Icovamenib in Type 1 Diabetes

COVALENT-112 Topline Results

BIOMEA FUSION CONFERENCE CALL
28 APRIL 2026

biomea FUSION™

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 U.S. 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 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.

Table of contents

Type 1 diabetes at-a-glance

~9.5M

People live with T1D globally in 2025[1]

- **~1.8M in the US[2]**

~513K

New diagnoses per year globally in 2025[1]

- **~64K new diagnoses/year in the US[3]**

T1D is caused by autoimmune destruction of insulin-producing pancreatic islet beta cells

- **T1D is considered a lifelong chronic disease and carries substantial acute risk** (severe hypoglycemia, DKA) as well as long-term complications including kidney disease, nerve damage, vision loss, and cardiovascular issues[4]
- **Patients with symptomatic T1D (Stage 3) typically lose yearly ~50%** of their beta cell capacity over the first 7 years[5]
- **There are no approved therapies** other than exogenous insulin that address the dysglycemia associated with the progressive decline of C-peptide in Stage 3 T1D[6]

1. *Ogle, et al. Diabetes Research and Clinical Practice 2025, 225, 112277*
2. *Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2023*
3. *Mayer-Davis et al., NEJM / CDC updates*
4. *American Diabetes Association. Standards of Care in Diabetes–2025*
5. *Diabetes Care. 2018 Jun 7;41(7):1486–1492*
6. *Front. Endocrinol., 05 November 2024*

Table of Contents

Lowering menin is a natural biological process that drives beta cell expansion and is expected to reduce diabetes risk

- **Physiologic evidence**
  Natural states such as pregnancy and lactation reduce menin, enabling beta cell expansion and increased insulin output

- **Preclinical and translational validation**
  Across animal models and human islet studies, reduced menin is consistently linked to improved beta-cell mass and function

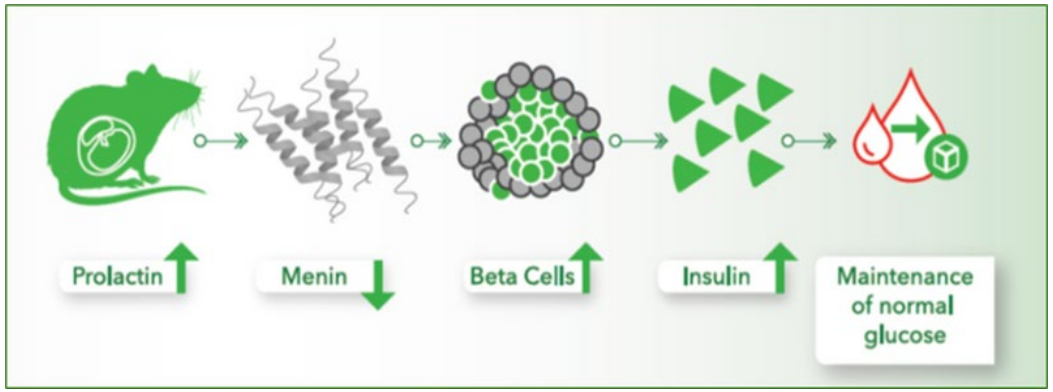
- **Icovamenib MOA**
  Icovamenib reduced menin levels to replicate a validated biological process and restore beta cell function

Science
AAAS

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

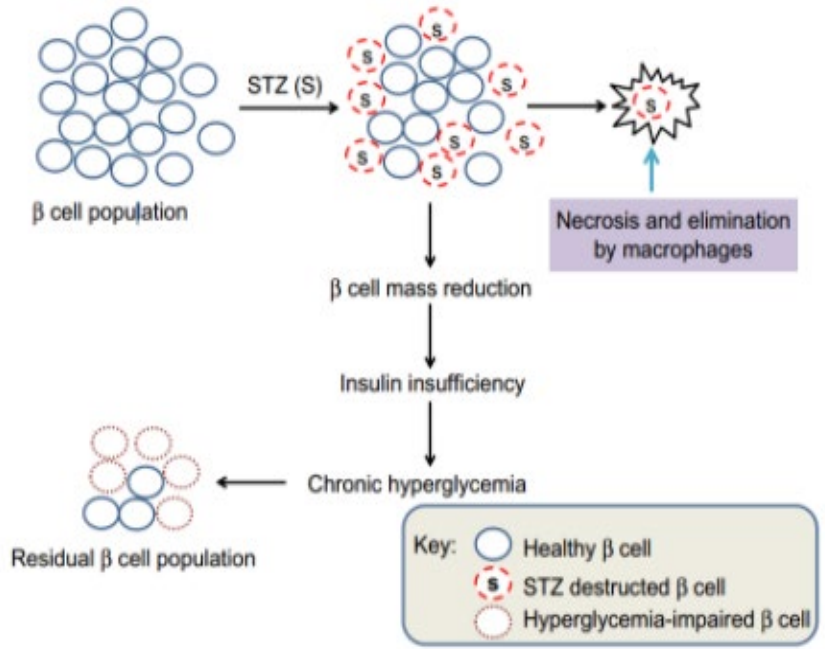
Satyajit K. Karnik,[1] Hainan Chen,[1*] Graeme W. McLean,[1*] Jeremy J. Heit,[1*] Xueying Gu,[1] Andrew Y. Zhang,[1] Magali Fontaine,[2] Michael H. Yen,[1,3] Seung K. Kim[1,3]†

