UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 17, 2024

Biomea Fusion, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-40335**	**82-2520134**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

900 Middlefield Road, 4th Floor **Redwood City, California**	**94063**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: 650 980-9099

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value	BMEA	The NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On December 17, 2024, Biomea Fusion, Inc. (the "Company") issued a press release announcing topline data from the Phase II portion of COVALENT-111, the Company's clinical trial of its lead product candidate, icovamenib, in type 2 diabetes. A copy of the press release is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K.

The Company also hosted a conference call and live webcast to discuss the interim clinical data on December 17, 2024 at 8:00 a.m. E.T. The Company has made available a slide presentation to accompany the call, a copy of which is furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Item 7.01, including Exhibit 99.1 and Exhibit 99.2 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On December 17, 2024, the Company reported positive topline results from its ongoing Phase II COVALENT-111 Study in patients with type 2 diabetes ("T2D"). Icovamenib met the primary endpoint, displaying a meaningful statistically significant placebo-corrected mean reduction in HbA1c at Week 26 in the prespecified per protocol patient population. Specifically, Arm B, the larger patient set from the two 12-week dosing arms, demonstrated a statistically significant reduction in HbA1c compared to placebo in all patients treated in the Per Protocol Patient population. In a post-hoc analysis of patients receiving at least one anti-diabetic medication, all active dosing arms combined as well as Arm B demonstrated a statistically significant reduction in HbA1c compared to placebo. Best response was achieved in target, beta-cell deficient patients on one or more antidiabetic agents at baseline (Arm B, n=7), showing a placebo-adjusted mean reduction of 1.47% in HbA1c at Week 26 with statistical significance, after only 12 weeks of dosing with 100 mg icovamenib. Additionally it was noted that icovamenib was generally well-tolerated, with no adverse-event related discontinuations, no hypoglycemic events, and no related serious adverse events.

The purpose of COVALENT-111 is to identify the optimal dose and the patient population to advance with icovamenib in late-stage clinical development. The topline data at Week 26 supports that 12-weeks of treatment of consistent 100 mg once-daily exposure, Arm B, was the best performing dose scheme, and the insulin-deficient patient population (SIDD and MARD patients) were the best responding subjects. The SIDD and MARD subgroups are known to demonstrate the lowest beta-cell function and lowest fasting c-peptide of the four phenotypes. COVALENT-111 is a double-blinded, randomized, 3:1 placebo-controlled trial that has enrolled adult patients diagnosed with T2D within the last 7 years, who had HbA1c levels between 7.0% and 10.5%, and a body mass index (BMI) between 25 and 40 kg/m^2. At baseline, all participants were receiving treatment with diet and exercise and were uncontrolled with up to three antidiabetic medications. Icovamenib was investigated in three different dosing arms with a primary follow up after 26 weeks, which the Company reported on: Arm A at 100mg QD (once daily) for 8 weeks, Arm B at 100mg QD for 12 weeks, and Arm C at 100 mg QD for 8 weeks and 100mg BID (twice daily) for 4 weeks. The study enrolled a total of 225 patients who received at least one dose of icovamenib and were considered evaluable for the modified intent-to-treat population. Dosing was interrupted for many patients due to an interim clinical hold imposed by the U.S. Food and Drug Administration (the "FDA"). This topline efficacy analysis focuses on those patients who had completed at least 80% of their assigned dosing schedule prior to the clinical hold, the Per Protocol Patient population, and includes a post-hoc analysis of the subgroup (90% of Per Protocol Patients) who were treated with one or more anti-hyperglycemic therapies at baseline (n=168).

Based on these initial results and the upcoming 52-week readout in the second half 2025, we plan to engage with the FDA to discuss the data. This meeting will provide an opportunity to align with FDA on how to further advance icovamenib as a first-in-class menin inhibitor therapy for T2D.

Cautionary Note Regarding Forward Looking Statements

This Current Report on Form 8-K and certain of the materials filed or furnished herewith contain certain statements which are not historical facts and are considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will," and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this contained in this Current Report on Form 8-K or the materials furnished or filed herewith that are not statements of historical fact, including statements regarding the clinical and therapeutic potential of the Company' product candidates and development programs, their mechanism of action, and their potential relative to approved products marketed by third parties; the potential benefits to future trial design and program development of subtyping diabetes patients; the Company's research, development and regulatory plans, including its plans to engage with the FDA regarding clinical data from COVALENT-111, the progress of the Company's ongoing and upcoming clinical trials and the timing of such events may be deemed to be forward-looking statements. The Company intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. Any forward-looking statements in this contained in this Current Report on Form 8-K or the materials furnished or filed herewith are based on the Company's current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, including the risk that preliminary or interim results of preclinical studies or clinical trials may not be predictive of future or final results in connection with future clinical trials that the Company's analysis of preliminary or interim data in subsets of patients may not be predictive of the Company's product candidate in a broader patient population, and the risk that the Company may encounter delays in preclinical or clinical development, patient enrollment and in the initiation, conduct and completion of the Company's ongoing and planned clinical trials and other research and development activities. These risks concerning Biomea Fusion's business and operations are described in additional detail in its periodic filings with the U.S. Securities and Exchange Commission (SEC), including its most recent periodic report filed with the SEC and subsequent filings thereafter. Biomea Fusion explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release titled "Biomea Fusion Announces Positive Topline Results from Ongoing Phase II COVALENT-111 Study in Patients with Type 2 Diabetes," issued by Biomea Fusion, Inc. on December 17, 2024, furnished herewith.
99.2	Corporate presentation titled "Covalent-111 Topline Results" dated December 17, 2024, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Biomea Fusion Inc.

