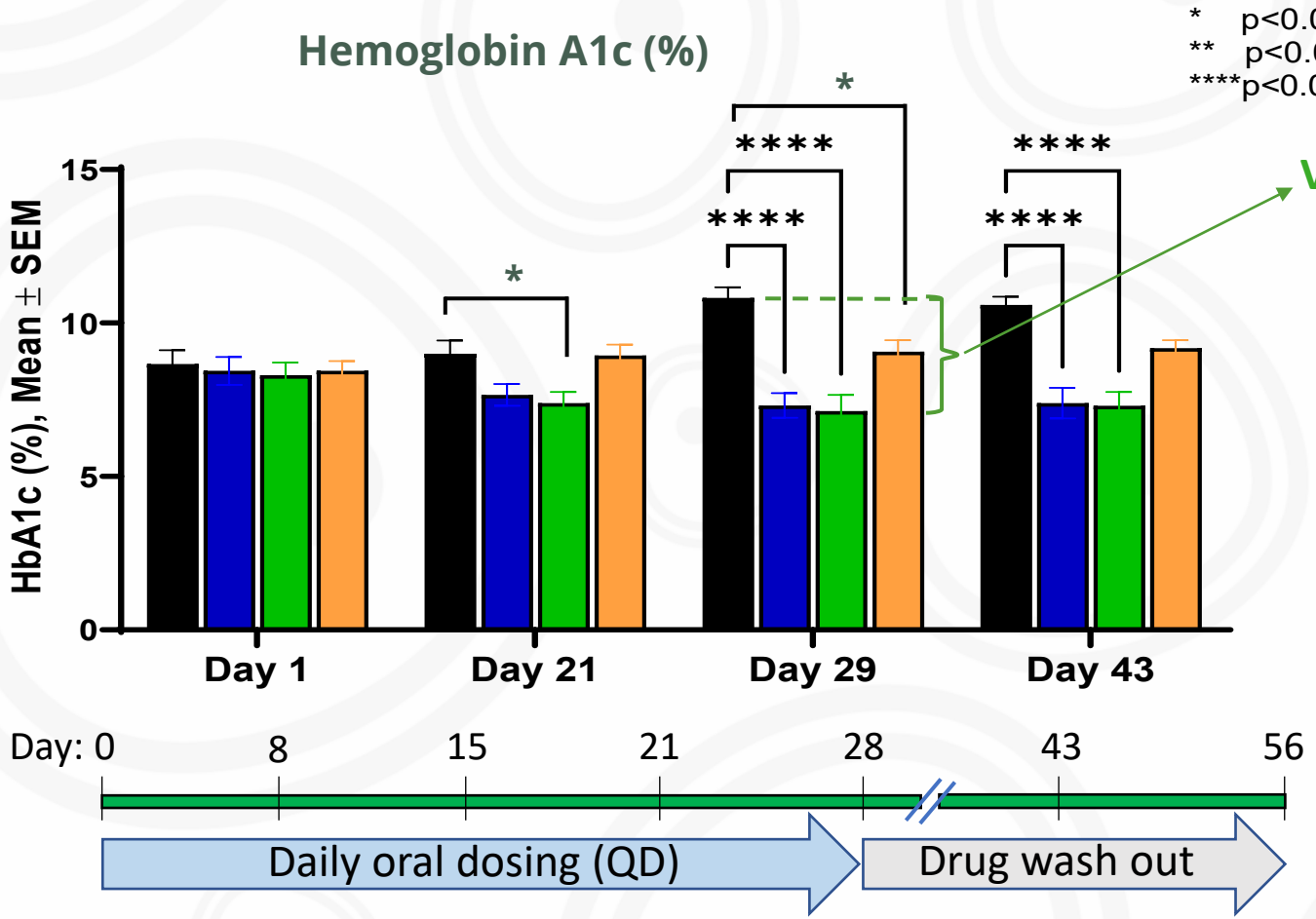
BMF-219 restores and maintains HOMA-B index to normal state (>201) over 4 weeks of treatment



Severity Grading Assessment for Pancreatic Beta-Cell Function	HOMA-B Index
Adequate (normal state)	≥ 201.00
Mild deficiency	134.00 to 200.99
Moderate deficiency	67.00 to 133.99
Severe deficiency	0.00 to 66.99

Table Source: Fasipe JO et al. 2020. Can J Diabetes 44 (2020) 663e669.

BMF-219 Significantly Reduces HbA1c (-3.5%) vs. Vehicle during Treatment and Maintains Lowering Effect during 2 Weeks of Drug Washout



HbA1c reduction in BMF-219 treated groups maintained through washout period

Group 1 dose increased from 40 to 200 mg/kg/day

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Summary of Key Animal Data

- BMF-219 was well-tolerated in all animals.
- BMF-219 displayed significant glycemic control in ZDF rats, outperforming liraglutide in reduction of fasting blood glucose by Day 29 and by OGTT on day 25.
- BMF-219 significantly reduced HbA1c levels (-3.5%) relative to vehicle control during treatment and during drug washout.
- Collectively, these data suggest a durable effect of BMF-219 on glycemic control and beta cell function, enabling further clinical studies.

