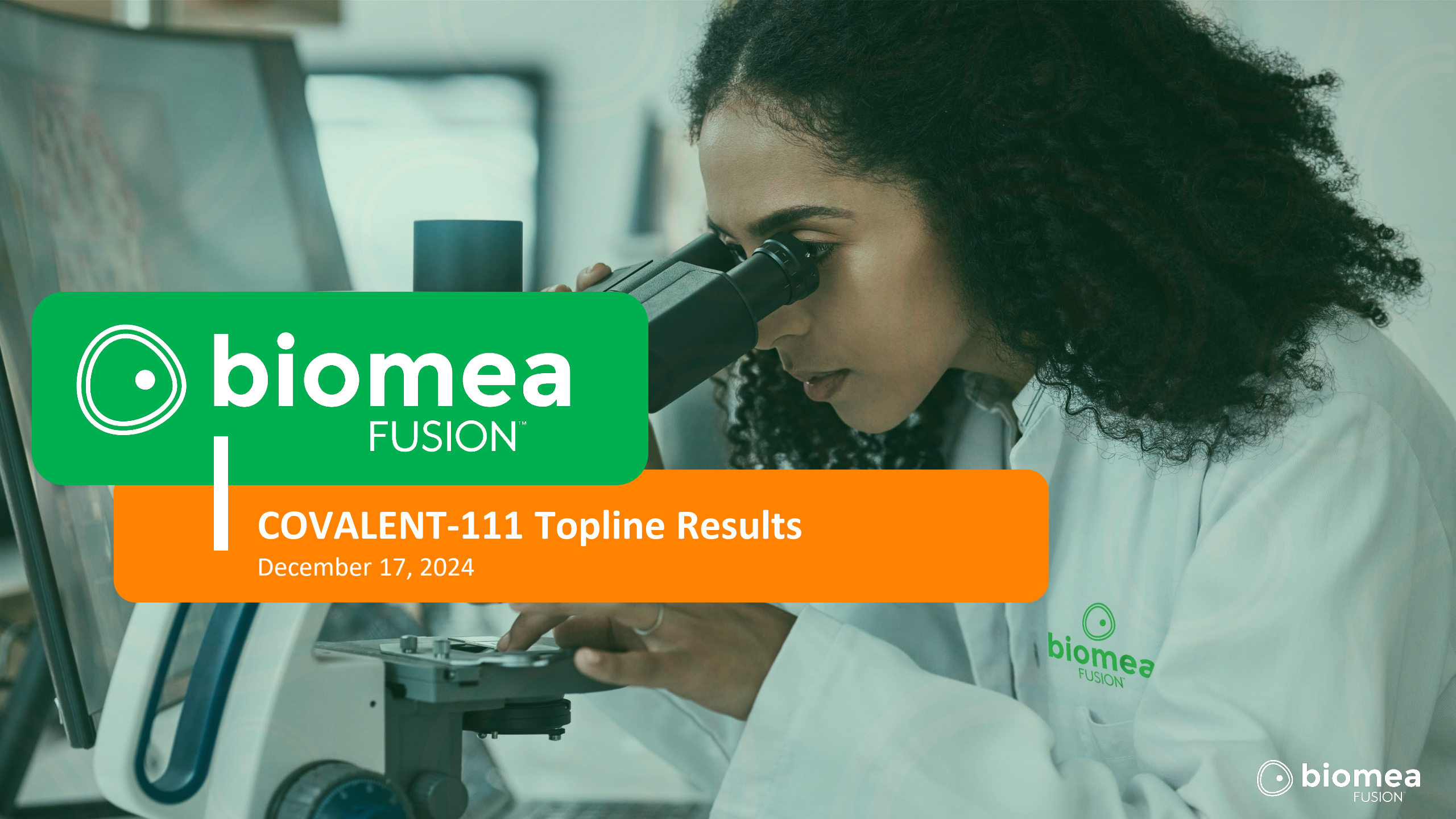
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COVALENT-111 Topline Results
December 17, 2024
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COVALENT-111 Topline Results - Conference Call December 17, 2024

Agenda

Introduction & Executive Summary		**Thomas Butler** *Chief Executive Officer, Chairman of the Board & Co-Founder of Biomea Fusion*
COVALENT-111 Topline Results		**Dr. Juan Pablo Frias** *Chief Medical Officer of Biomea Fusion*
Key Opinion Leader Insights		**Dr. Alex Abitbol** *LMC Healthcare, Endocrinologist, Scientific Advisory Board Member of Biomea Fusion*

Question & Answer Session

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 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; any statements of expectation or belief regarding future events, potential markets or market size, or technology developments, unfavorable global economic conditions, including inflationary pressures, market volatility, acts of war and civil and political unrest, and other factors affecting the Company's financial condition or operations. 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, as well as discussions of potential risks, uncertainties, and other important factors in our other subsequent filings with the Securities and Exchange Commission. 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 forward-looking 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.

Introduction & Executive Summary

COVALENT-111 Topline Results

December 17, 2024

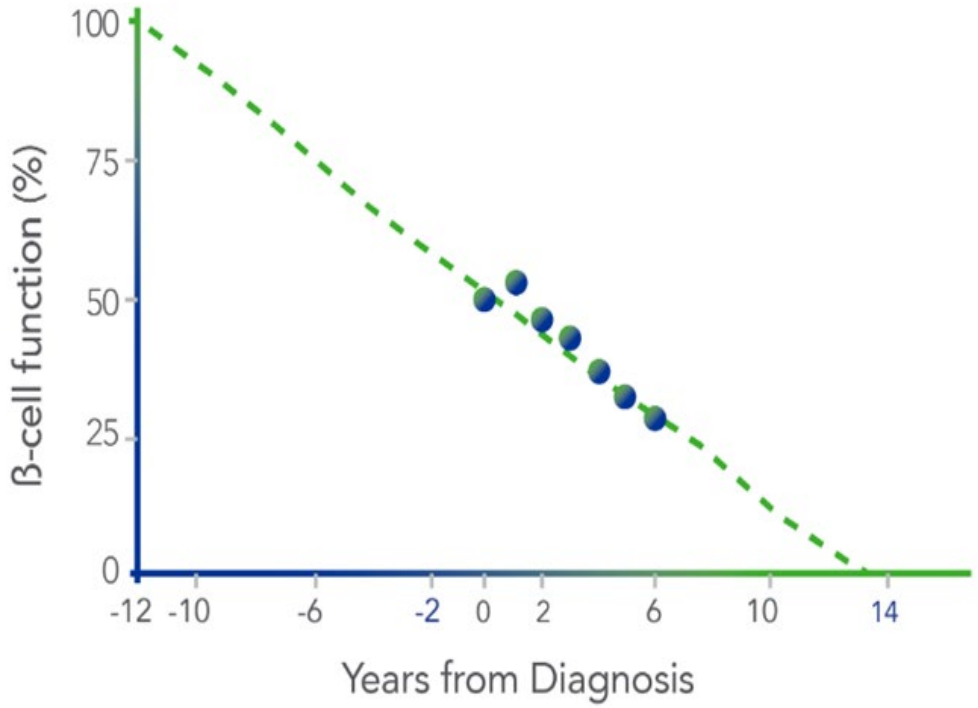
Thomas Butler
Chief Executive Officer,
Chairman of the Board & Co-Founder of Biomea Fusion

