

## **Corporate Presentation**

43rd Annual J.P. Morgan Healthcare Conference - January 15, 2025



#### Legal Disclaimer & Forward-Looking Statements

Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future business and financial performance of Biomea Fusion, Inc. (the "Company") and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "potential" or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including any projections of financial information or profitability, the initiation, timing and results of pending or future preclinical studies and clinical trials, the actual or potential actions of the Food and Drug Administration (FDA), the status and timing of ongoing research, development and corporate partnering activities, any statements about historical results that may suggest trends for the Company's business; any statements of the plans, strategies, and objectives of management for future operations and any statements of expectation or belief regarding future events, potential markets or market size, or technology developments. The Company has based these forward-looking statements on its current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company's control. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K filed with the Securities and Exchange Commission (the SEC), as well as discussions of potential risks, uncertainties, and other important factors in our other subsequent filings with the SEC. The forward-looking statements in this presentation are made only as of the date hereof. Except as required by law, the Company assumes no obligation and does not intend to update these forwardlooking statements or to conform these statements to actual results or to changes in the Company's expectations. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.



### **Biomea Fusion: A Diabetes and Obesity Medicines Company**





## A Long History of Developing Multi-Billion Dollar Drugs - Together



**Thomas Butler** Chairman & CEO

#### biomea •) FUSION

**Co-Founder** 

The FUSION<sup>™</sup> SYSTEM icovamenib\* **Co-Inventor** 

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

**Veklury**<sup>®</sup> remdesivir NUECTION **Co-Inventor** 



**Ramses Erdtmann** President & COO

biomea FUSION

**Co-Founder** imbruvicã<sup>®</sup>

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



Juan Frías, M.D. **Chief Medical** Officer once weekly mouniaro (tirzepatide) injection 0.5 mL 2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | 15 mg Jardiance<sup>®</sup> farxida (empagliflozin) tablets (dapagliflozin)







Chief of People

```
imbruviča®
(ibrutinib)
```

560, 420, 280, 140 mg tablets | 140, 70 mg capsules





**Heow Tan** Chief Technical & **Quality Officer** 

ZADAXIN

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









**Franco Valle Chief Financial** Officer









 $\bigcirc$ 

sitagliptin

## Icovamenib & BMF-650 (Oral Small Molecule GLP-1 RA) to Become Cornerstones of Our Metabolic Franchise

#### **Our Strategic Focus**

- Biomea to prioritize the development of icovamenib to address critical needs in the metabolic disease space
- Previously announced COV-111 positive topline data and in-vivo GLP-1 RA combination data supports focus
- Icovamenib development in type 2 diabetes to focus on patients with severe insulin deficiency and on patients treated with GLP-1 RA therapies

#### **Anticipated Key Milestones for 2025**

#### 1H: 2025

• Meet with the FDA to discuss icovamenib clinical development plan

#### 2H:2025

- COV-111 52-Week Data
- COV-112 Open Label Data
- IND filing for BMF-650
- Advance icovamenib in late-stage development for type 2 diabetes
- Initiate Phase I for BMF-650



#### **Icovamenib Value Proposition**

#### **Key Benefits of Icovamenib**

- First-in-class therapy with a novel mechanism of action
- Unique treatment effect: Durable treatment impact on beta cell function and incretin effect
- Oral, once-daily, 12-week treatment
- Has enhanced endogenous insulin production
- Has improved beta cell function\*
- Has promoted body weight loss \*
- Has increased proportion of lean mass / preserve lean mass\*

#### **Development Rationale**

- People with the lowest insulin production demonstrate the highest all-cause mortality, and the highest treatment failure
- Icovamenib has demonstrated superior treatment efficacy in this patient population
- Has promoted weight loss and increases muscle mass pct when combined with a GLP-1 RA therapy\*
- Supports GLP-1 RA combination, GLP-1 RA mono as maintenance post combination
- Supports Novel-Novel combo with oral small molecule GLP-1 RA

\*in preclinical studies



### 1 in 3 Americans will Develop Diabetes During Their Lifetime - CDC

In the U.S. 80% of people with diabetes will die from diabetes.<sup>1</sup> Premature mortality caused by diabetes results in an estimated 12-14 years of life lost.<sup>2</sup>

Diabetes creates one of the largest economic burdens on the U.S. health care system. **\$1 out of every \$4 in U.S. health care** costs is being spent on caring for people with diabetes.