Date: December 20, 2024

By: /s/ Thomas Butler
Thomas Butler
Principal Executive Officer

Biomea Fusion Announces Positive Topline Results from Ongoing Phase II COVALENT-111 Study in Patients with Type 2 Diabetes

December 17, 2024

- *Icovamenib met the primary endpoint, displaying a meaningful statistically significant placebo-corrected mean reduction in HbA1c in the prespecified per protocol patient population*
- *Best response achieved in target, beta-cell deficient patients on one or more antidiabetic agents at baseline, showing a placebo-adjusted mean reduction of 1.47% in HbA1c at Week 26 with statistical significance, after only 12 weeks of dosing icovamenib with 100 mg*
- *Icovamenib was well-tolerated, with no adverse-event related discontinuations, no hypoglycemic events and no serious adverse events*

REDWOOD CITY, Calif., Dec. 17, 2024 (GLOBE NEWSWIRE) — Biomea Fusion, Inc. ("Biomea" or "Biomea Fusion" or "the Company") (Nasdaq: BMEA), a clinical-stage biopharmaceutical company dedicated to discovering and developing oral covalent small molecules to improve the lives of patients with diabetes, obesity, and genetically defined cancers, today announced positive topline results from the ongoing COVALENT-111 study, evaluating the efficacy, safety and tolerability of icovamenib in patients with type 2 diabetes (T2D).

COVALENT-111 is a double-blinded, randomized, 3:1 placebo-controlled trial that has enrolled adult patients diagnosed with T2D within the last 7 years, who had HbA1c levels between 7.0% and 10.5%, and a body mass index (BMI) between 25 and 40 kg/m². At baseline, all participants were receiving treatment with diet and exercise and were uncontrolled with up to three antidiabetic medications. Icovamenib was investigated in three different dosing arms with a primary follow up after 26 weeks which we are reporting on today: Arm A at 100mg QD (once daily) for 8 weeks, Arm B at 100mg QD for 12 weeks, and Arm C at 100 mg QD for 8 weeks and 100mg BID (twice daily) for 4 weeks. The study enrolled a total of 225 patients that received at least one dose of icovamenib and were considered evaluable for the modified intent-to-treat population (mITT). Dosing was interrupted for many patients due to an interim clinical hold imposed by the U.S. Food and Drug Administration (FDA). This topline efficacy analysis focuses on those patients who had completed at least 80% of their dosing prior to the clinical hold and who at baseline were treated with one or more anti-hyperglycemic therapy, the Per Protocol Patient population (n=168).

The study showed positive topline results at Week 26, demonstrating statistically significant and clinically meaningful reductions in HbA1c, the gold standard for assessing glycemic control in T2D. In patients who completed dosing per protocol and were suboptimally controlled at baseline on one or more prior agent, icovamenib showed meaningful reductions in HbA1c with statistical significance in all major categories. Here icovamenib showed a mean reduction in HbA1c of 0.36% (p=0.022). The strongest performing arm was Arm B (icovamenib dosed at 100mg QD for 12 weeks) with a mean HbA1c reduction of 0.5% (p=0.012). In the analysis of the T2D phenotypes, icovamenib showed further improved reduction in the insulin deficient patients. Within the mild age-related diabetes (MARD) and severe insulin-deficient diabetes (SIDD) patients the mean HbA1c reduction was 0.73% (p=0.009) and in Arm B these patient subtypes reduced the mean HbA1c by 1.05% (p=0.004). Patients who were considered most severe insulin deficient, the SIDDs, demonstrated the best response with a mean HbA1c reduction in Arm B of 1.47% (p=0.022). Importantly, MARD and SIDD represent more than 50% of the US patient population. Of note, in the patients that failed on a GLP-1 based therapy an HbA1c reduction of 0.84% was demonstrated.

Throughout the 26-week period there were no serious adverse events or discontinuations due to adverse events observed. No drug-to-drug interactions were observed during the study. Overall, icovamenib was well tolerated and demonstrated a favorable safety profile in the COVALENT-111 study.

The company used clinical biomarker data to categorize participants into prespecified subtypes (SIDD, MARD, SIRD, and MOD) during screening:

- **SIDD**: Characterized by low insulin secretion, high HbA1c, and reduced beta-cell function (low HOMA-B)
- **MARD**: Characterized by mild age-related diabetes, typically older age at onset, with mild hyperglycemia and fewer metabolic disturbances
- **SIRD**: Defined by significant insulin resistance, high HOMA-IR, and potential complications like liver disease
- **MOD**: Identified by mild obesity, less severe insulin resistance, and relatively mild hyperglycemia

The study will further assess secondary endpoints (e.g., HbA1c reduction, fasting glucose, HOMA-B and HOMA-IR) within each pre-specified subtype to identify distinct patterns of response. Analysis of the full Phase II COVALENT-111 data is ongoing and Biomea Fusion plans to present detailed results at an upcoming medical conference in 2025.