Karnik SK, et al. Science. 2007;318:806-809

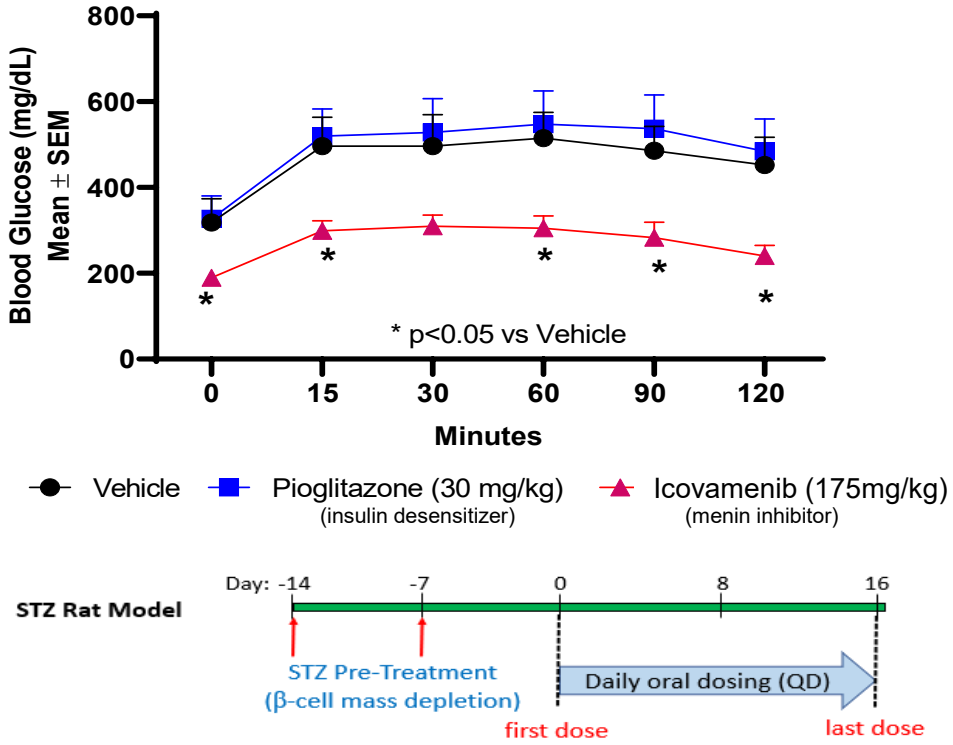


Icovamenib significantly reduced blood glucose in STZ rats (a model in which only insulin decreases blood glucose levels)

STZ TREATMENT TYPICALLY RESULTS IN ~50% BETA CELL LOSS



ORAL GLUCOSE TOLERANCE TEST (DAY 17)

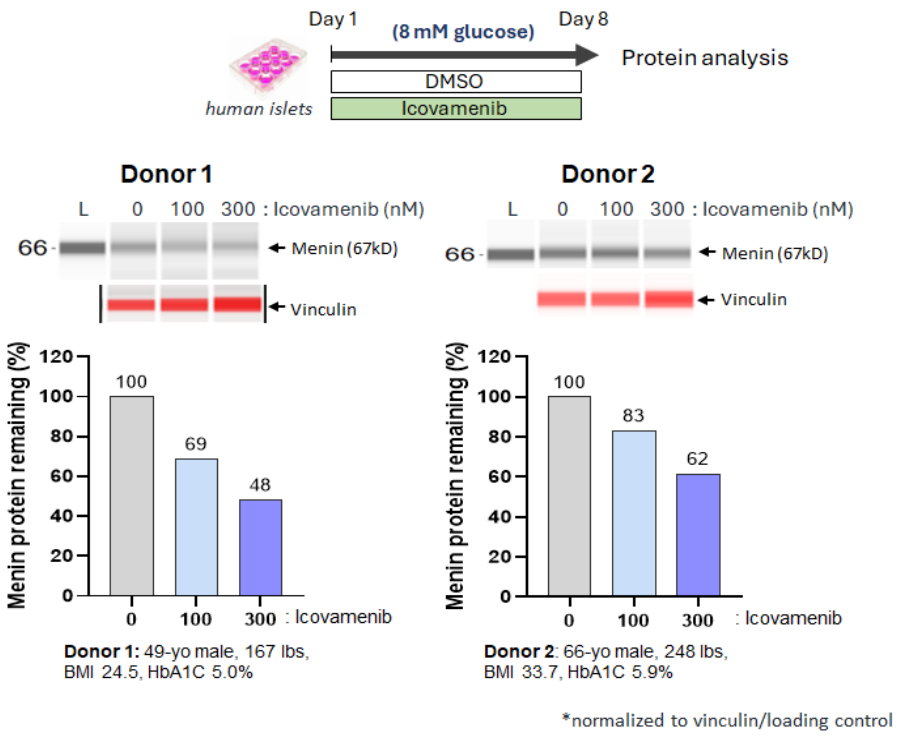


Butler, et al. Diabetologia 65 (Suppl 1), 1–469 (2022) presentation #197

STZ=Streptozotocin, an antibiotic that produces pancreatic islet beta cell destruction and is widely used experimentally to produce a model in diabetes

Icovamenib decreased menin protein levels & promoted beta cell proliferation in ex vivo human islet cultures