There are over 60+ approved type 2 diabetes therapies but **none of them address the root cause of the disease.** 



### Over 800 million adults globally are living with diabetes<sup>4</sup>

## Today diabetes remains poorly controlled in approximately 50% of patients treated with standard of care agents<sup>4</sup>



- 1. Tabish Int J Health Sci. 2007 Jul;1(2):V–VIII.
- 2. National library of Medicine 1(2); 2007 Jul PMC3068646
- 3. CDC National Diabetes Statistics Report accessed January 2025
- 4. Zohu Lancet 2024; 404: 2077–93

#### **Challenges with Current Standard of Care**





## Current Diabetes Treatments: Despite Initial Effectiveness There is No Lasting Impact



Mean time to Loss of Glucose Control (A1c>7%)

Nathan, et al. N Engl J Med 2022;387:1063-107

• Average time to loss of glucose control ranges from less than 2 years to just over 2.4 years • Highlights the progressive nature of diabetes and the inability of current therapies to provide lasting glycemic control

#### Impact of tirzepatide on HbA1c: Sustained Reduction During Treatment, Rebound After Discontinuation



Kubota M, et al. Cureus. 2023 Oct 4;15(10)

• HbA1c levels rebound during the 52-week offtreatment phase, approaching baseline levels

- Continuous therapy is necessary to sustain glycemic control with current treatments
- There is a need for novel, durable solutions to improve long-term outcomes for diabetes patients



## Type 2 Diabetes Today - Chronic and Stacked Treatments to Overcome B-cell Loss





J.P. Morgan Healthcare Conference – January 15, 2025

## **Current Treatment Landscape in Type 2 Diabetes**



- Adults with type 2 diabetes see multiple agents over time
- Agents are prescribed to drive patients to glycemic target
- Agents are prescribed for extra-glycemic benefit
- Higher the baseline HbA1c, higher # of agents are needed

Current type 2 diabetes agents yield poor compliance

Oral is the preferred route versus injectable

Difficult to continue "medication for life"

Poor tolerability at the most effective dose levels



#### Adults with Type 2 Diabetes Cycle Through Many Therapies to Tackle Their Disease



### Type 2 Diabetes (T2D) is a Heterogeneous Disease – Two Core Drivers

Analysis from two independent 4,000 patient studies, (ADOPT and RECORD)

#### **INSULIN DEFICIENT DIABETES**

Severe insulindeficient diabetes (SIDD)

low BMI, severe betacell dysfunction, low insulin resistance, and high HbA1c, often with early onset and a high risk of complications.

**18%** 

Median HOMA-B	49%	
Median HbA1c	8.3%	
Median BMI	29 kg/m <sup>2</sup>	



39%

Median HOMA-B	64%
Median HbA1c	7.0%
Median BMI	29 kg/m <sup>2</sup>
	29 kg/m²

Adjusted from: https://www.thelancet.com/journals/landia/article/PIIS2213-8587(18)30051-2/abstract "Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables"

Ahlqvist et al. Diabetes 2020;69:2086-2093 | https://doi.org/10.2337/dbi20-0001

#### INSULIN RESISTANT DIABETES

Mild obesityrelated diabetes (MOD)

high BMI, insulin resistance, preserved beta-cell function, and a strong link to obesity with moderate HbA1c levels.

22%

Median HOMA-B	74%
Median HbA1c	7.2%
Median BMI	36 kg/m <sup>2</sup>

Severe insulin resistant diabetes (SIRD)

high BMI, severe insulin resistance, normal or elevated insulin production, and a high risk of cardiovascular disease and metabolic complications.



Median HOMA-B	101%		
Median HbA1c	7.0%		
Median BMI	34 kg/m <sup>2</sup>		



#### What is a SIDD patient?

- SIDD Patients have the lowest insulin production out of all adults with type 2 diabetes
- They represent the highest unmet medical need, displaying the highest all-cause mortality and worst CV outcomes
- They have the highest treatment failure rate among adults with type 2 diabetes
- They represent approximately 18% of the type 2 diabetes patient population (approx. 14M U.S./EU and 50 Million in Asia)
- They typically present with a BMI less than 32 kg/m<sup>2</sup> and a baseline HbA1c of at least 8.5%

Reduce the proportion of adults with diabetes who have an A1c value above 9 percent — D-03 -Healthy People 2030 | odphp.health.gov