"I am very excited about these initial results we are presenting today. We believe we now have a defined path to further develop icovamenib in diabetes. We have identified the optimal dose, the patient population to target, and most importantly, we now have strong efficacy and safety data," says Thomas Butler, CEO and Chair of Biomea Fusion. "These results validate our approach and highlight that icovamenib has the potential to address an aspect of diabetes that no other current therapy can. We are excited to continue advancing this promising molecule and bring a new treatment option to patients who need it most."

Based on these initial results and the upcoming 52-week readout in the second half 2025, Biomea plans to engage with the FDA to discuss the data. This meeting will provide an opportunity to align with FDA on how to further advance icovamenib as a first-in-class menin inhibitor therapy for T2D.

“The topline data from the COVALENT-111 Phase II study are incredibly promising, showing that icovamenib delivers significant and clinically meaningful reductions in HbA1c. We now understand the duration of dosing and target patient population. This study confirms the potential of menin inhibition as a novel mechanism for treating type 2 diabetes. Achieving a HbA1c reduction of this magnitude without chronic treatment is paradigm shifting in diabetes therapy,” said Dr. Juan Pablo Frias, Chief Medical Officer of Biomea Fusion.

Conference Call and Webcast Details

Webcast of Biomea’s investor update on Tuesday, December 17, 2024, at 8:00 am EST will be available to registered attendees under the Investors and Media section of the company’s website at https://investors.biomeafusion.com/news-events/events. A replay of the presentation will be archived on Biomea’s site following the event.

The clinical hold which was placed on icovamenib was due to data FDA had observed during the Escalation Phase, when higher dosages of icovamenib were tested. The clinical hold led to a disruption for patients enrolled in the COVALENT-111 study. It had a more profound impact on the ongoing Phase II COVALENT -112 study in type 1 diabetes, where over 90% of the targeted patient population were not able to complete dosing due to the clinical hold. We are therefore planning to continue the enrollment in COVALENT-112 so we can provide a more complete update in this patient population in 2025.

About Icovamenib

Icovamenib is an investigational, orally bioavailable, potent, and selective covalent inhibitor of menin. The molecule was built using Biomea Fusion’s FUSION™ System and is designed to regenerate insulin-producing beta cells with the aim to cure diabetes. Icovamenib’s proposed mechanism of action in diabetes is to enable the proliferation, preservation, and reactivation of a patient’s own healthy, functional, insulin-producing beta cells. As the potentially first disease-modifying therapy for T1D and T2D, icovamenib could become an important addition and complement to the diabetes treatment landscape once it has successfully completed its ongoing clinical studies.

About Menin’s Role in Diabetes

Loss of functional beta cell mass is a core component of the natural history in both types of diabetes — type 1 diabetes (mediated by autoimmune dysfunction) and T2D (mediated by metabolic dysfunction). Beta cells are found in the pancreas and are responsible for the synthesis and secretion of insulin. Insulin is a hormone that helps the body use glucose for energy and helps control blood glucose levels. In patients with diabetes, beta cell mass and function have been observed to be diminished, leading to insufficient insulin secretion and hyperglycemia. Menin is thought to act as a brake on beta cell turnover and growth, supporting the notion that inhibition of menin could lead to the regeneration of normal, healthy beta cells. Based on these and other scientific findings, Biomea is exploring the potential for icovamenib-mediated menin inhibition as a viable therapeutic approach to potentially halt or reverse progression of T2D.

About Type 2 Diabetes

Diabetes is considered a chronic health condition that affects how the body turns food into energy and results in excessive glucose in the bloodstream. Over time, this can cause serious health problems and damage vital organs. Most people with diabetes have a shorter life expectancy than people without this disease. The Centers for Disease Control and Prevention estimates about two in five adults in the United States are now expected to develop diabetes during their lifetime. More than 37 million people of all ages (about 11% of the US population) have diabetes today. 96 million adults (more than one in three) have pre-diabetes, blood glucose levels that are higher than normal but not high enough to be classified as diabetes. Diabetes is also one of the largest economic burdens on the United States health care system with one dollar out of every four dollars in US health care costs spent on caring for people with diabetes. Despite the current availability of many diabetes medications, there remains a significant need in the treatment and care of patients with diabetes.

About Biomea Fusion

Biomea Fusion is a clinical-stage biopharmaceutical company focused on the discovery and development of oral covalent small molecules to improve the lives of patients with diabetes, obesity, and genetically defined cancers. A covalent small molecule is a synthetic compound that forms a permanent bond to its target protein and offers a number of potential advantages over conventional non-covalent drugs, including greater target selectivity, lower drug exposure, and the ability to drive a deeper, more durable response.

We are utilizing our proprietary FUSION™ System to discover, design and develop a pipeline of next-generation covalent-binding small-molecule medicines designed to maximize clinical benefit for patients. We aim to have an outsized impact on the treatment of disease for the patients we serve. We aim to cure.

Visit us at biomeafusion.com and follow us on LinkedIn, X, and Facebook.