MENIN LEVELS DECREASED

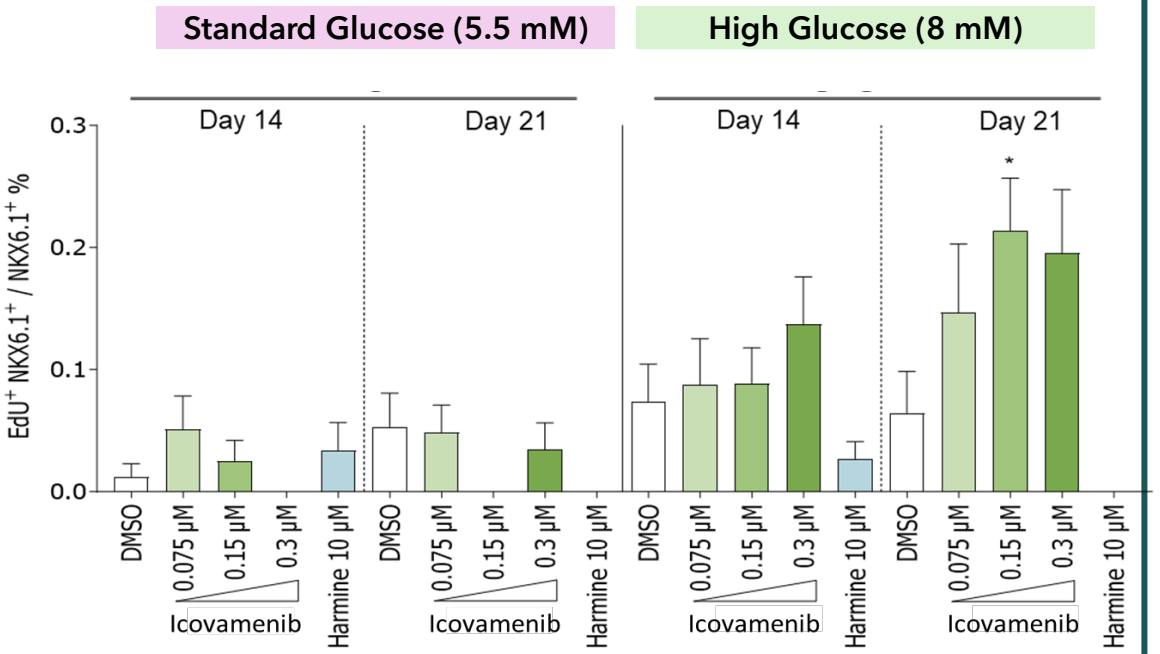


Donor 1: 49-yo male, 167 lbs, BMI 24.5, HbA1C 5.0%

Donor 2: 66-yo male, 248 lbs, BMI 33.7, HbA1C 5.9%

*normalized to vinculin/loading control

ICOVAMENIB CONDITIONALLY PROMOTED BETA CELL PROLIFERATION ONLY UNDER HYPERGLYCEMIC CONDITIONS



Somanath, et al. Diabetologia 68 (Suppl 1), 1–754 (2025). Oral presentation #66

Frias, et al. Metabolism,Vol153, Supplement,2023,#88

Table of contents

Treatment Landscape:
Limitations of current approaches in stage 3 T1D

- Most investigational therapies in T1D focus on immune modulation to slow autoimmune destruction or on preserving residual beta cell function[1]
- C-peptide area under the curve (AUC) has become the accepted endpoint, driving enrollment early after diagnosis (<90 days, new-onset T1D) to preserve residual beta-cell function[2]
- To date, most investigational therapies have not demonstrated durable restoration of beta cell function or sustained increases in C-peptide, outside of cell-based transplantation approaches[3]

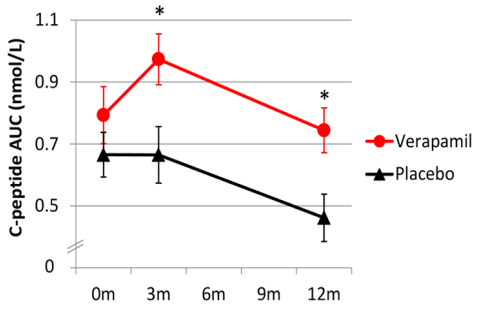
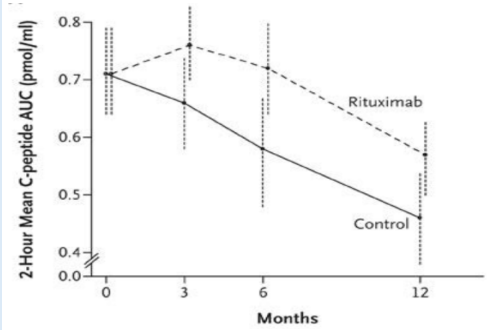
The Next Frontier:

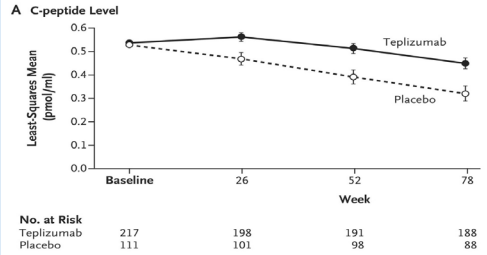
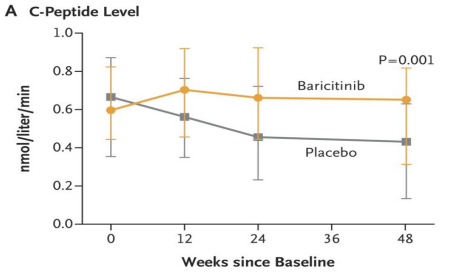
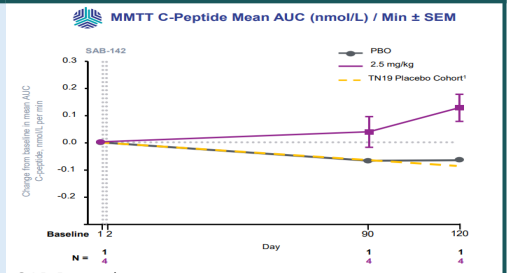
- Restoring beta cell function and mass, beyond only slowing the decline of C-peptide
- Expanding the treatment window beyond early, new onset T1D populations
- Enabling persistence of newly generated beta cells despite autoimmune pressure