### Icovamenib: First-in-Class Product Candidate for the Treatment of Diabetes







## **COVALENT-111**

Phase 2a Double-Blinded, Randomized Placebo Controlled Study in Type 2 Diabetes



## Phase 2a Double-Blinded, Randomized Placebo Controlled Study in Type 2 Diabetes (T2D)

An ongoing dose-finding study evaluating the addition of icovamenib in T2D patients with uncontrolled glycemia on standard of care

Patients receive icovamenib for a fixed treatment period, up to 12 weeks Durability of treatment effect is measured at Week 26 and Week 52



FUSION

#### Phase 2a Double-Blinded, Randomized Placebo Controlled Study in Type 2 Diabetes

A dose-finding study in T2D patients on standard of care with uncontrolled glycemia





## Icovamenib Displayed a 100% Response Rate and 1.5% Reduction in HbA1c at Week 26 in Patients Uncontrolled on Standard of Care



## Icovamenib Dosed at 100mg for 12 Weeks Demonstrated Statistically Significant **Reductions in HbA1c Across All Patient Segments**

MARD SIDD All (Arm B) -0.1 -Subtypes SIDD N=7 (Arm B) (Arm B) -0.2 -N=37 N=22 -0.3 -90 Million -0.4 -Patients HbA1c in U.S./EU -0.5 --0.50 \* 14 Million baseline, 45 Million (p=0.012) **Patients** -0.6 -Patients in in U.S./EU U.S./EU -0.7 -Severe % change from -0.8 insulindeficient -0.9 diabetes -1.0 -(SIDD) -1.05 \* -1.1 -(p=0.004) -1.2 -Severe Insulin -1.3 -\_\_ **Deficient Patient Population Showed** -1.4 -**Greatest Reduction** -1.5 --1.47 \* in HbA1c (p=0.038) -1.6 -

0.0 -

Placebo-Adjusted Mean Change in HbA1c at Week 26 Patients Uncontrolled with at Least 1 Prior Therapy

The SIDD Patient population is approximately 14 Million in the U.S./EU and 50 Million in Asia

Arm B: 12 weeks of dosing 100 mg QD

MARD/SIDD: Mild Age-Related and Severe Insulin-**Deficient Diabetes** (insulin deficient)

Ahlqvist et al. Diabetes 2020;69:2086–2093 | https://doi.org/10.2337/dbi20-0001



\*statistical significance

### HbA1c Reduction Has Continued Over Time – Outside the Treatment Period

#### Severe Insulin Deficient Diabetes (SIDD) Patients Mean Change in HbA1c – All Arms



**biomea** FUSION" We Aim to Cure"

#### **Summary Table of Efficacy Analysis**

Targeted Patients – Severe Insulin Deficient Patients (SIDD)

		Number of Patients	Reduction in HbA1C	P Value	
ARM B & C	All patients 12 weeks dosing	69	-0.42%	0.015	*
ARM B & C	SIDD/MARD (12 weeks)	22	-0.84%	0.008	*
ARM B & C	SIDD (12 weeks)	11	-1.17%	0.038	*
		Number of	Reduction in		
		Patients	HbA1C	P Value	
ARM B	All patients 12 weeks dosing	Patients 37	HbA1C -0.50%	P Value 0.012	*
ARM B ARM B	All patients 12 weeks dosing SIDD/MARD (12 weeks)	Patients 37 13	HbA1C -0.50% -1.05%	P Value 0.012 0.004	*

\* Statistically Significant

#### icovamenib has the potential to be the only disease modifying agent in diabetes

Arm B: 12 weeks of dosing at 100 mg QD Arm C: 8 weeks of 100 mg QD + 4 weeks of 100 BID MARD/SIDD: insulin deficient diabetes patients



Arm C: 2/4Arm B: 6/7SIDD ptsSIDD ptscompleted fullcompleted full12 weeks12 weeksJ.P. Morgan Healthcare Conference – January 15, 2025