Forward-Looking Statements

Statements we make in this press release may include statements which are not historical facts and are considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These statements may be identified by words such as “aims,” “anticipates,” “believes,” “could,” “estimates,” “expects,” “forecasts,” “goal,” “intends,” “may,” “plans,” “possible,” “potential,” “seeks,” “will,” and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact, including statements regarding the clinical and therapeutic potential of our product candidates and development programs, their mechanism of action, and their potential relative to approved products marketed by third parties; the potential benefits to future trial design and program development of subtyping diabetes patients; our research, development and regulatory plans, the progress of our ongoing and upcoming clinical trials and the timing of such events may be deemed to be forward-looking statements. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. Any forward-looking statements in this press release are based on our current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, including the risk that preliminary or interim results of preclinical studies or clinical trials may not be predictive of future or final results in connection with future clinical trials that our analysis of

preliminary or interim data in subsets of patients may not be predictive of our product candidate in a broader patient population, and the risk that we may encounter delays in preclinical or clinical development, patient enrollment and in the initiation, conduct and completion of our ongoing and planned clinical trials and other research and development activities. These risks concerning Biomea Fusion's business and operations are described in additional detail in its periodic filings with the U.S. Securities and Exchange Commission (SEC), including its most recent periodic report filed with the SEC and subsequent filings thereafter. Biomea Fusion explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

Contact:
Ramses Erdtmann
COO & President of Biomea Fusion
re@biomeafusion.com

Exhibit 99.2


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FUSION
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.

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Introduction & Executive Summary

COVALENT-111 Topline Results

December 17, 2024

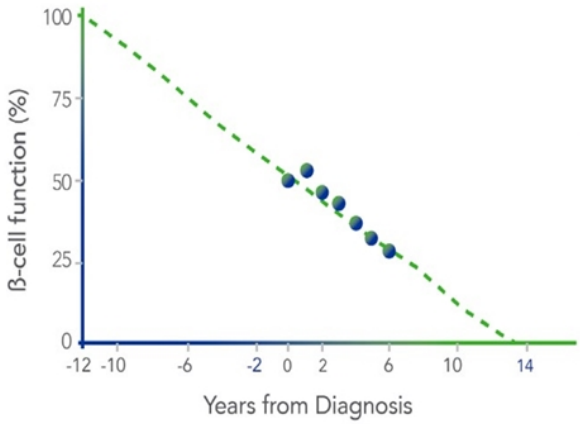
Thomas Butler
Chief Executive Officer,
Chairman of the Board & Co-Founder of Biomea Fusion

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

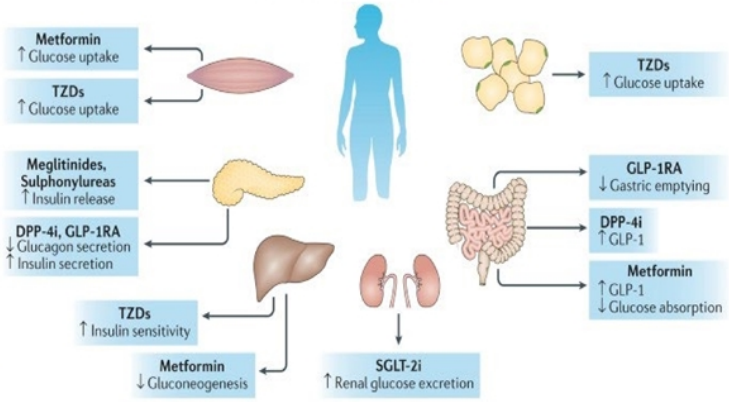


Adapted from DeFronzo RA. Diabetes. 2009;58(4):773-795.

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

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COVALENT-111 Top-Line Results