None of Today's Type 2 Diabetes Agents Address the Root Cause of Diabetes

- The Progressive Decline of Beta Cell Mass and Function -

Loss of Beta Cell Function

The Root Cause of Diabetes

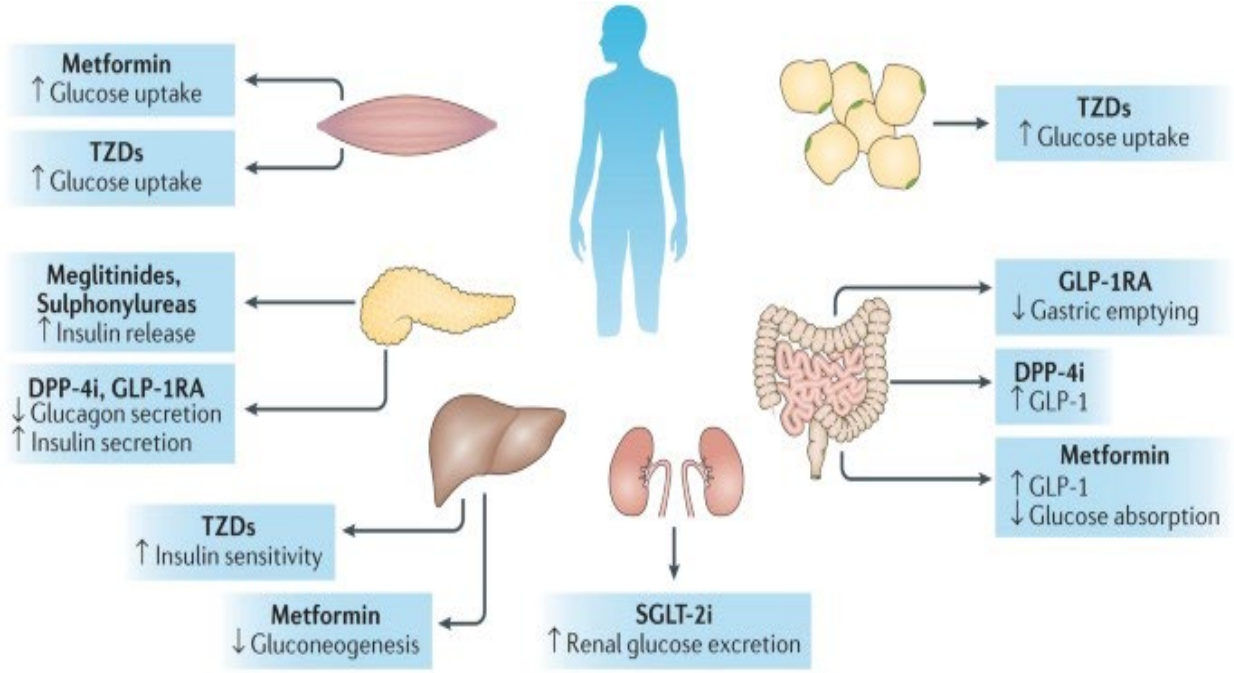


Adapted from DeFronzo RA. Diabetes. 2009;58(4):773-795.