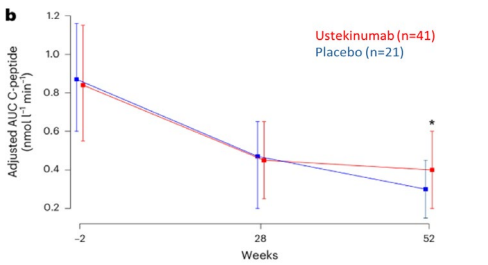
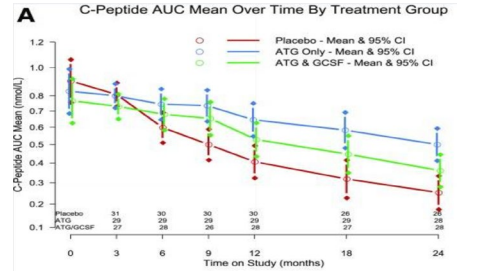
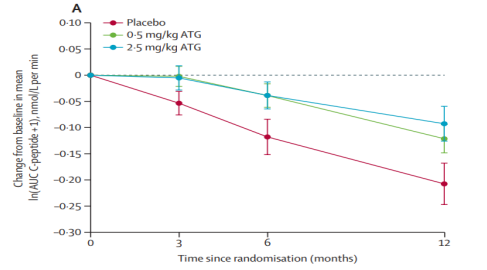
1. *Zarei M et al. Diabetes Epidemiology and Management 2025;17*
2. *Diabetes Care 2025*
3. *NIDDK. Diabetes in America, 2024*

Most therapies in development for stage 3 T1D show limited and non-durable C-peptide impact

biomea FUSION

DRUG	Mean C-PEPTIDE AUC VS PLACEBO
Verapamil	 *Nature. 2018 Aug;24(8):1108-1112*
Rituximab	 *NEJM. 2009 361:2143–2152*

DRUG	Mean C-PEPTIDE AUC VS PLACEBO
Teplizumab (Tzield)	 *ESPE Yearbook of Paediatric Endocrinology (2024) 21 10.2*
Baricitinib	 *N Engl J Med 2023;389:2140-2150*
SAB-142	 *SAB Bio website corporate presentation (March 10, 2026) https://www.sab.bio/*

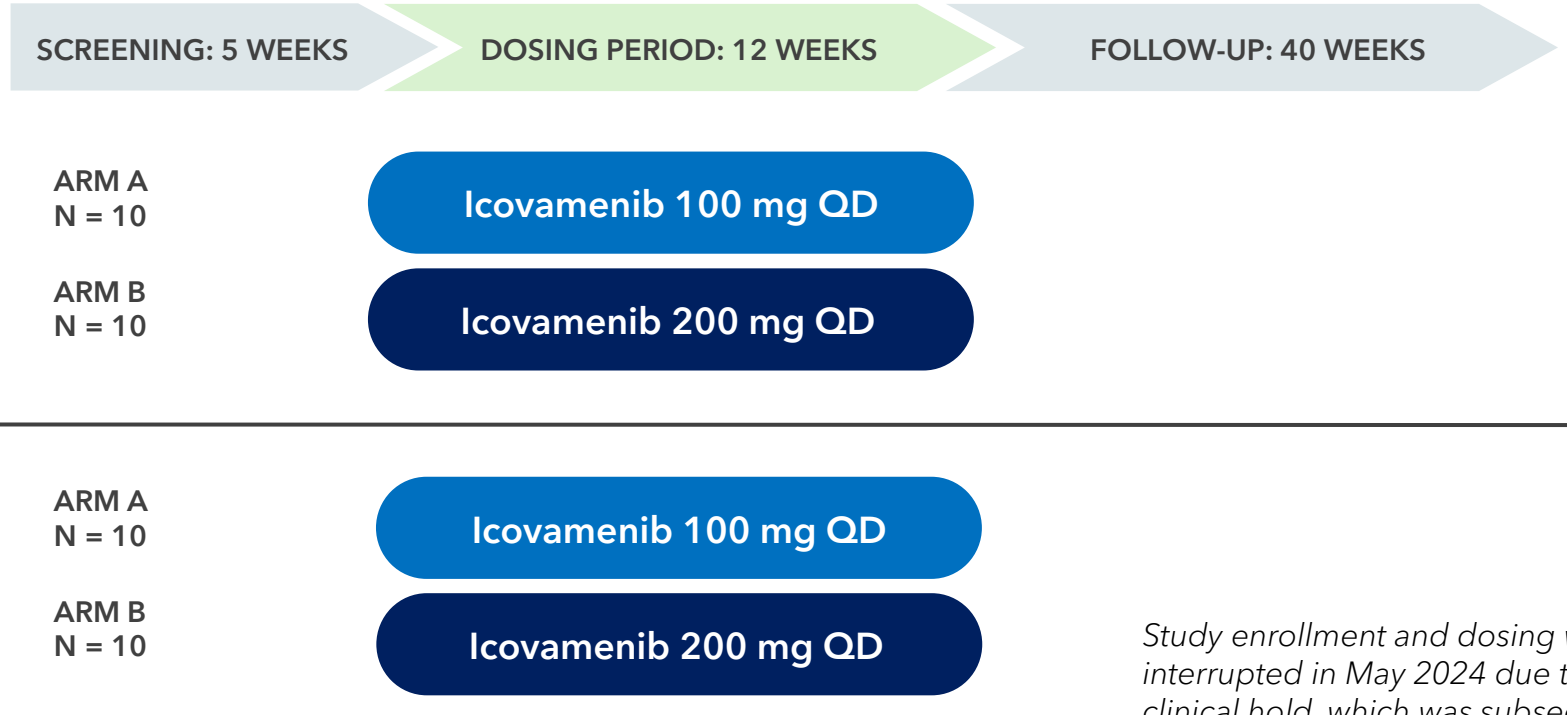
DRUG	Mean C-PEPTIDE AUC VS PLACEBO
Ustekinumab	 *Nature Medicine 2024 vol 30, 2657–2666*
ATG (TrialNet)	 *Diabetes Care 2018 Jul 16;41(9):1917–1925*
MELD-ATG	 *Lancet 2025 Sep 27;406(10510):1375-1388*