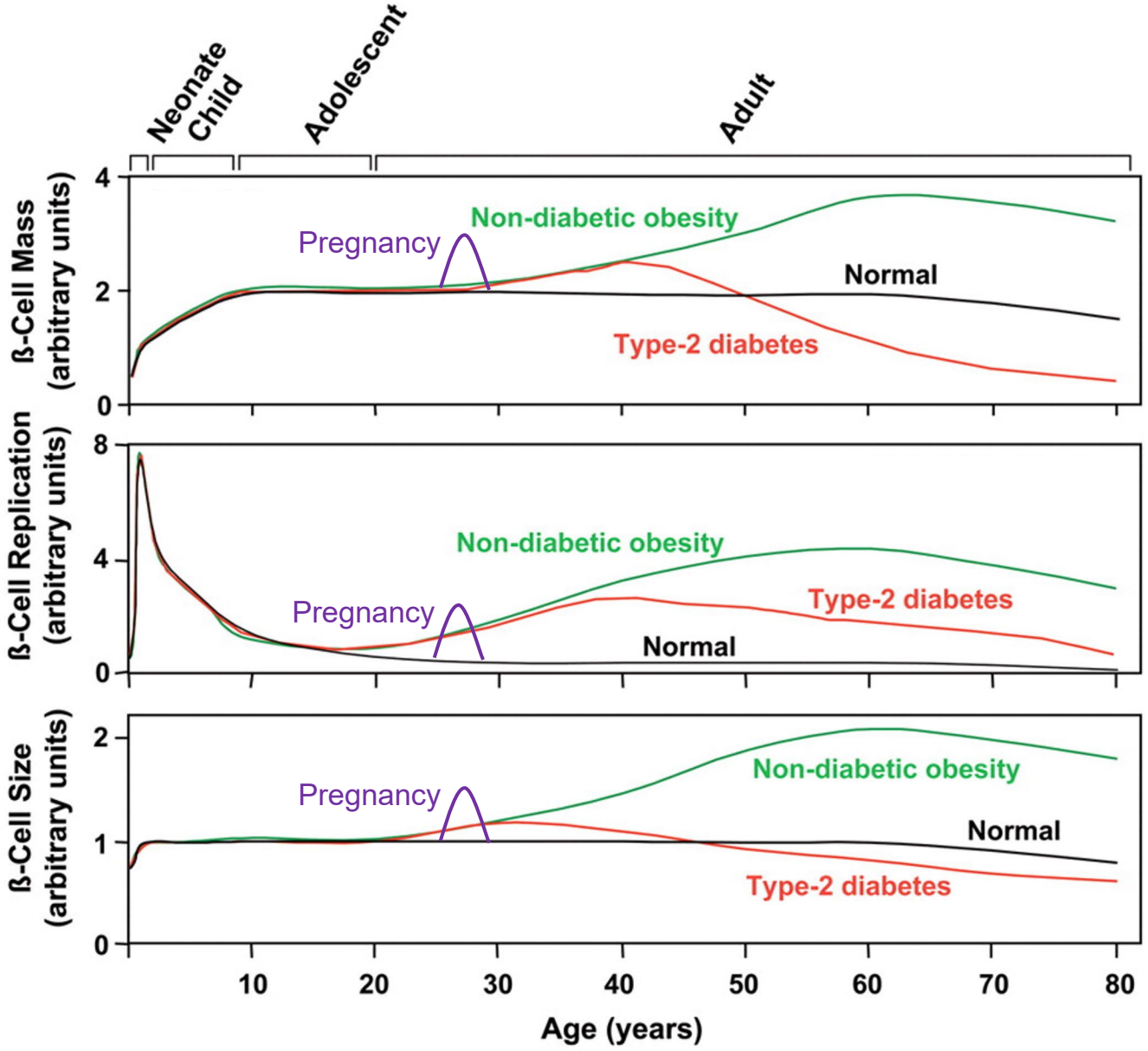
Joslin Diabetes

Harvard Medical School

Menin Inhibition: What May Explain the Effects of BMF-219 on β-Cell Function and Glycemic Control?