### Prespecified SIDD Subgroup Performed In-line with GLP-1 RA Based Therapies

Currently Approved Type 2 Diabetes Agents w/Chronic Dosing						
Drug (Mechanism of Action)	Dosing Frequency	Medication Route	Observation Period	Mean HbA1c Reduction (placebo adj., %)		
ICOVAMENIB (Menin Inhibitor)	12 Weeks	Oral	Week 26	-1.5% (100mg)		
Ozempic (GLP 1 Agonist)	Chronic Dosing	Injectable	Week 30	-1.2 (0.5mg) -1.5 (1mg)		
Mounjaro (GLP-1/GIP Agonist)	Chronic Dosing	Injectable	Week 40	-1.7 (5mg) -1.6 (15mg)		
Jardiance (SGLT2 Inhibitor)	Chronic Dosing	Oral	Week 24	-0.7 (10mg) -0.9 (25mg)		
Januvia (DPP4 Inhibitor)	Chronic Dosing	Oral	Week 24	-0.8 (100mg)		
Summary		-	-	0.7% ~ 1.7%		

Note: data shown are not from head-to-head studies and no head-to-head studies have been conducted

Mounjaro FDA Label; Ozempic FDA Label; Jardiance FDA Label; Januvia Label



biomea We Aim to Cure" **FUSION** 

#### J.P. Morgan Healthcare Conference – January 15, 2025

### **Baseline HbA1c and BMI Can Enrich for the Desired Phenotype**

#### BMI and baseline HbA1c inclusion criteria can enrich for SIDD to over 90%





Adapted from Ahlqvist et al. Diabetes 2020;69:2086–2093 | https://doi.org/10.2337/dbi20-0001





## icovamenib

### in combination with GLP-1 based therapies



#### Menin Suppresses GLP-1 Receptor Transcript Levels



**Fig 1.** Menin, in complex with PRMT5, is a suppressor of GLP1-R expression, leading to reduced CREB phosphorylation and GLP1 pathway function. Decreased GLP1-R expression reduces insulin secretion and expression of beta cell proliferative genes leading to blunted glycemic control.





## Combination Treatment: Icovamenib Enhanced Responsiveness of Islets to GLP-1/GIP Dual Receptor Agonist - Tirzepatide





J.P. Morgan Healthcare Conference – January 15, 2025

## **Combination Treatment: Icovamenib Enhanced Responsiveness of Islets to GLP-1** Receptor Agonist - Semaglutide



J.P. Morgan Healthcare Conference – January 15, 2025

FUSION

**Combination Treatment: Icovamenib Enhanced Responsiveness of Islets to** the Small Molecule GLP-1 Receptor Agonists - Orforglipron and BMF-650



Glucose Stimulated Insulin Secretion



## Combination Treatment of Icovamenib and Low Dose Semaglutide Extends Marked Glycemic Control in Diabetic Animals



## Fasting blood glucose reduced to normal range in combination group



Significant reduction in combination group vs. semaglutide





#### J.P. Morgan Healthcare Conference – January 15, 2025

## Combination Treatment of Icovamenib and Low Dose Semaglutide Significantly Reduced Insulin Resistance and Elevates C-peptide Index



Significant reduction in combination group vs. semaglutide



#### **C-peptide Index**







J.P. Morgan Healthcare Conference – January 15, 2025

## Combination Treatment of Icovamenib and Low Dose Semaglutide Reduces Body Weight and Boosts Lean Mass





J.P. Morgan Healthcare Conference – January 15, 2025

14

28

Day 0

#### Icovamenib Drove Additional HbA1c Reduction in Patients on a GLP-1 RA Based Therapy

Icovamenib displays clinically meaningful 1.0% reduction in HbA1c in patients currently uncontrolled on GLP-1 RA based therapies

- 5/5 pts on 0.25mg to 1mg Ozempic lost additional weight when initiating icovamenib
- Up to 14% of additional weight loss observed at Week 26
- ~1.0% reduction in HbA1c of add-on therapy
- COV-111 did not have meal requirements during study



Placebo-Adjusted Mean Change in HbA1c at Week 26 Uncontrolled with GLP-1 Agonist-Based Therapy

Arm A: 8 weeks of dosing 100mg QD; Arm B: 12 weeks of dosing 100 mg QD; Arm C: 8 weeks of 100 mg QD + 4 weeks of 100 BID



### **Overview of Adverse Events Through 26 Weeks (mITT Population, N=225)**

Parameter	Arm A icovamenib (N=59)	Arm B icovamenib (N=54)	Arm C icovamenib (N=55)	Combined Arms icovamenib (N=168)	Combined Arms placebo (N=57)
Patients with ≥1 TEAE	18 (31)	19 (35)	13 (24)	50 (30)	18 (32)
SAEs	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Treatment Discontinuation due to AE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Study Discontinuation due to AE	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Deaths	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Data are n (%) TEAE, treatment-emergent adverse event SAE, serious adverse event