**__Ladarixin and Diamyd,__ both Immune modulating, not mentioned here as they demonstrated no meaningful difference compared to placebo*

Table of contents

COVALENT-112 | Study Design

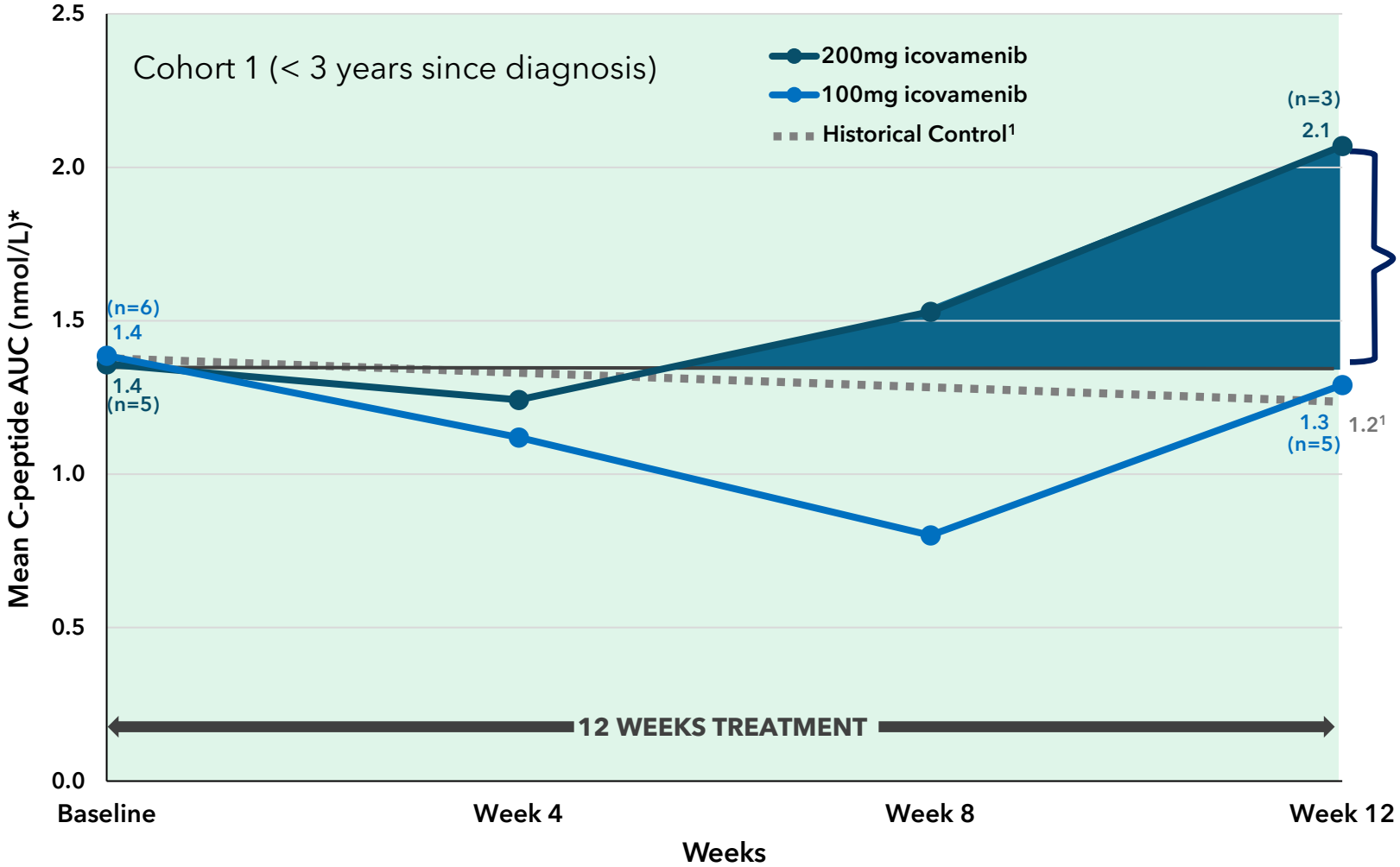
COVALENT-112 (NCT06152042) was a Phase 2 trial designed to examine beta cell function (as measured by C-peptide change and the change of exogenous insulin usage) and glucose and lipid metabolism in participants with T1D treated with standard of care insulin and icovamenib.