Rohit N. Kulkarni MD PhD

β-Cell Compensation in Physiological and Pathophysiological States in Mammals



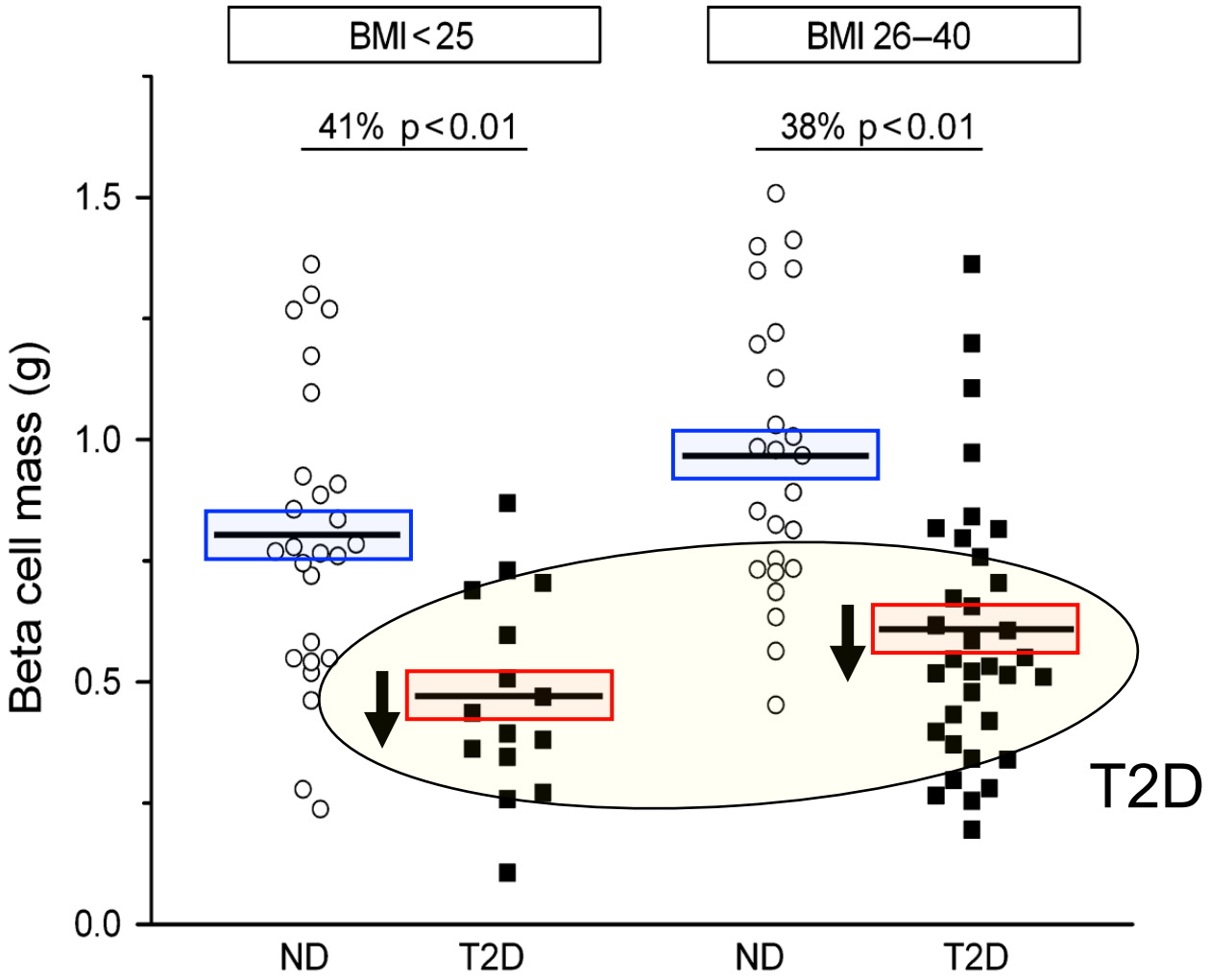
β-Cell Mass

β-Cell Replication

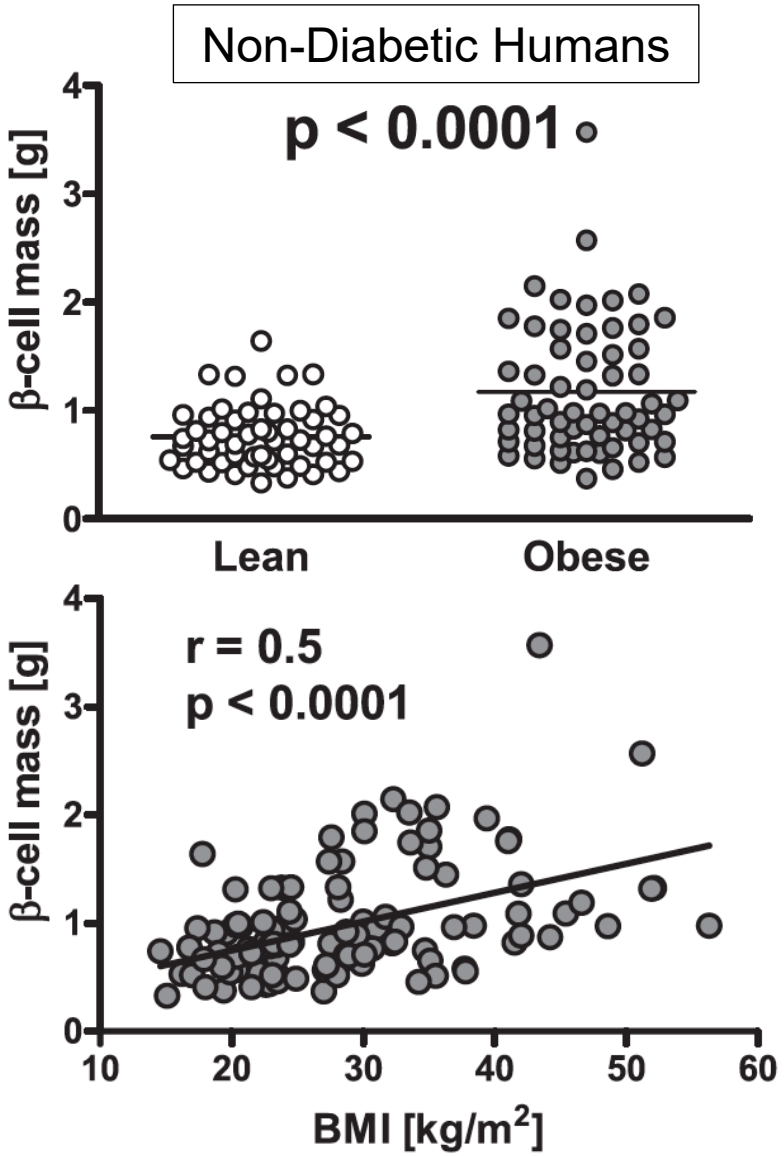
β-Cell Size

Adapted from Science. 2005

Evidence for Enhanced β-Cell Mass in Humans



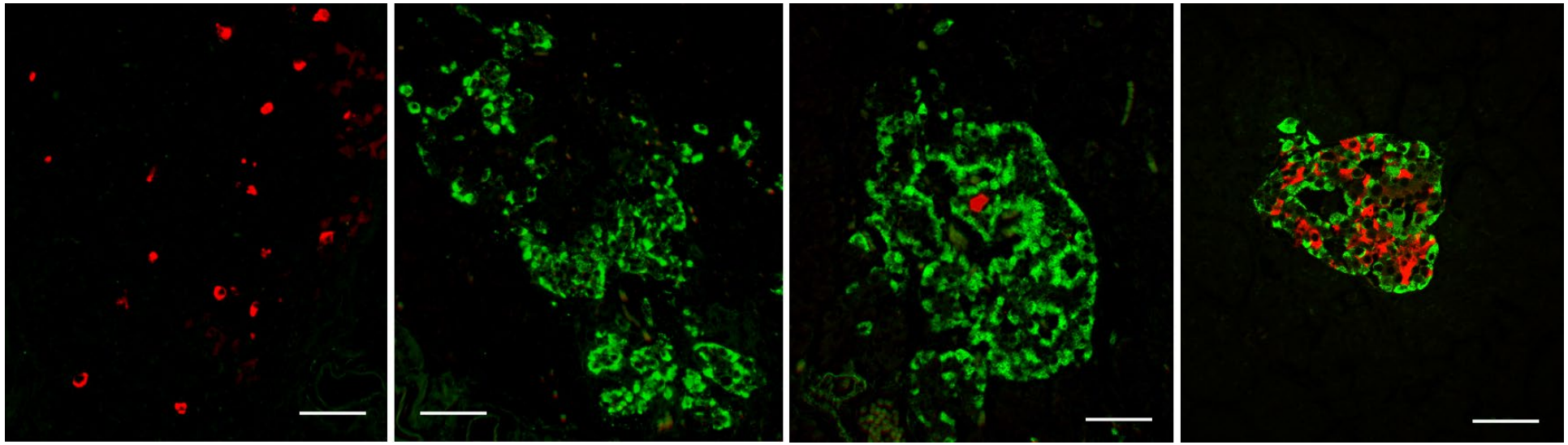
Rahier et al. Diabetes, Obesity and Metabolism. 2008



Saisho et al. Diabetes Care. 2012

Evidence for Replicating and Functional β-cells in Patients with Long-Standing (>50 yrs) Type 1 Diabetes

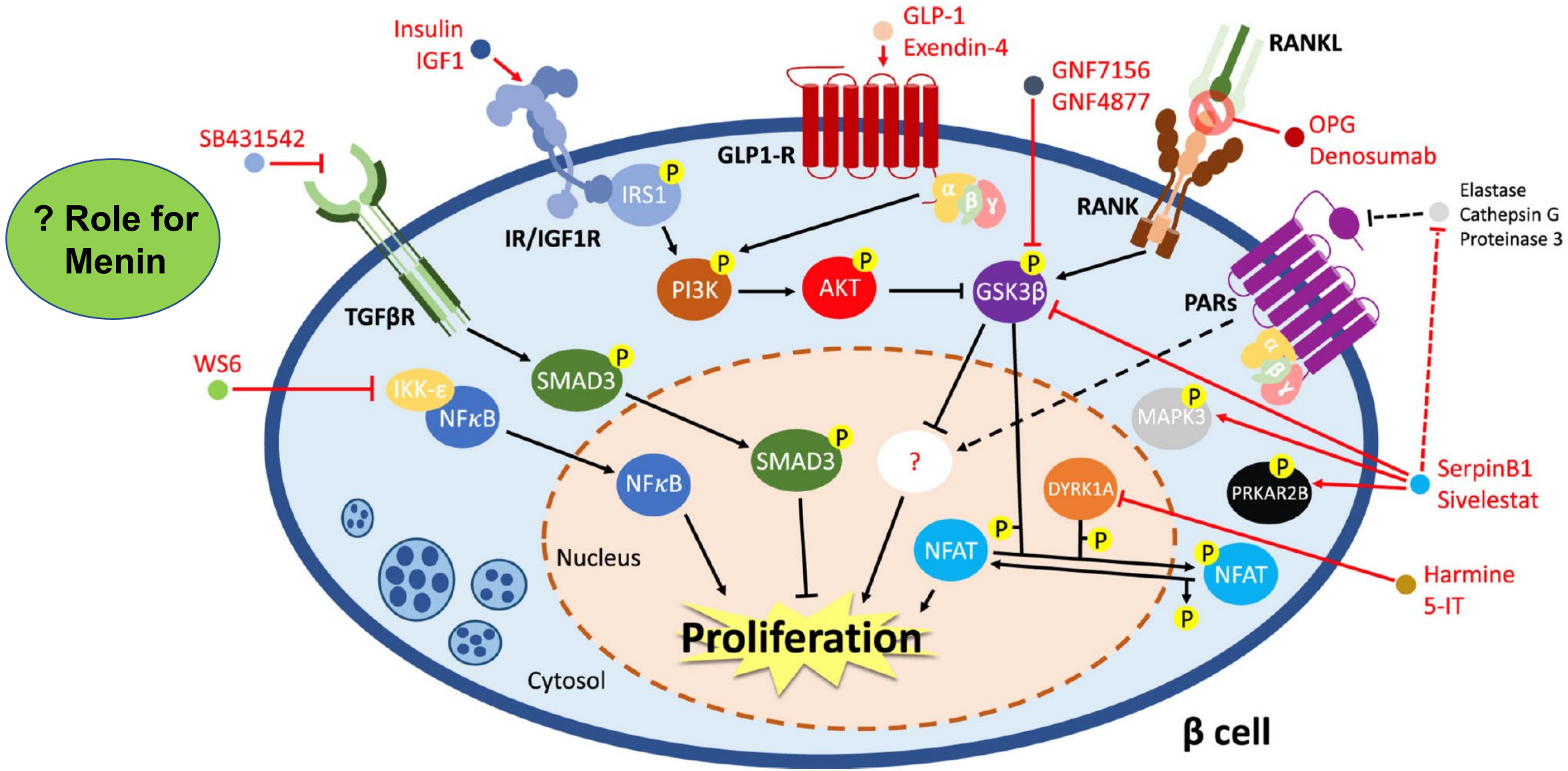
Medalists: 50+ yrs with insulin-dependent diabetes, mean duration= 65 yrs



Singlets outside islet	Few within a few islets	Several in islets in few lobes
48/48	36/48	7/48