Currently Approved Therapies

Targeting the Symptoms of Type 2 Diabetes

HYPERGLYCEMIA



Nat Rev Endocrinol 12, 337–346 (2016). https://doi.org/10.1038/nrendo.2016.51

COVALENT-111 Top-Line Results

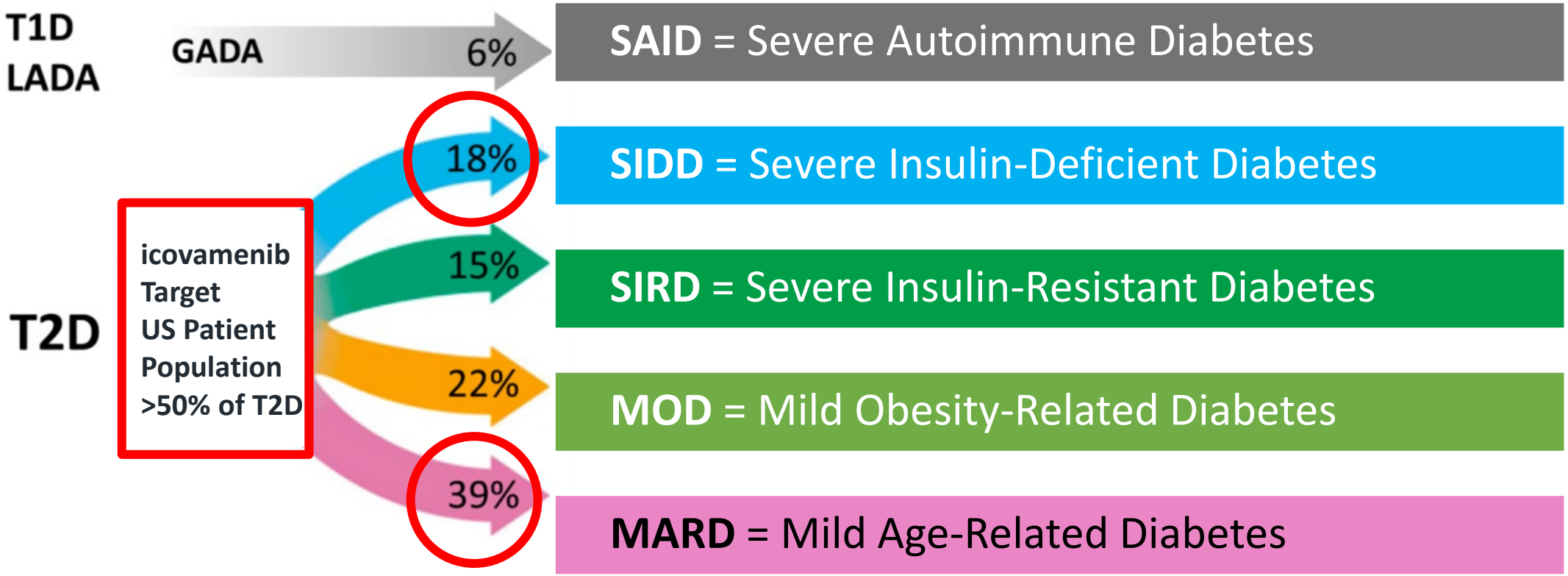
COVALENT-111 Topline Results

December 17, 2024

Dr. Juan Pablo Frias
Chief Medical Officer of Biomea Fusion

Heterogeneity in Type 2 Diabetes

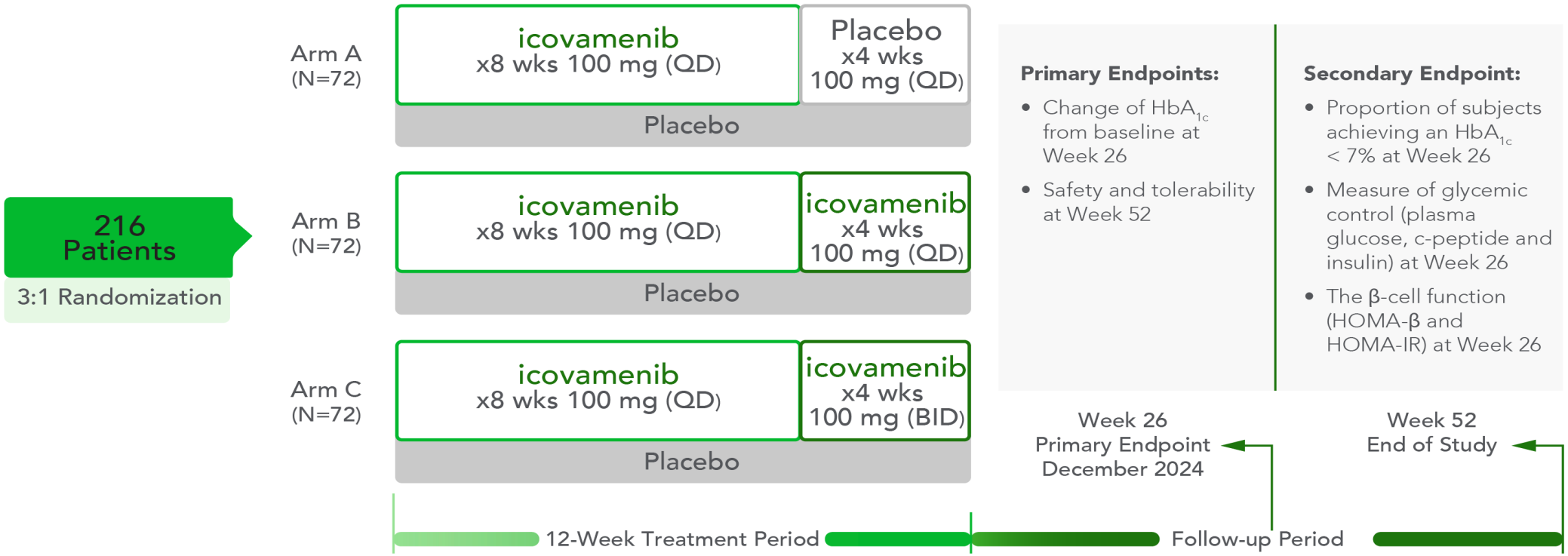
"While diabetes is diagnosed on the basis of a single metabolite, glucose, hyperglycemia can arise due to multiple complex etiological processes that can vary between individuals."[1,2]



1. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2019. Diabetes Care 2019;42(Suppl. 1):S13–S28
2. Ahlqvist E, et al. Diabetes 2020;69:2086–2093
3. Ahlqvist E, et al. Lancet Diabetes Endocrinol. 2018;6:361-369
4. Zaghlool SB, et al. Nat Commun. 2022;13:7121

Key Eligibility Criteria and Study Design

- Adults (18-65 years old) with T2D (<7 yr T2D duration)
- HbA1c 7.0-10.5%; BMI 25-40 kg/m^2
- Treated with up to 3 antidiabetic agents (excluding insulin or insulin secretagogues)
- N=72 participants per arm (3:1 ratio, icovamenib:Placebo)

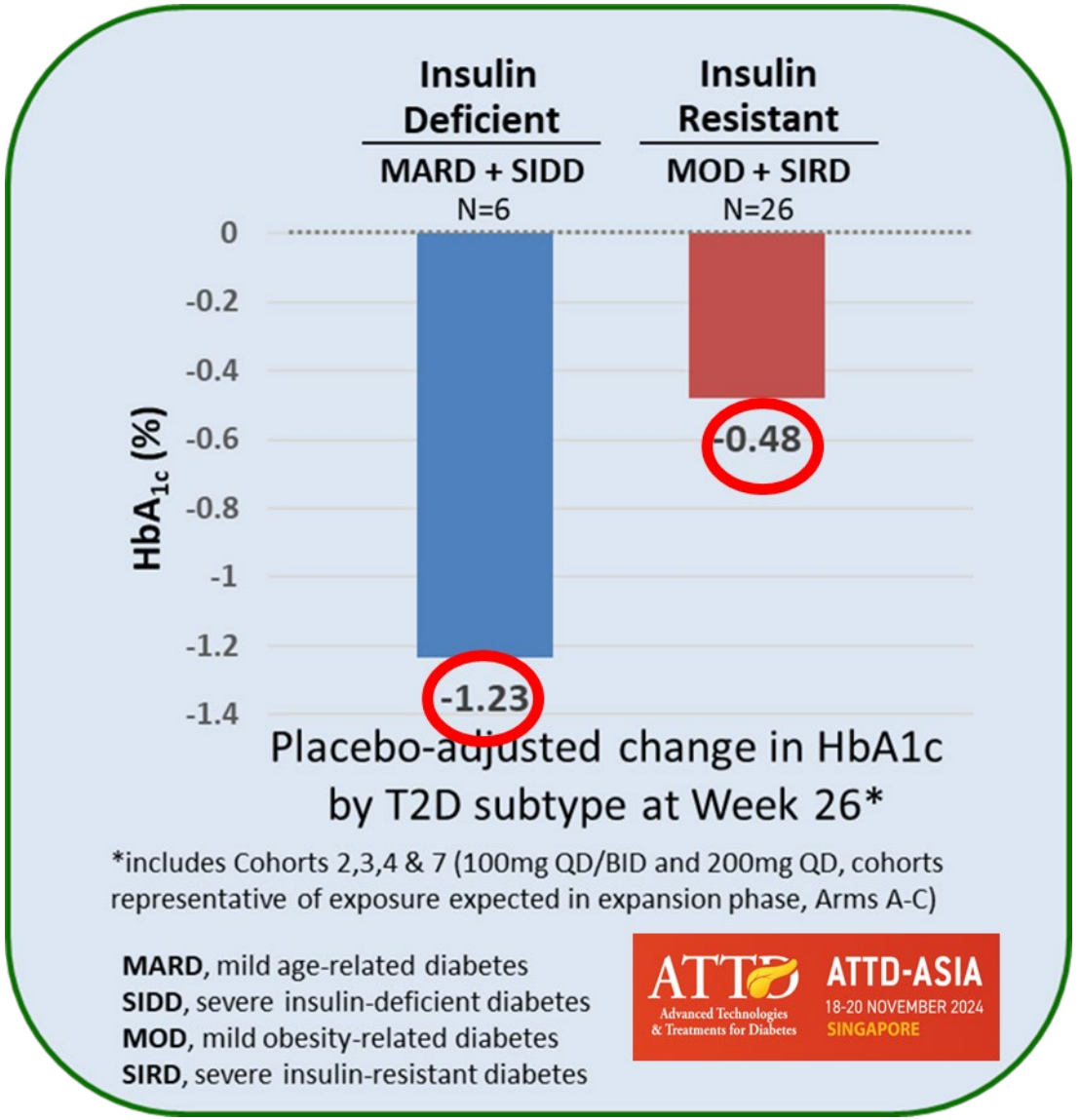


Placebo-Adjusted Change in HbA1c as Presented during ATTD ASIA 18 Nov. 2024

Week 26 from cohorts dosed during the Escalation Phase of COVALENT-111

SIDD and MARD are insulin deficient patients
They make up approx. 50% -70% of T2D

MOD and SIRD are insulin resistant patients
They make up approx. 30% - 50% of T2D



Frías JP, et al. (ATTD-Asia 2024, November 19, 2024)
Subtyping per Ahlqvist E, et al. Lancet Diabetes Endocrinol. 2018;6:361-369

Baseline Patient Population

- mITT population:
  Defined as all randomized participants who took at least one dose of study drug (N=225)