Study enrollment and dosing were interrupted in May 2024 due to an FDA clinical hold, which was subsequently resolved, but reduced the number of patients enrolled and followed through to the 52-week readout.

Readout at Week 12

52% mean increase in C-peptide during the 12 weeks treatment period of icovamenib



52% mean increase from baseline

+0.7
P<0.001

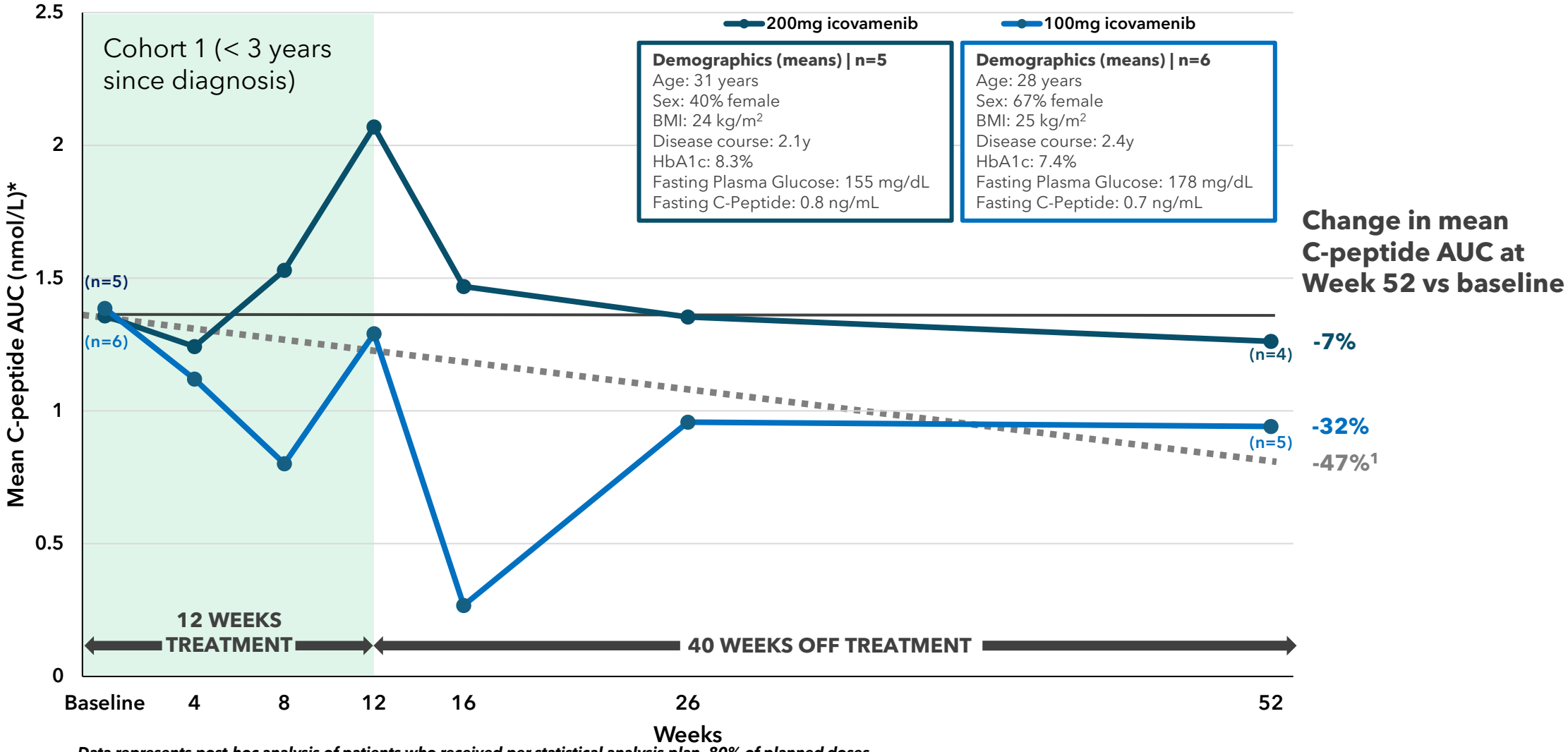
Data represents post-hoc analysis of patients who received per statistical analysis plan, 80% of planned doses

[1] Historical control in T1D patients (n=1549) C-peptide declining over first 7 years at 47% yearly. Diabetes Care. 2018 Jun 7;41(7):1486–1492

** 4-hour Mixed Meal Tolerance Test (MMTT)*

Readout at week 52

Baseline C-peptide levels sustained through week 52 with minimal decline (only -7.1%) observed post 12 weeks of 200mg daily icovamenib



Data represents post-hoc analysis of patients who received per statistical analysis plan, 80% of planned doses

[1] Historical control in T1D patients (n=1549) C-peptide declining over first 7 years at 47% yearly. Diabetes Care. 2018 Jun 7;41(7):1486–1492

** 4-hour Mixed Meal Tolerance Test (MMTT)*

Topline results of icovamenib demonstrated marked C-peptide increase in T1D with observed persistence