Keenan, Bonner-Weir, King et al, *Diabetes* 2010

Molecular Mechanisms Regulating Human β-Cell Proliferation



Basile et al. Current Diabetes Reports. 2019

Science
AAAS
2007

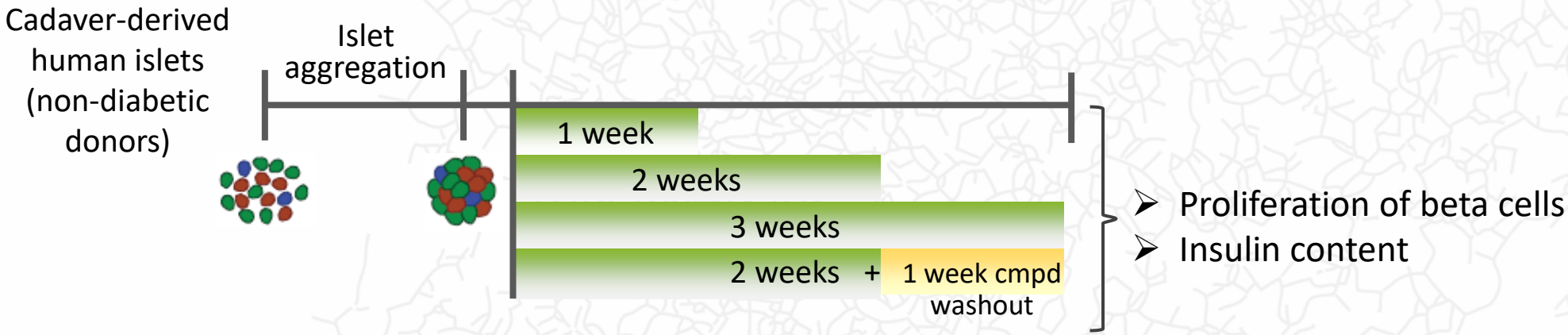
Menin Controls Growth of Pancreatic β-Cells in Pregnant Mice and Promotes Gestational Diabetes Mellitus

Satyajit K. Karnik,[1] Hainan Chen,[1*] Graeme W. McLean,[1*] Jeremy J. Heit,[1*] Xueying Gu,[1] Andrew Y. Zhang,[1] Magali Fontaine,[2] Michael H. Yen,[1,3] Seung K. Kim[1,3]†

During pregnancy, maternal pancreatic islets grow to match dynamic physiological demands, but the mechanisms regulating adaptive islet growth in this setting are poorly understood. Here we show that menin, a protein previously characterized as an endocrine tumor suppressor and transcriptional regulator, controls islet growth in pregnant mice. Pregnancy stimulated proliferation of maternal pancreatic islet β-cells that was accompanied by reduced islet levels of menin and its targets. Transgenic expression of menin in maternal β-cells prevented islet expansion and led to hyperglycemia and impaired glucose tolerance, hallmark features of gestational diabetes. Prolactin, a hormonal regulator of pregnancy, repressed islet menin levels and stimulated β-cell proliferation. These results expand our understanding of mechanisms underlying diabetes pathogenesis and reveal potential targets for therapy in diabetes.

Ex-Vivo Human Islet Microtissues: Assay Set-Up and Read Outs

- Compound treatment 1-3 weeks (+/- compound washout)
- Assayed under standard (5.5 mM) and high (8.0 mM) glucose

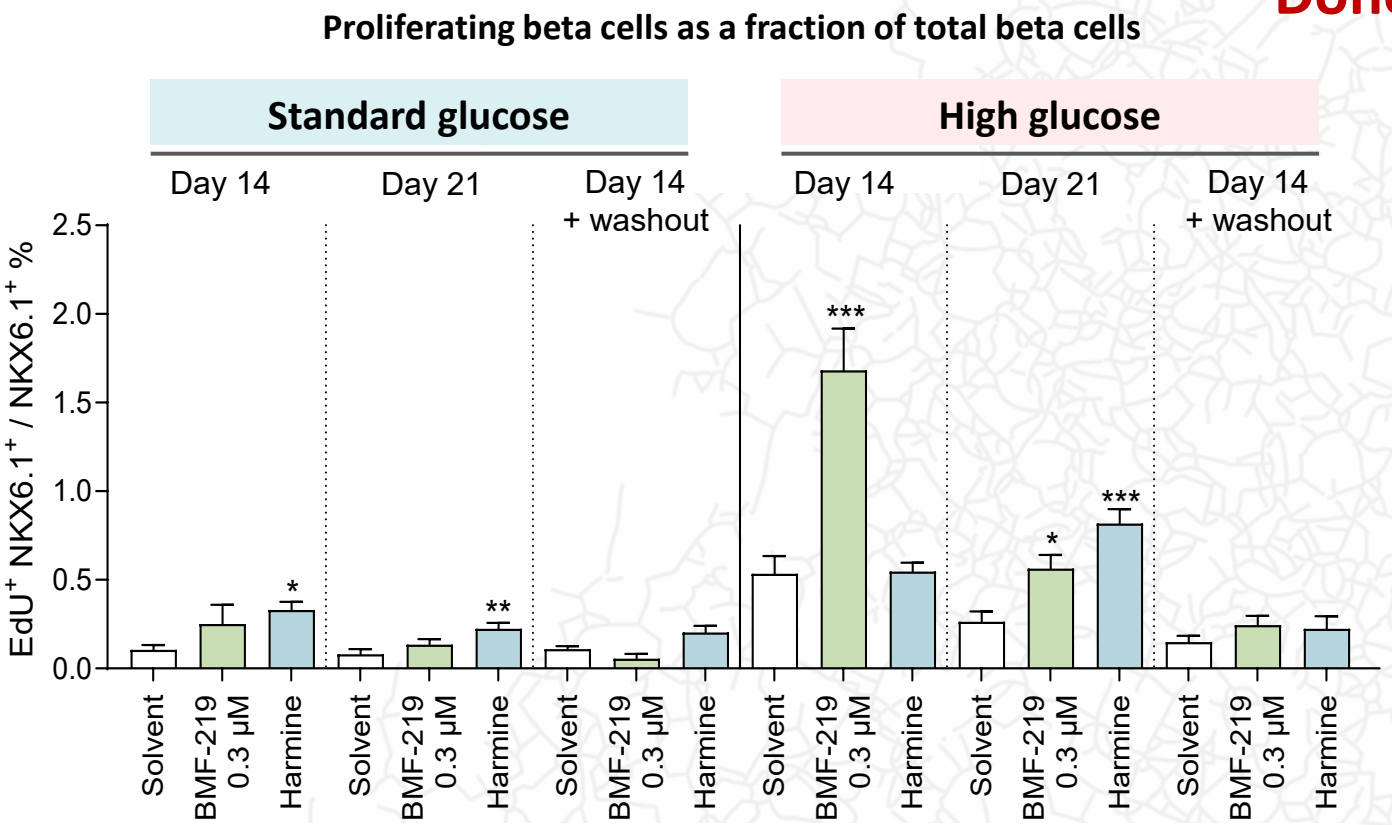


Donor characteristics:

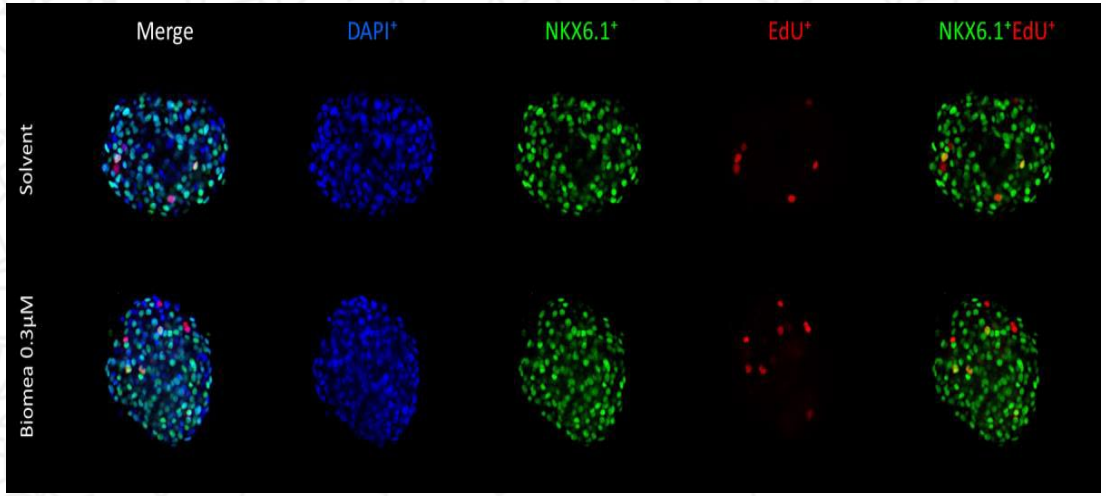
Donor	Age	BMI	HbA1c
#1	19	23.2	5.8
#2	32	25.0	5.2

BMF-219 Induced a Glucose-Dependent Enhancement in β-Cell Proliferation

Donor 1



Donor 1; Day 14, High glucose



Data represent mean ±SEM of 1 donor with n = 6-10 technical replicates.
One-way ANOVA with Dunnett's post hoc test rel. to DMSO control. *p < 0.05, **p < 0.01, ***p < 0.001

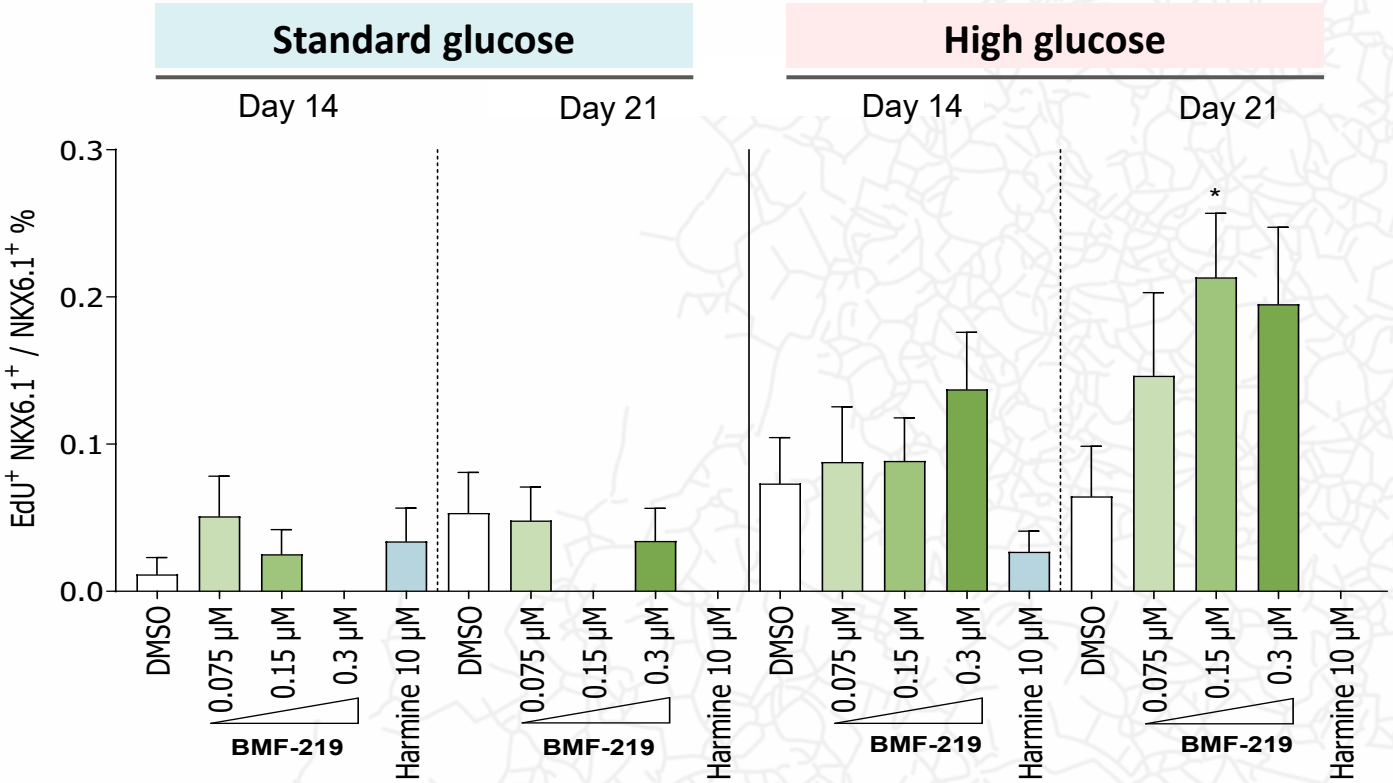
Donor #1	Age	BMI	HbA1c
White	19	23.2	5.8

Proliferation observed only under elevated glucose conditions, which mimic diabetic levels, and with continuous drug exposure.

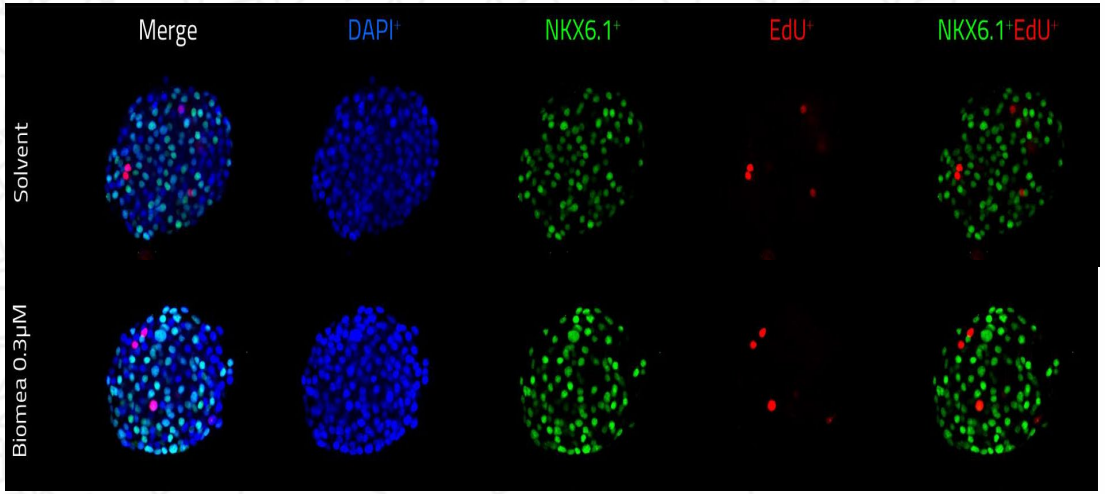
BMF-219 Induced a Glucose-Dependent Enhancement in β-Cell Proliferation