## Safety and Tolerability (mITT Population, N=225)

Parameter	Arm A icovamenib (N=59)	Arm B icovamenib (N=54)	Arm C icovamenib (N=55)	Combined Arms icovamenib (N=168)	Combined Arms placebo (N=57)
Diarrhea	4 (7)	2 (4)	1 (2)	7 (4)	0 (0)
Nausea	2 (3)	3 (6)	2 (4)	7 (4)	1 (2)
Hyperglycemia	1 (2)	4 (7)	1 (2)	6 (4)	3 (5)
Headache	0	3 (6)	1 (2)	4 (2)	3 (5)
ALT increase	2 (3)	0	2 (4)	4 (2)	0
AST increase	2 (3)	0	1 (2)	3 (2)	0

Data are n (%) of TEAE with ≥5% frequency in any arm and ALT or AST increase irrespective of incidence; mITT population (safety analysis set) TEAE, treatment-emergent adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase

Diarrhea: In icovamenib arms, all 7 events were Grade 1.

Nausea: In icovamenib arms, 6 of 7 events were Grade 1 and 1 event was Grade 2 (Arm B). In placebo arm, the 1 event was Grade 1.

Hyperglycemia: In icovamenib and placebo arms, all events were Grade 2.

Headache: In icovamenib arms, 3 of the 4 events were Grade 1 and 1 event was Grade 2 (Arm B). In the placebo arm, 3 of the 4 events were Grade 1 and 1 event was Grade 2.

ALT increase: In the icovamenib arms, 3 of the 4 events were Grade 1 and 1 event was Grade 2 (Arm A).

AST increase: In the icovamenib arms, all 3 events were Grade 1.

#### Icovamenib: Late-Stage Clinical Development in Type 2 Diabetes

#### Development of icovamenib to focus on two key patient segments

- Severe Insulin Deficient Diabetes Patients
- All Patients in Combination with a GLP-1 RA

#### 1. <u>Severely Insulin Deficient Diabetes (SIDD) Subjects</u>

We aim to improve glycemic control in the patient population with the highest unmet medical need in type 2 diabetes

#### 2. GLP-1 Combination

We aim to maximize the incretin effect while preserving lean mass and increasing body weight loss

- A. Subjects initiating a GLP-1 RA based therapy
- B. Subject uncontrolled on a GLP-1 RA based therapy



### **Biomea Fusion: A Diabetes and Obesity Medicines Company**





#### JP MORGAN 2025 Summary Advancing a First-in-Class, Precision-Based Treatment for Diabetes

- Icovamenib is an oral, once daily, simple, 12-week treatment for diabetes
- Icovamenib displayed comparable efficacy to a GLP-1 RA chronic therapy in the target patient population at Week 26, with just 12 weeks of treatment
- Icovamenib displayed in the pre-specified severe insulin deficient diabetes (SIDD) patients a placebo-adjusted mean reduction in HbA1c 1.5%
- The SIDD patient population represents the highest unmet medical need and approx 18% of the diabetes population
- Icovamenib was well tolerated with no study drug discontinuations due to TEAEs
- Icovamenib added on top of an existing GLP-1 RA therapy demonstrated a clinically meaningful 1% reduction in HbA1c in study participants with uncontrolled diabetes
- BMF-650 a next generation oral GLP-1 RA to treat diabetes and obesity is on schedule, advancing towards the clinic with IND filing in 2H 2025.



## **Company Financials (NASDAQ: BMEA)**

As of September 30, 2024

		Three Months Ended September 30, 2024
Operating expenses:		50, 2024
R&D		\$ 27,244
G&A		6,795
Total Operating Expenses		34,039
Loss from operations		(34,039)
Interest and other income, net		1,252
Net loss		\$ (32,787)
Other comprehensive loss:		
Changes in unrealized gain on short term investments, net		_
Comprehensive loss		\$ (32,787)
Net loss per common share, basic and diluted		\$ (0.91)
Weighted-average number of common shares used to compute basic and diluted net lo	oss per	
common share		36,220,736
Q3 Operating Expenses minus Stock Based Comp	\$29.3 M	
Cash, Cash Equivalents, Investments, and Restricted Cash as of 30 September 2024	\$88.3 M	



# Thank you