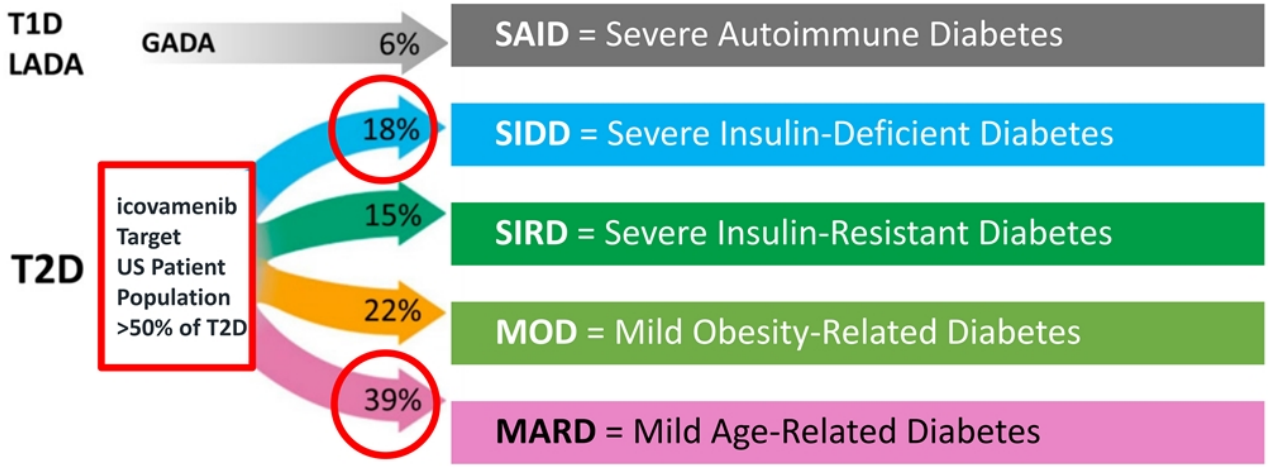
COVALENT-111 Topline Results

December 17, 2024

Dr. Juan Pablo Frias
Chief Medical Officer of Biomea Fusion

Heterogeneity in Type 2 Diabetes

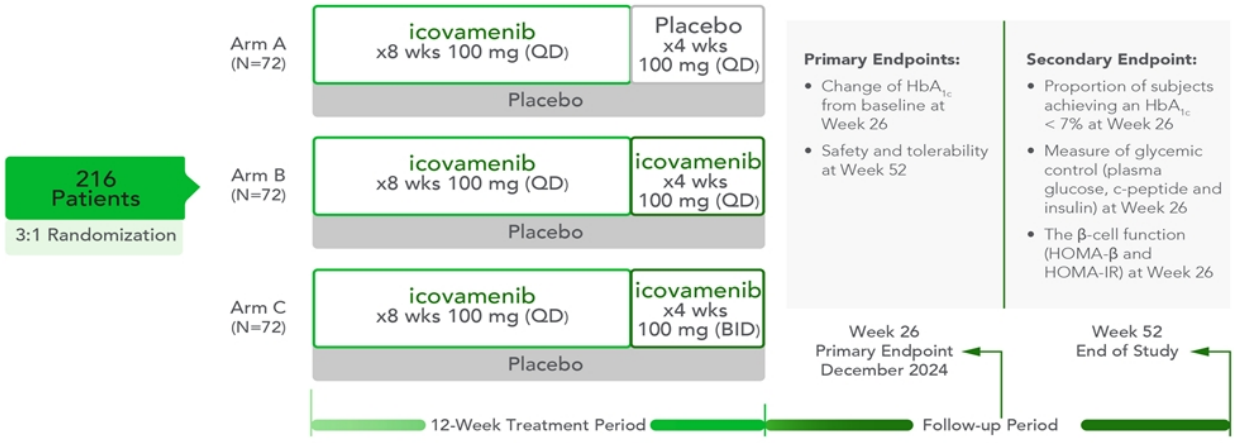
"While diabetes is diagnosed on the basis of a single metabolite, glucose, hyperglycemia can arise due to multiple complex etiological processes that can vary between individuals."[1,2]



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)

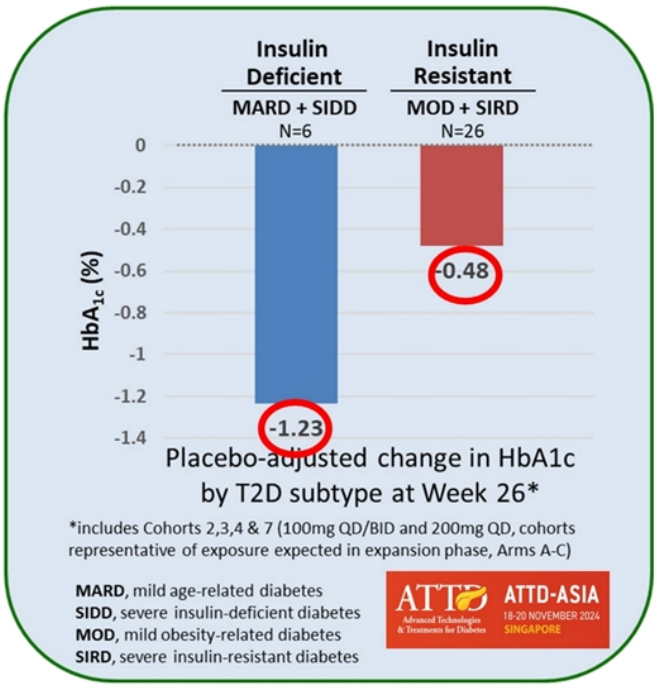


Placebo-Adjusted Change in HbA1c as Presented during ATTD ASIA 18 Nov. 2024

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 %

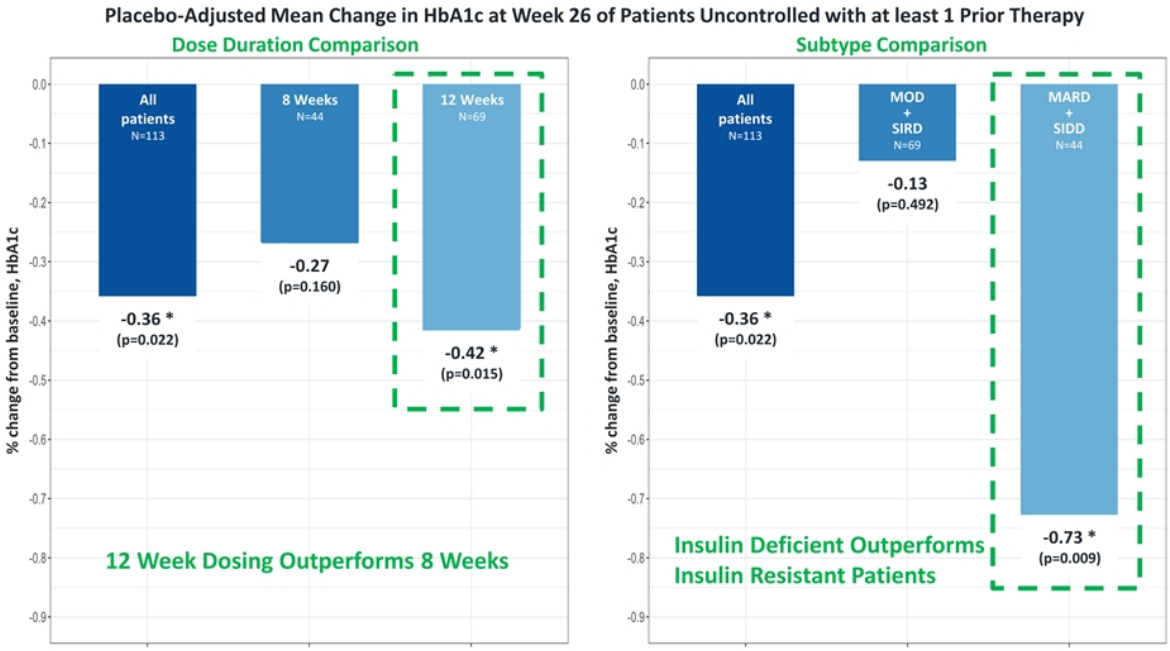
Placebo-Adjusted Change in HbA1c at 26 Weeks