- The efficacy analysis focuses on those patients that completed the dosing period prior to the clinical hold and were “uncontrolled” on at least one anti-diabetic medication at baseline (N=168)
  Per Protocol Patients = 113
  Placebo patients = 55

- 10% of all patients enrolled were on no background therapy
  69% were on metformin alone
  15% were on two therapies
  5% were on three therapies

Baseline Demographics and Characteristics (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)
Age (yr)	55 (7)	55 (8)	53 (9)	55 (8)	54 (8)
Duration of T2D Diagnosis (yr)	4.2 (1.9)	4.6 (1.9)	4.2 (2.1)	4.3 (2.0)	4.2 (2.1)
Sex (% Female)	32	50	35	39	42
Ethnicity (%)					
Hispanic	54	39	45	46	67
Non-Hispanic	46	61	55	54	33
Race (%)					
Asian	12	9	9	10	7
Black	25	20	29	25	16
White	63	65	62	63	77
Other	0	6	0	2	0
HbA1c (%)	8.2 (1.0)	8.2 (1.0)	8.2 (1.0)	8.2 (1.0)	8.3 (0.9)
BMI (kg/m^2)	31.3 (4.6)	32.3 (4.5)	31.9 (4.8)	31.8 (4.6)	32.2 (4.3)
BMI <30 kg/m^2 (%)	42	30	36	36	30
BMI ≥30 kg/m^2 (%)	58	69	64	64	70

Mean (SD) or %

Placebo-Adjusted Change in HbA1c at 26 Weeks

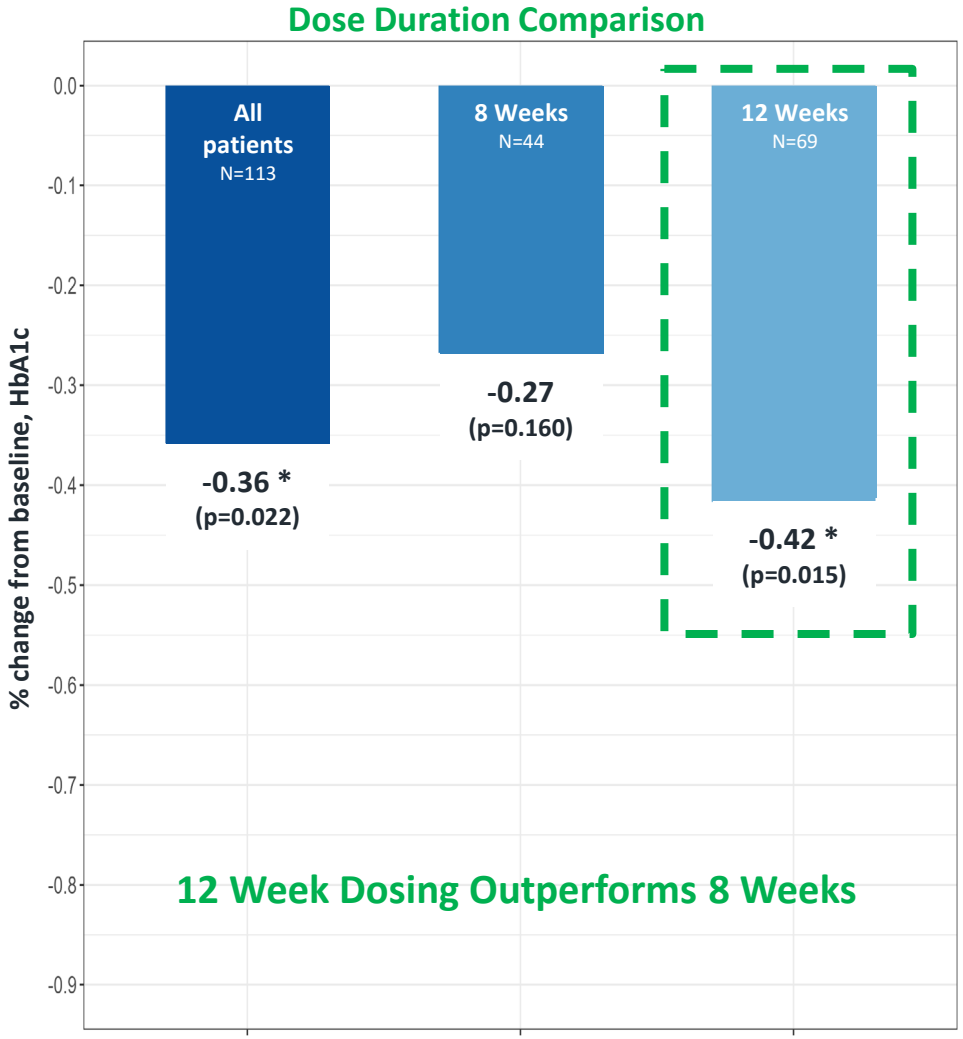
Per Protocol Patients Uncontrolled with at least 1 Medication at Baseline (N=113)

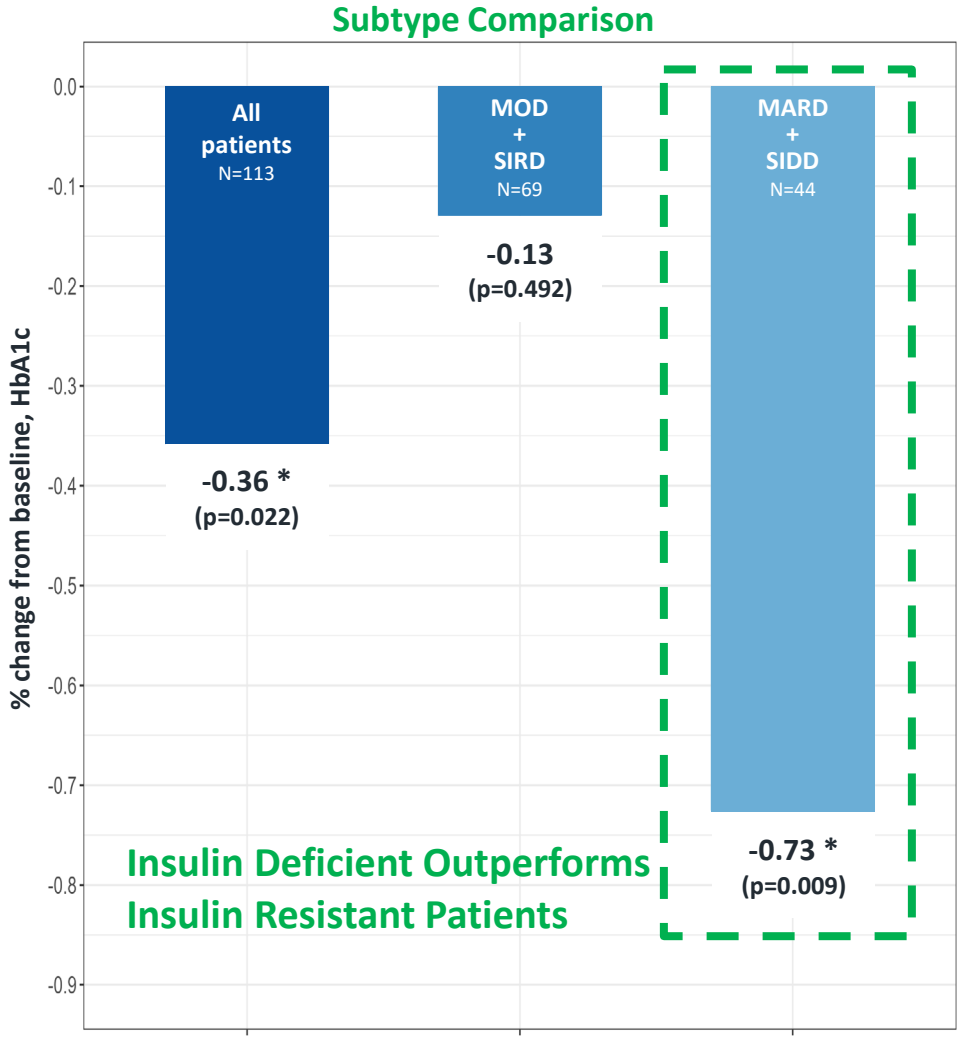
Arm A: 8 weeks of dosing 100mg QD
Arm B: 12 weeks of dosing 100 mg QD
Arm C: 8 weeks of 100 mg QD + 4 weeks of 100 BID