- **Observed 52% increase in mean C-peptide AUC at Week 12** ($p < 0.001$) in Cohort 1 patients dosed at 200 mg (diagnosed within 0–3 years; n=5), a magnitude of improvement not commonly reported in published T1D studies
- **Mean C-peptide AUC remained largely preserved through Week 52** in Cohort 1 patients dosed at 200 mg (~7% decline from baseline), supporting persistence of effect. Patients dosed in Cohort 2 demonstrated stable AUC during and post dosing.
- **Generally well-tolerated,** with a favorable safety profile throughout the 52-week observation period
- **Validation of menin as a target for diabetes (T1D & T2D)** further supported by these results
- **Presentation at American Diabetes Association's (ADA) Scientific Session,** comprehensive dataset of Cohort 1 and Cohort 2 to be presented (full release on June 5th at 6:30 pm CST)

Table of contents

Optimal dose and target population identified for T1D phase 2 program

ICOVAMENIB

T1D insights:

- ✓ Dose response: 200 mg demonstrated stronger clinical activity vs 100 mg
- ✓ Potential early intervention advantage: T1D patients dosed ≤3 years showed greater response vs those 3-15 years from diagnosis
- ✓ 12-week treatment showed continuous and improved responses, supporting potential for greater benefit with extended dosing
- ✓ Preclinical chronic toxicology studies support longer term dosing
- ✓ Generally well-tolerated, with a favorable safety profile maintained through the 52-week observation period

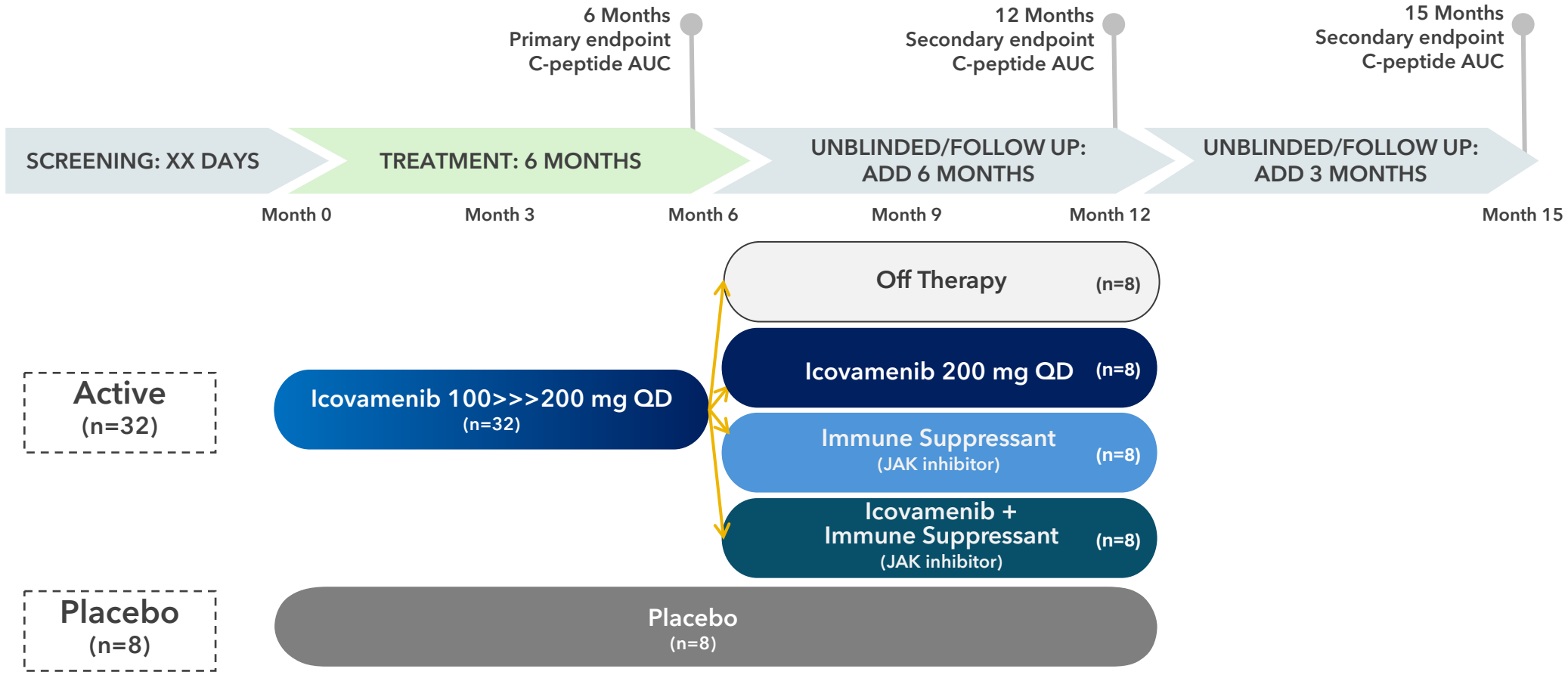
T1D development focus:

- Potential to further increase C-peptide AUC in T1D with extended or continuous dosing
- Opportunity to potentially enhance outcomes through combination with immunomodulation therapies

Proposed phase 2 trial design*

Inclusion Criteria

- Adult participants with T1D diagnosed within 3 years with a C-peptide ≥0.2 nmol/L
- Background therapy maintained unless rescue required



*Subject to regulatory and investigator alignment, and feedback from applicable health authorities.

Table of Contents

Thank you

(NASDAQ: BMEA)

For questions or inquiries, please reach out to Meichiel Weiss at ir@biomeafusion.com

www.biomeafusion.com

biomea FUSION™

Exhibits

biomea FUSION™

KOL perspectives across clinical significance, biology, and future development in T1D

Efforts to intervene against type 1 diabetes (T1D) have historically focused on preserving remaining insulin secretion in people just diagnosed with T1D. These icovamenib data are unique in showing increased C-peptide-reflected insulin secretion in patients with established T1D during dosing and persistence of this effect after treatment was stopped. In people with established T1D, endogenous insulin secretion progressively declines to very low levels. Any evidence of improvement in endogenous insulin secretion—even among a few T1D individuals—is unprecedented and of immense biologic and clinical significance. These findings warrant rigorous and longer-term evaluation.