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)



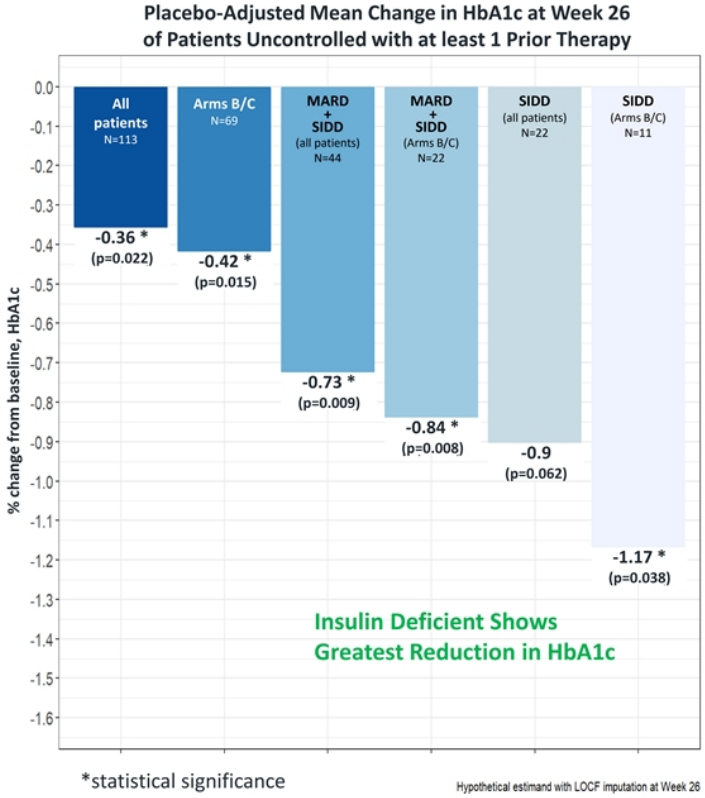
*statistical significance
Hypothetical estimand with LOCF imputation at Week 26

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

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)

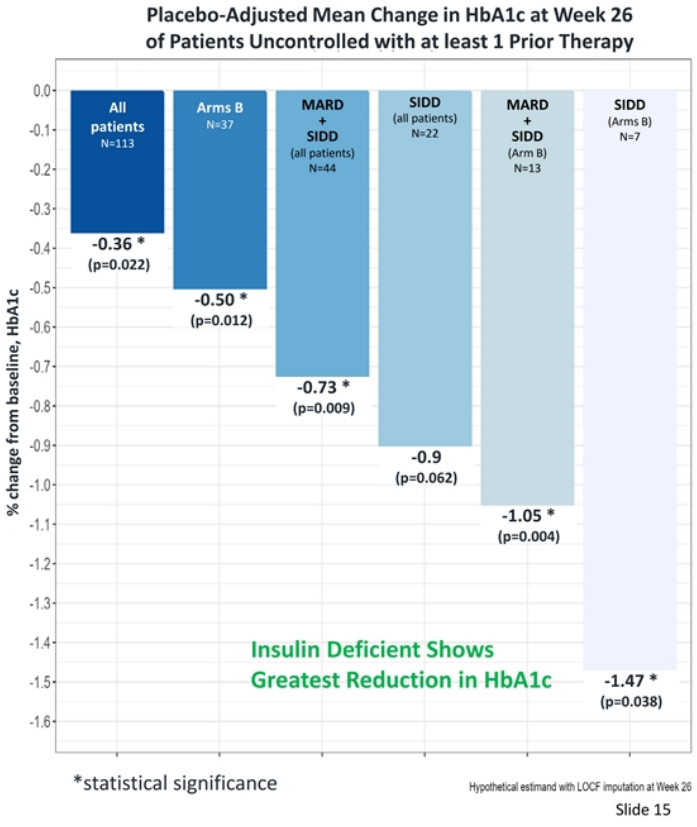


Placebo-Adjusted Mean Change in HbA1c at 26 Weeks in Per Protocol Patients Uncontrolled with at least 1 Medication at Baseline (N=113)

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)