Donor 2

Proliferating beta cells as a fraction of total beta cells



Donor 2; Day 14, High glucose



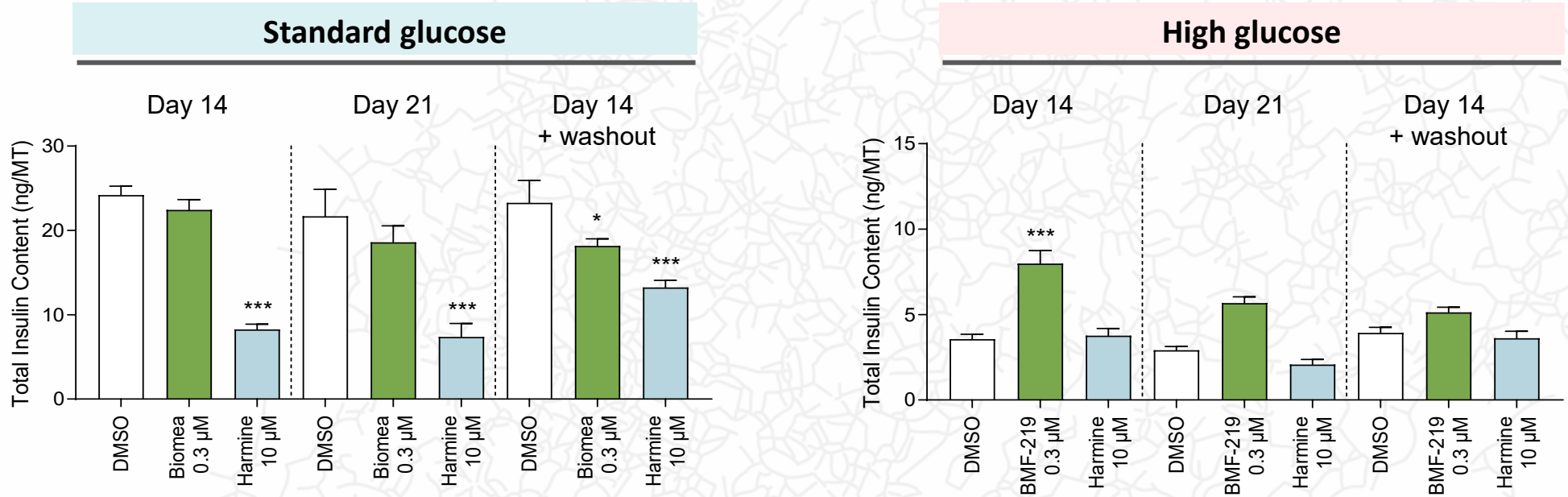
Data represent mean ±SEM of 1 donor with n = 9-12 technical replicates.
One-way ANOVA with Dunnett's post hoc test rel. to DMSO control. *p < 0.05, **p < 0.01, ***p < 0.001

Donor 2	Age	BMI	HbA1c
Caucasian	32	25.0	5.2

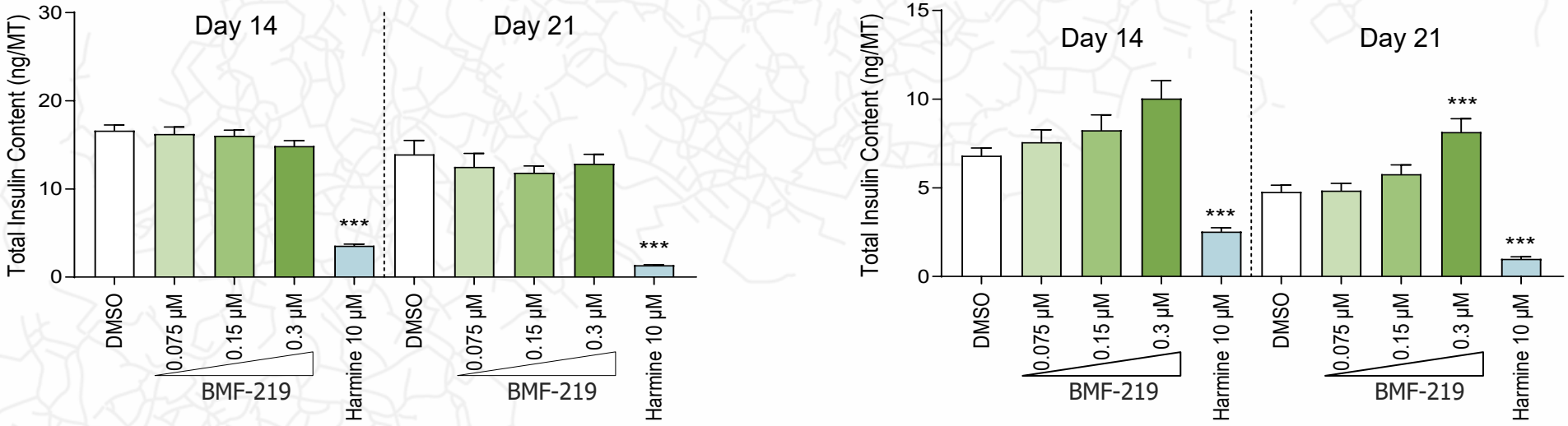
Proliferation observed only under elevated glucose conditions, which mimic diabetic levels.

BMF-219 Induced a Glucose-Dependent Enhancement in β-Cell Insulin Content

Donor 1



Donor 2



Summary and Ongoing Studies on BMF219

- BMF-219 promotes controlled proliferation and enhances insulin content in β-cells in human islets *ex vivo* in a glucose- and dose-dependent manner
- Data suggests induction of β-cell proliferation as a mechanism for the improved glycemic control in BMF-219-treated patients with diabetes
- Ongoing studies aim to explore changes in gene and protein signatures of human β-cells treated with BMF-219 using RNA sequencing and proteomics to dissect signaling pathways for the safe activation and re-activation of human β-cell cycle proliferation

BMF-219 in People with T2D

Select Results of a Multiple Ascending Dose Study

Juan Pablo Frias, MD
Chief Medical Officer, Head of Diabetes
Biomea Fusion

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Study Objectives of T2D Multiple Ascending Dose (MAD) Cohorts

Primary Objective:

To assess the **safety and tolerability** of multiple ascending oral doses of BMF-219

Key Secondary Objectives:

- To determine the **pharmacokinetics** following multiple ascending doses of BMF-219
- To determine the impact of multiple ascending doses of BMF-219 on **glycemic parameters**
- To assess changes in **beta-cell function** after multiple ascending doses of BMF-219

COVALENT-111 Study

Key Eligibility Criteria and Study Design

Eligibility Criteria

- T2D, age 18-65 years
- Duration of diabetes ≤15 years
- HbA_{1c} 7.0-10.0%, inclusive
- Treated with diet/exercise ± up to 3 antihyperglycemic agents (insulin secretagogues and insulin excluded)