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

MOD/SIRD: Mild Obesity-Related Diabetes and Severe Insulin-Resistance Diabetes
(insulin resistant)

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





*statistical significance
Hypothetical estimand with LOCF imputation at Week 26

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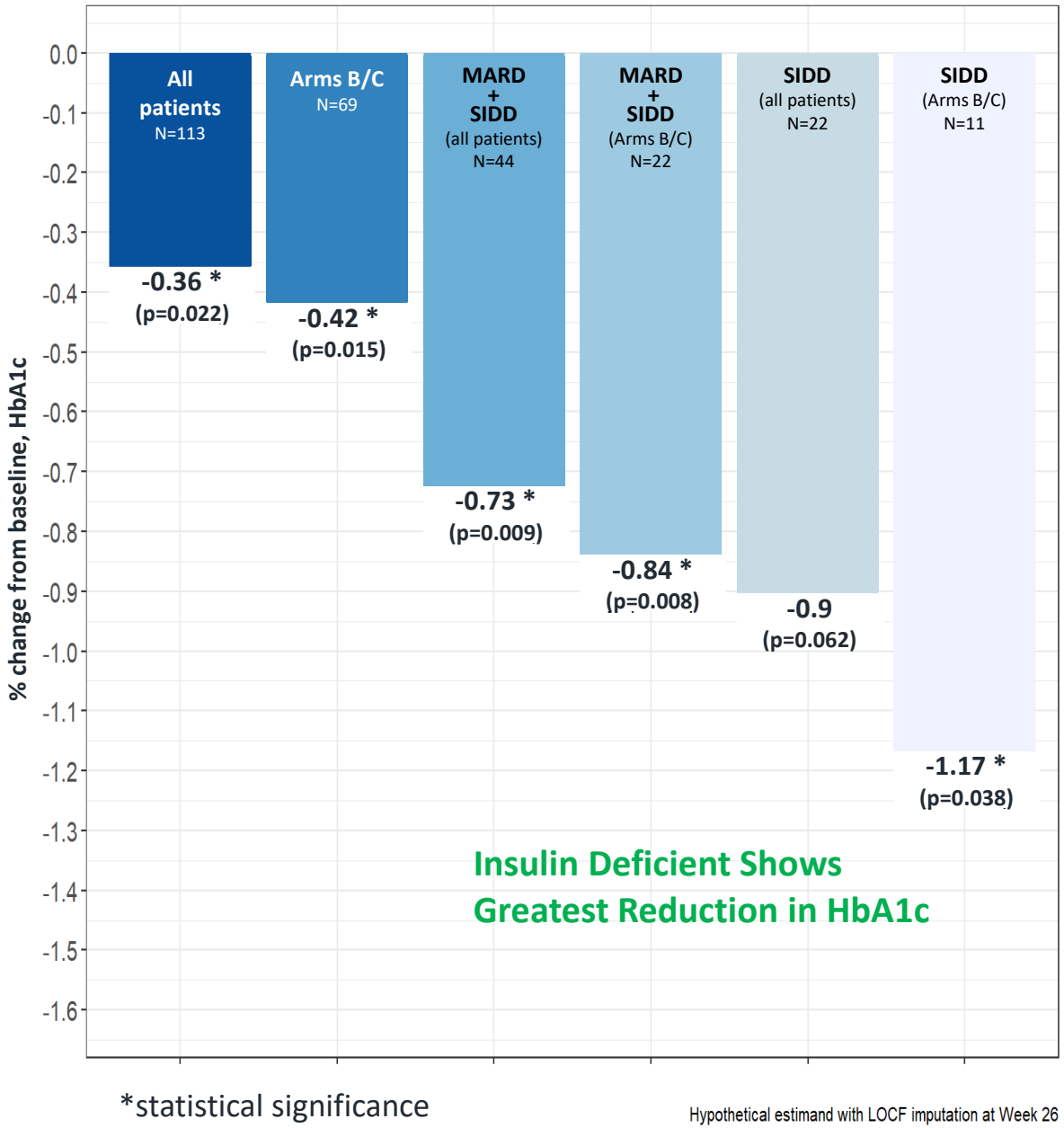
Placebo-Adjusted Mean Change in HbA1c at 26 Weeks in Per Protocol Patients Uncontrolled with at least 1 Medication at Baseline (N=113)

12 weeks of dosing with icovamenib (Arms B and C) in insulin deficient patients (MARD and SIDD) shows clinically meaningful and statistically significant mean reductions in HbA1c

Legend
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

MARD/SIDD: Mild Age-Related and Severe Insulin-Depleted Diabetes (Insulin deficient)
MOD/SIRD: Mild Obesity-Related Diabetes and Severe Insulin Resistance Diabetes (Insulin resistant)