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*

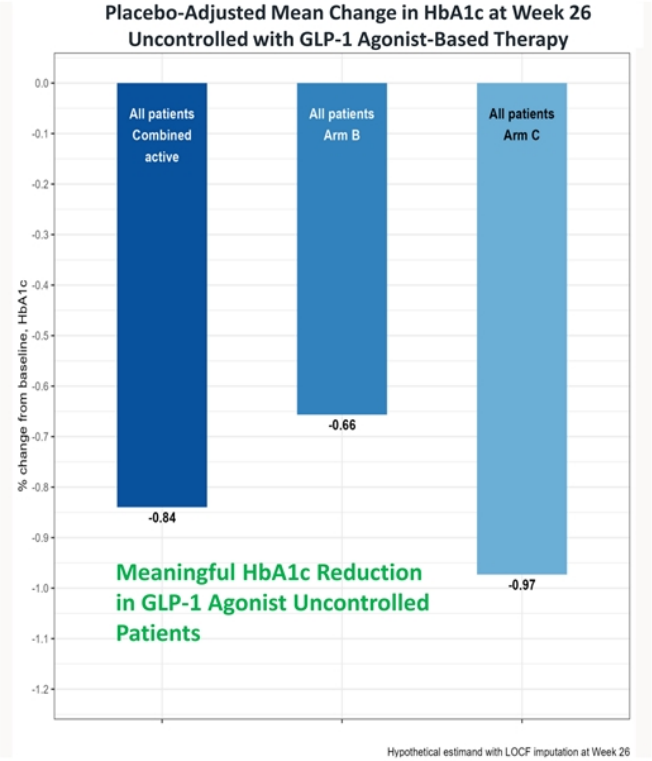
Legend
Arm A: 8 weeks of dosing 100mg QD
Arm B: 12 weeks of dosing 100 mg QD
Arm C: 8 weeks of 100 mg QD + 4 weeks of 100 BID

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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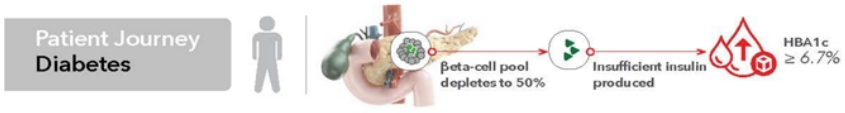
Key Opinion Leader INSIGHTS