COVALENT-111 T2D MAD Cohorts

50 mg QD, without food
x 4 weeks

100 mg QD, without food
x 4 weeks

100 mg QD, with food
x 4 weeks

BMF-219 (n=10) and placebo (n=2) per cohort

200 mg QD, without food
x 4 weeks

200 mg QD, with food
x 4 weeks

100 mg BID, without food
x 4 weeks

200 mg QD x 2 weeks	**400 mg QD** x 2 weeks

without food

4 weeks once-daily oral dosing + 22 weeks follow-up

QD, once daily

COVALENT-111 Study

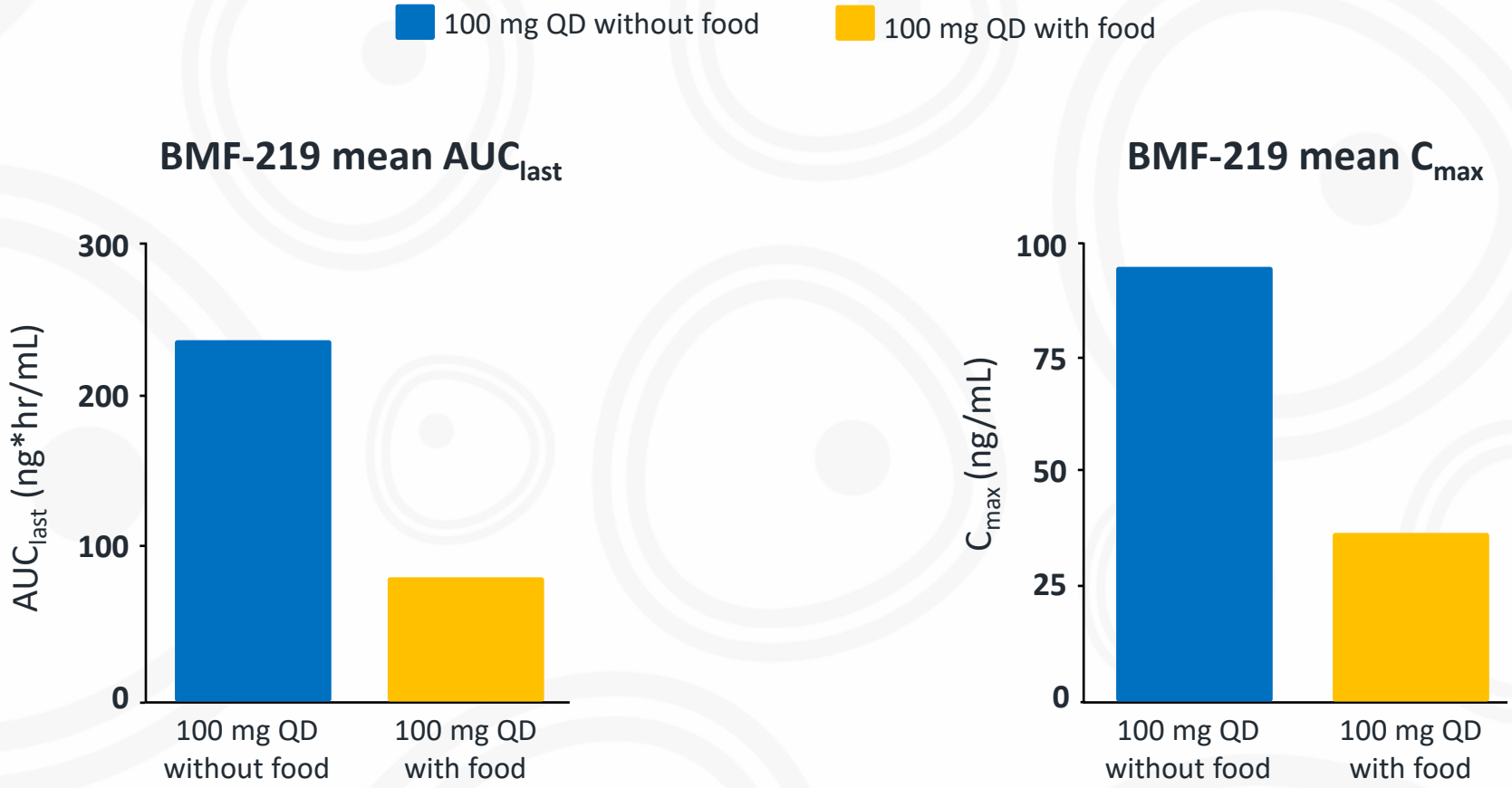
Baseline Characteristics and Demographics

	BMF-219 100mg QD without food (n=10)	BMF-219 100mg QD with food (n=10)	Placebo (n=4)
Age (year, min-max)	52 (38-63)	51 (35-60)	47 (35-61)
Sex (n, M/F)	6/4	7/3	4/0
Duration of diabetes (year, min-max)	4.2 (0.5-9.0)	8.7 (4.0-14.0)	4.3 (0.75-9.0)
HbA_{1c} (%-point, mean, SD)	8.1 (0.9)	8.0 (0.6)	8.1 (7.4)
Diet and exercise alone (n, %)	0 (0%)	1 (10%)	0 (0%)
1 antihyperglycemic agent (n, %)	9 (90%)	7 (70%)	3 (75%)
2 antihyperglycemic agent (n, %)	0 (0%)	2 (20%)	1 (25%)
3 antihyperglycemic agent (n, %)	1 (10%)	0	0

COVALENT-111 Study

Pharmacokinetics:

100 mg QD without food resulted in approximately 2.7-fold greater BMF-219 exposure than 100 mg QD with food



COVALENT-111 Study

Summary of Glycemic Results at Week 12 (8 Weeks after Final BMF-219 Dose)

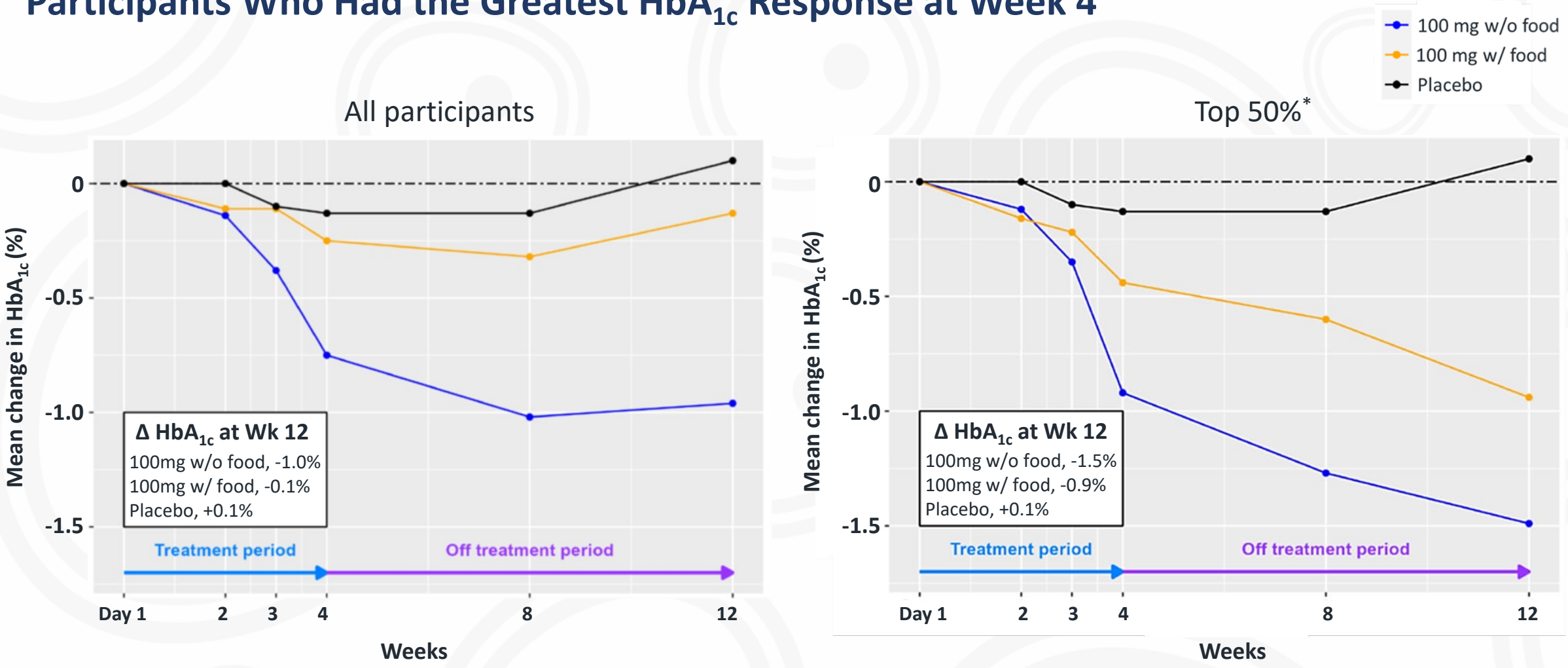
	BMF-219 100mg QD without food (n=10)	BMF-219 100mg QD with food (n=10)	Placebo (n=6)
Mean change in HbA_{1c} (%)	-1.0	-0.1	1.0
Mean placebo-corrected change in HbA_{1c} (%)	-1.1	-0.2	-
Percent of participants with any reduction in HbA_{1c}	90*	60	33
Percent of participants with ≥0.5% reduction in HbA_{1c}	80*	40	17
Percent of participants with ≥1.0% reduction in HbA_{1c}	40*	30	0
Percent of participants achieving HbA_{1c} <7.0%	40	0	0
Top 50%† mean change in HbA_{1c} (%)	-1.5	-0.9	-