*statistical significance

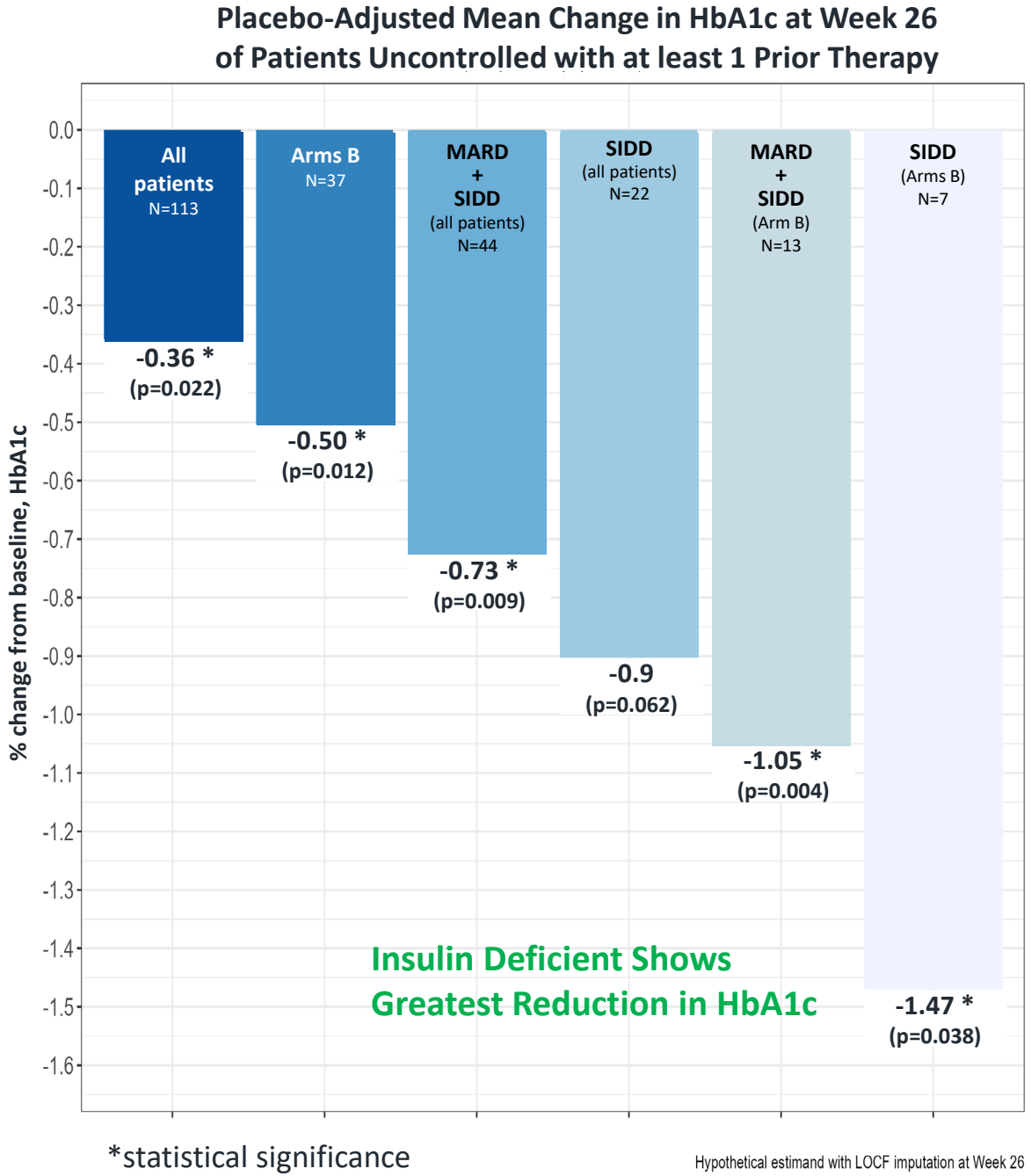
Hypothetical estimand with LOCF imputation at Week 26

Placebo-Adjusted Mean Change in HbA1c at 26 Weeks in Per Protocol Patients Uncontrolled with at least 1 Medication at Baseline (N=113)

100 mg for 12 weeks of dosing with icovamenib (Arm B) in insulin deficient patients (MARD and SIDD) shows the strongest effect across all groups

Legend
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

MARD/SIDD: Mild Age-Related and Severe Insulin-Depleted Diabetes (Insulin deficient)
MOD/SIRD: Mild Obesity-Related Diabetes and Severe Insulin Resistance Diabetes (Insulin resistant)



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Summary Table of Efficacy Analysis

Targeted Patients - Insulin Deficient

		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 Patients	Reduction in HbA1C	P Value	
ARM B	*All patients 12 weeks dosing*	**37**	**-0.50%**	**0.012**	*
ARM B	*SIDD/MARD (12 weeks)*	**13**	**-1.05%**	**0.004**	*
ARM B	*SIDD (12 weeks)*	**7**	**-1.47%**	**0.022**	*

** Statistically Significant*

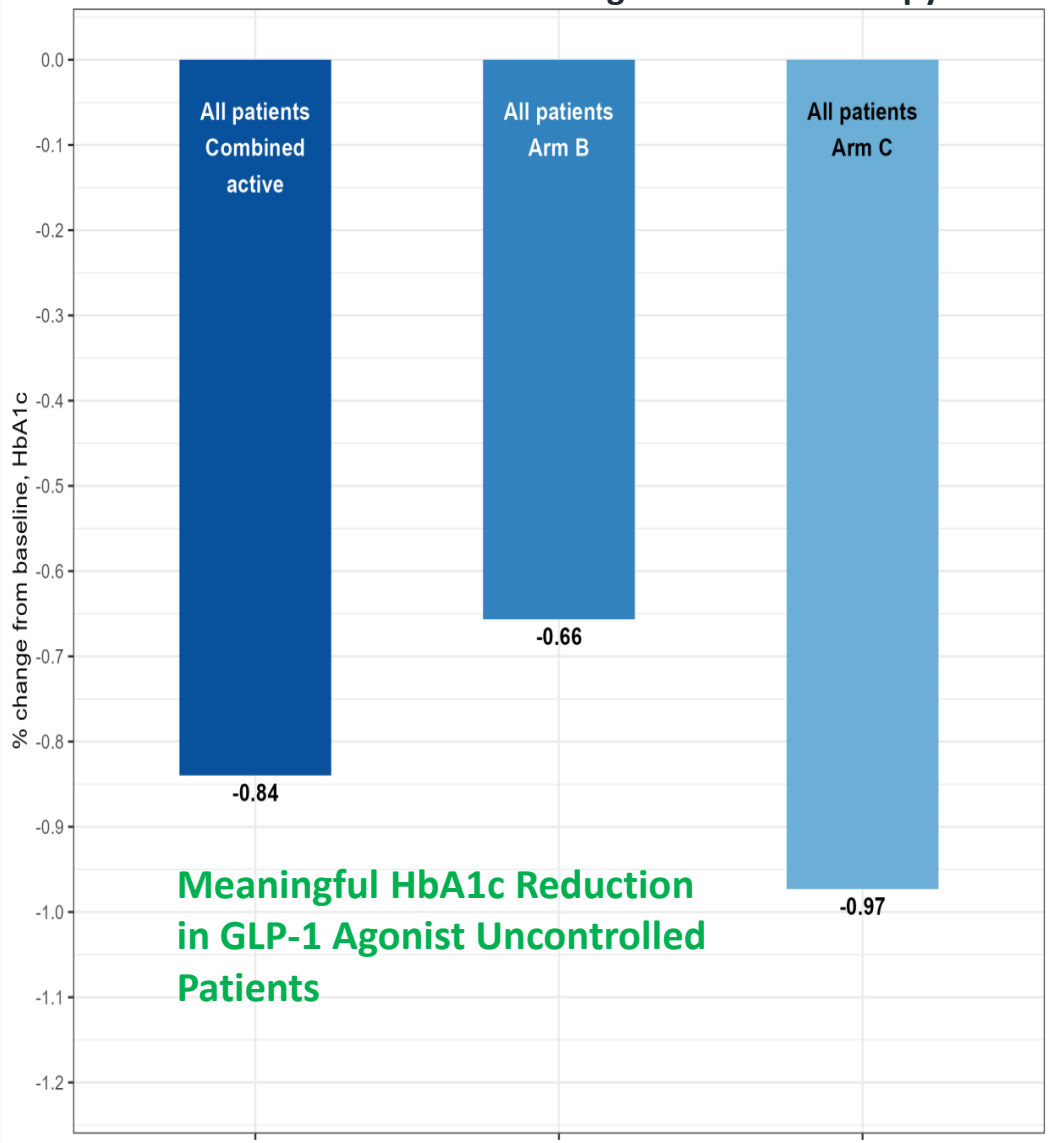
Legend
Arm A: 8 weeks of dosing 100mg QD
Arm B: 12 weeks of dosing 100 mg QD
Arm C: 8 weeks of 100 mg QD + 4 weeks of 100 BID

MARD/SIDD: Mild Age-Related and Severe Insulin-Depleted Diabetes (Insulin deficient)
MOD/SIRD: Mild Obesity-Related Diabetes and Severe Insulin Resistance Diabetes (Insulin resistant)

Interesting Finding in Other Subtypes

Insulin Resistant Patients

icovamenib displays clinically meaningful reductions in HbA1c also in the insulin resistant population (MOD) currently uncontrolled on GLP-1 agonist-based therapies



Legend
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

MARD/SIDD: Mild Age-Related and Severe Insulin-Depleted Diabetes (Insulin deficient)
MOD/SIRD: Mild Obesity-Related Diabetes and Severe Insulin Resistance Diabetes (Insulin resistant)

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 4 events were Grade 1.