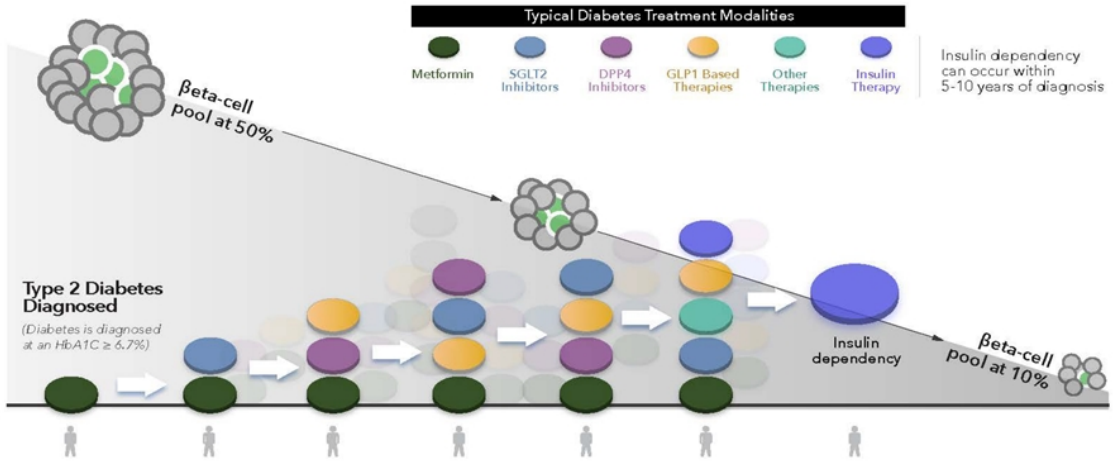
COVALENT-111 Topline Results

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

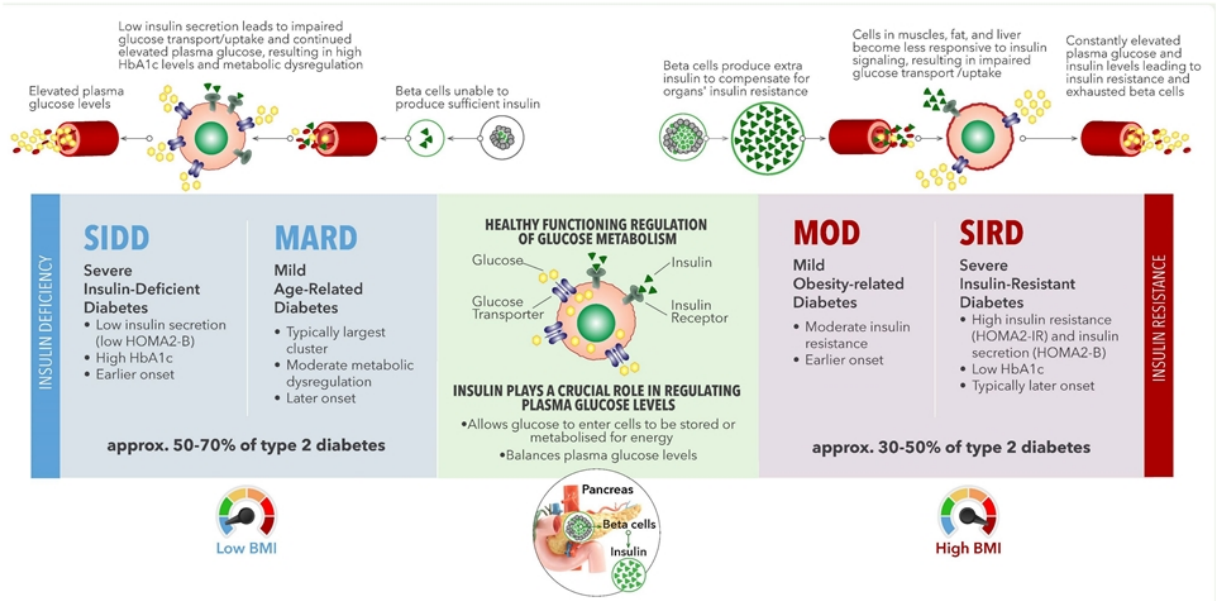
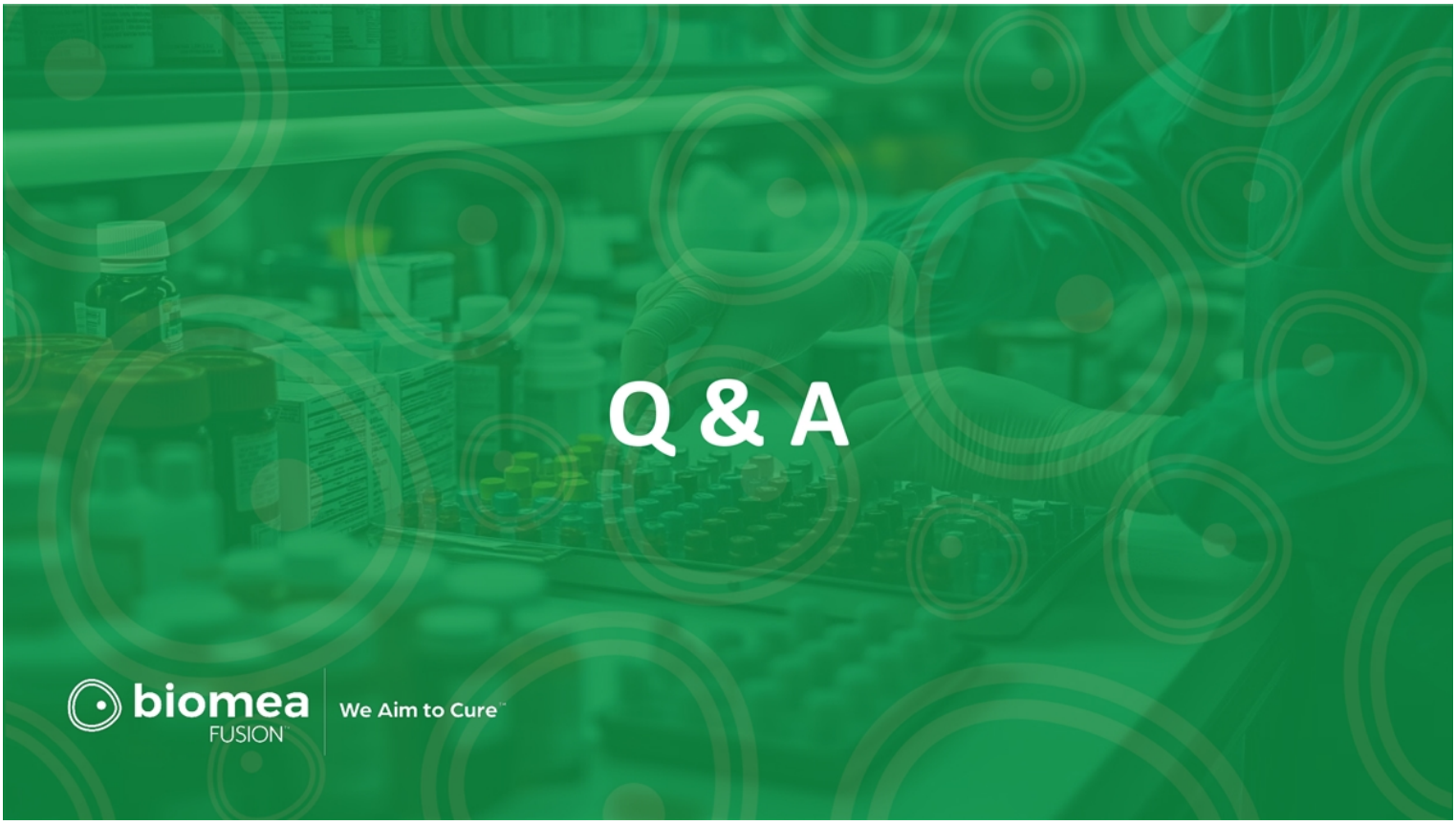


Fig. The phenotype characteristics were identified using five clinical parameters (age at diabetes onset, HbA1c, BMI, and measures of insulin resistance (HOMA2-IR) and insulin secretion (HOMA2-B)) to cluster adult-onset diabetes patients into four subtypes. These subtypes are associated with different 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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