*Note: Linear imputation used for single data point with results available before and after missing data

†Top 50% represents median participants with the greatest reduction in HbA_{1C} at Week 4

COVALENT-111 Study

Change in HbA_{1c} from Baseline at Week 12 for All Participants and for the 50% of Participants Who Had the Greatest HbA_{1c} Response at Week 4



*Top 50% represents median participants with the greatest reduction in HbA_{1c} at Week 4

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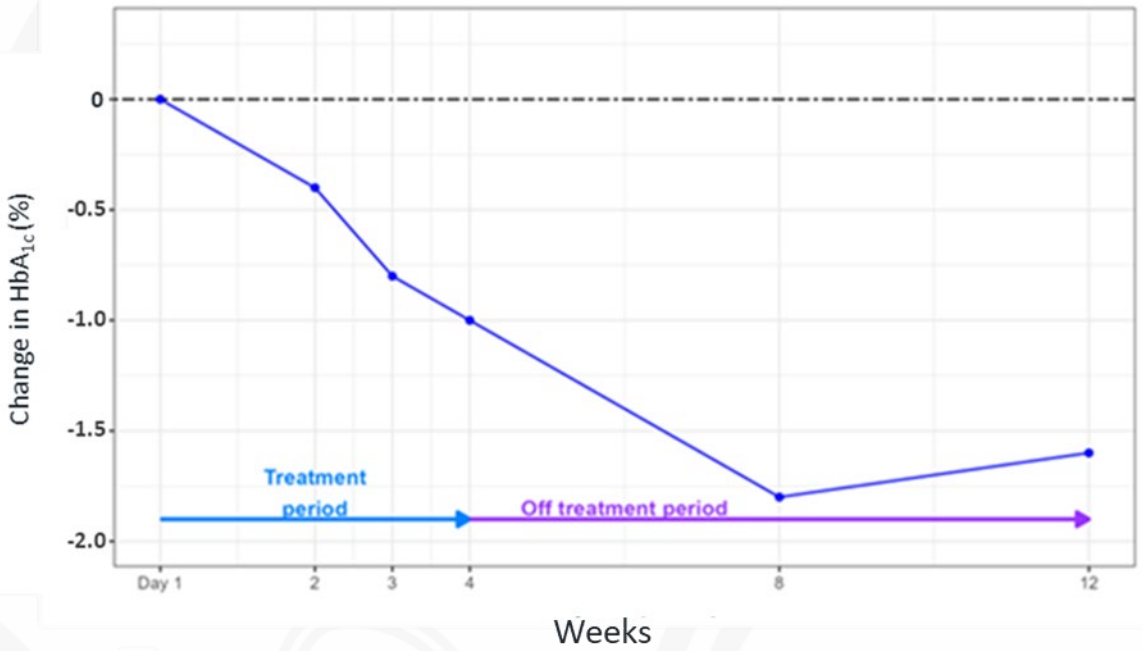
COVALENT-111 Study

Case Study: 51-Year-Old Man with 4-Year History of T2D

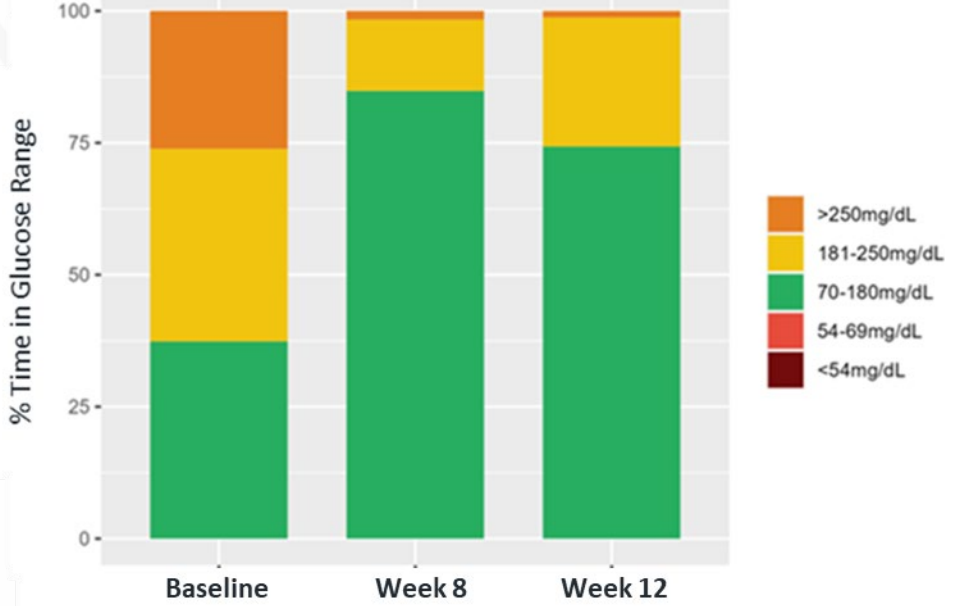
- 51-year-old man with 4-year history of T2D
- Metformin 500mg BID
- HbA_{1c} 8.9%; FPG 184 mg/dL; BMI 32 kg/m^2

- BMF-219 100 mg QD without food for 4 weeks
- Metformin continued
- No tolerability issues or adverse events reported

Change in HbA_{1c}



Continuous Glucose Monitoring



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COVALENT-111 Study

Safety and Tolerability

- BMF-219 was generally well tolerated and safe
- There were no severe or serious adverse events reported
- No dose discontinuations or modifications
- No symptomatic or clinically significant hypoglycemia

Summary and Conclusions

- In patients with T2D, 4 weeks of BMF-219 100 mg once-daily resulted in clinically meaningful improvements in glycemic control at Week 12 (8 weeks after the final dose)
- Higher BMF-219 exposure, as measured by BMF-219 AUC at Week 4, resulted in greater improvement in glycemic control
- BMF-219 was generally well tolerated and safe
- Higher BMF-219 doses and longer exposure (8-12 weeks) are being assessed in an ongoing Phase 2 study in patients with T2D and a study in patients with T1D has been initiated

Question & Answer Session

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Poster Presentation

- Thursday, Dec. 7th 6:35-7:30pm
- Exhibit Hall/Sierra Ballroom A
- Abstract #0088

Oral Presentation

- Friday, December 8th 7:30-9:00pm
- Sierra Ballroom B – Lobby Level

Tabletop Exhibit

- Thursday, December 7th
- Friday , December 8th
- Exhibit Hall/Sierra Ballroom A