Efficacy and Safety Analysis of Per Protocol Patient Population

- Icovamenib met the primary endpoint, displaying a clinically meaningful and statistically significant placebo-corrected reduction in HbA1c in the prespecified Per Protocol Patient population
- Icovamenib was well tolerated with no study drug discontinuations due to TEAEs
- Icovamenib displayed the greatest statistically significant mean HbA1c reduction in Patients dosed for 12 weeks and in the T2D subtypes characterized by insulin-deficiency.
  - SIDD (Arms B and C combined) mean HbA1c reduction = 1.17%
  - SIDD (Arm B) mean HbA1 reduction = 1.47%
- Icovamenib demonstrated also a clinically meaningful reduction in HbA1c in the T2D subtype characterized by insulin resistance (MOD), in study participants uncontrolled on a GLP-1 RA-based therapy at baseline

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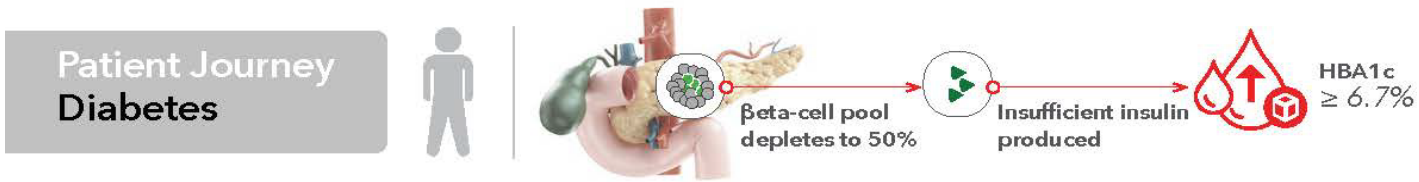
Key Opinion Leader INSIGHTS

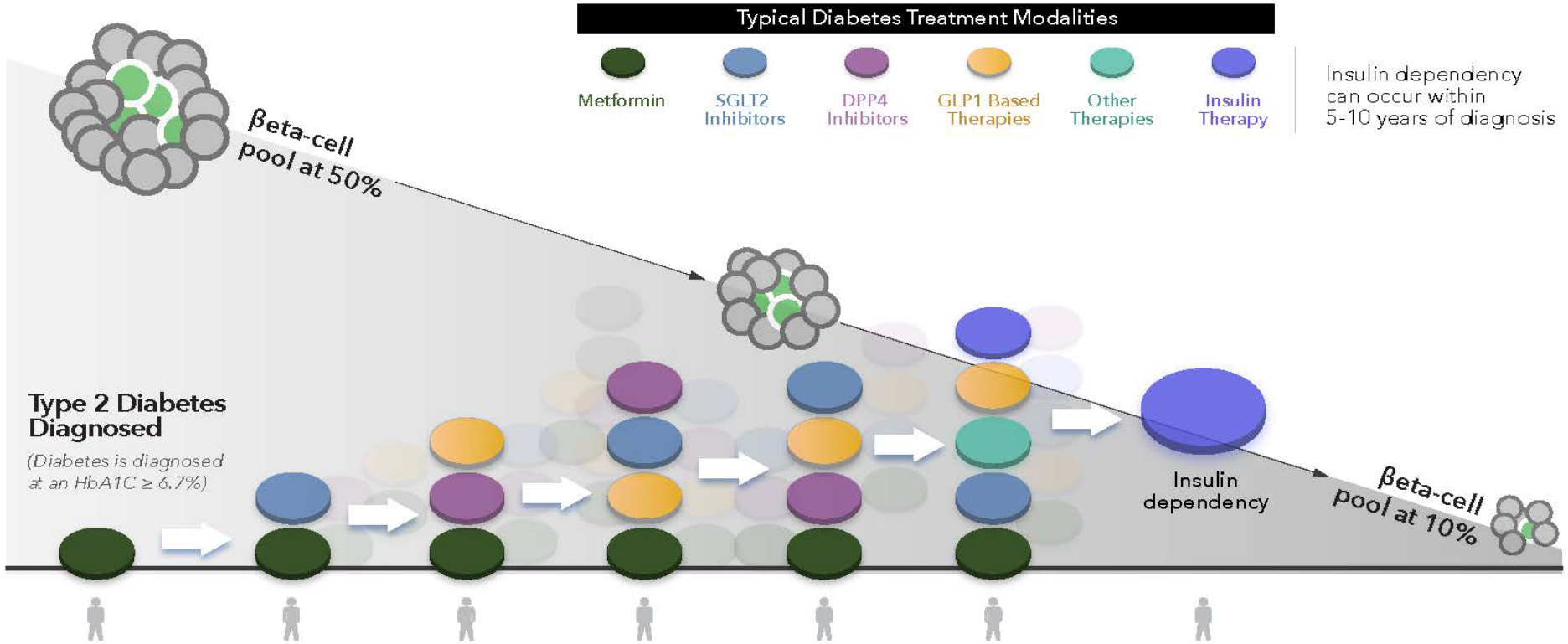
COVALENT-111 Topline Results

December 17, 2024

Dr. Alex Abitbol
Endocrinologist,
Scientific Advisory Board Member of Biomea Fusion

Typical Treatment Sequence/Stacking of Therapeutics in Type 2 Diabetes





- Initiation of therapy typically begins with an oral anti-diabetic drugs, like metformin, added/followed by DPP-4 Inhibitors, SGLT2 Inhibitors and oral / injectable GLP-1 based therapies
- Once all drugs and drug combinations are no longer supporting the patient then injection of pure insulin is the only available treatment ~30% of T2D patients take insulin

Type 2 Diabetes – Phenotypic Subtypes

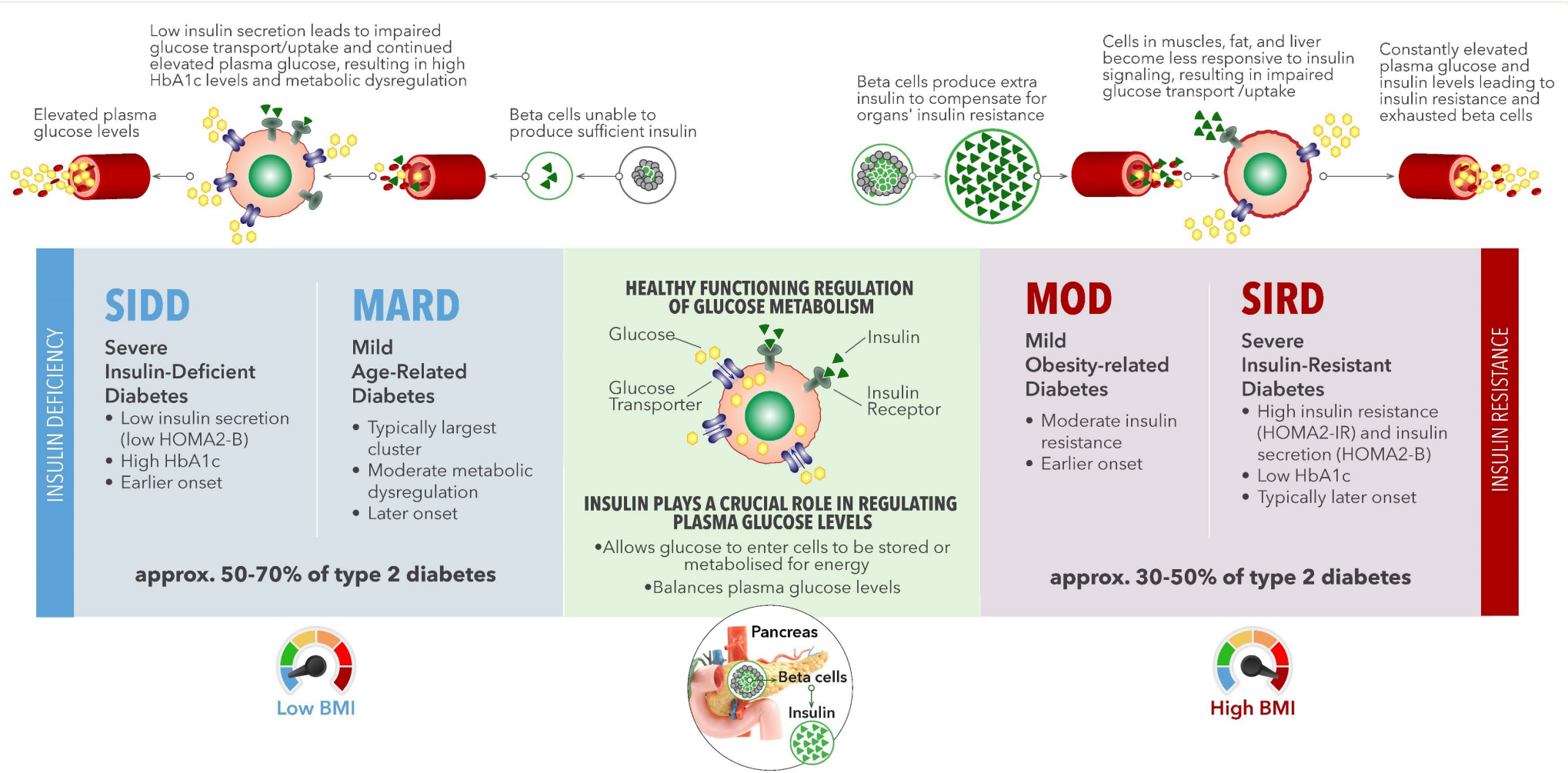
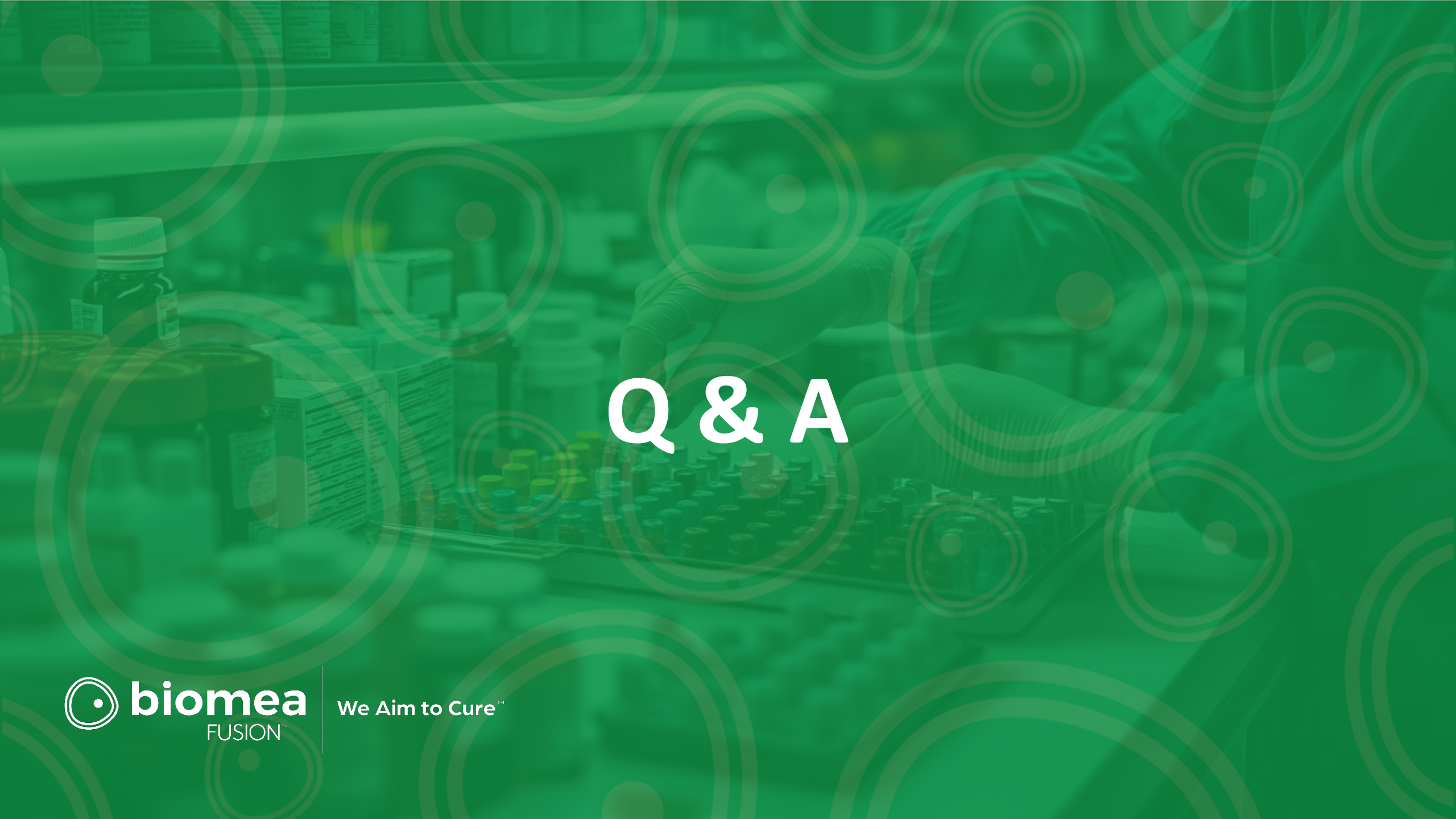


Fig. The phenotype characteristics were identified using five clinical parameters (age at diabetes onset, HbA1c, BMI, and measures of insulin resistance (HOMA2-IR) and insulin secretion (HOMA2-B)) to cluster adult-onset diabetes patients into four subtypes. These subtypes are associated with different risks of complications, comorbidities, genetic factors, and responses to treatment and may provide a framework for personalized and precision medicine in diabetes. *(Adjusted from Ahlqvist E et al. 2020 Diabetes)*



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