G. Alexander "Zan" Fleming, MD

FOUNDER & EXECUTIVE CHAIRMAN, KINEXUM
FORMER FDA SENIOR MEDICAL OFFICER AND DIVISION LEADER FOR METABOLIC & ENDOCRINE DRUGS, INVOLVED IN THE REVIEW OF LANDMARK DIABETES AND METABOLIC THERAPIES INCLUDING METFORMIN, THE FIRST RAPID-ACTING INSULIN ANALOGS, EARLY STATINS, AND PPAR AGONISTS

The new data presented today with icovamenib in patients with type 1 diabetes suggest a potential new therapeutic avenue in a disease where fundamental unmet need has long persisted. To date, approved therapies have not directly addressed the progressive loss of functional beta cells that underlies diabetes. Biomea has made critical progress in identifying and characterizing this molecule, which has demonstrated the ability to reduce menin protein levels and activate pathways associated with beta cell function. Today's icovamenib type 1 data further validates and deepens our understanding of icovamenib's mechanism of action. Congratulations to the Biomea team on reaching this important therapeutic milestone.

Rohit Kulkarni, MD, PhD

PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL | SENIOR INVESTIGATOR & SECTION CO-HEAD (ISLET CELL & REGENERATIVE BIOLOGY), JOSLIN DIABETES CENTER

What stands out to me in the icovamenib diabetes data is not only the emerging signal of biological activity, but also the safety profile observed to date with using icovamenib in diabetes studies. That combination is important, because safety ultimately determines whether rational combination strategies can be explored as the program moves forward. Looking ahead, future studies will be critical in determining whether the improvements observed in beta cell function of these Type 1 diabetes patients can be maintained over time, particularly in the presence of ongoing immune activity. It will also be important to understand whether combination approaches—including immunomodulatory therapies— are needed and can further enhance or stabilize the observed effects. These are key questions that will inform the long term clinical potential of this approach.

David Baidal, MD

ASSISTANT PROFESSOR DIABETES RESEARCH INSTITUTE, UNIVERSITY OF MIAMI MILLER SCHOOL OF MEDICINE

KOL perspectives across clinical significance, biology, and future development in T1D

The icovamenib data in Type 1 diabetes naturally makes us pause and reflect on what it could ultimately mean for people living with Type 1 diabetes. While these early findings require confirmation, they suggest a different way of thinking about treatment, one that extends beyond glucose management and begins to engage underlying disease biology. For younger individuals in particular, the possibility of preserving or improving endogenous beta cell function over time could have meaningful implications for lifelong disease burden.
Results like these invite consideration of how the treatment landscape in Type 1 diabetes may evolve if such approaches prove durable and safe.

Alice Cheng, M.D.

ENDOCRINOLOGIST, ASSOCIATE PROFESSOR OF MEDICINE UNIVERSITY OF TORONTO

The icovamenib data in type 1 diabetes are encouraging, this is particularly interesting as icovamenib targets a pathway that has not been meaningfully explored in this disease. Despite advances in insulin delivery and glucose monitoring, disease-modifying options remain limited for patients. These findings support the need for focused, proof-of-concept studies in well-characterized patient populations to better understand this signal, its durability, and the underlying biology.
An important next step will be examining the interplay between beta cell effects and the autoimmunity inherent in type 1 diabetes, and whether combination approaches with immunomodulatory therapies could further enhance or stabilize these beta cell effects.

Jason Gaglia, MD, MMSc

ASSISTANT PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL | STAFF PHYSICIAN, JOSLIN DIABETES CENTER – ONE OF THE WORLD'S LEADING DIABETES CENTERS

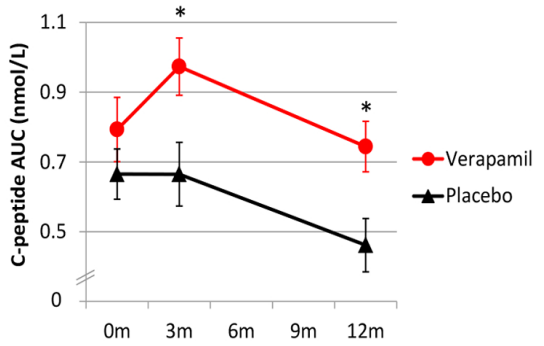
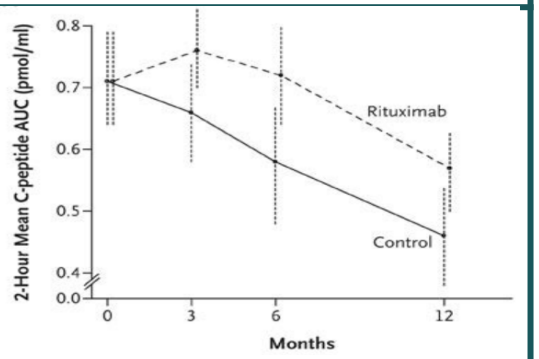
While insulin therapy is life saving for people with Type 1 diabetes, chronic exogenous insulin use is not without consequence. Over time, it is associated with well recognized iatrogenic risks, including hypoglycemia, diabetic ketoacidosis, weight gain, lipohypertrophy, and increased cardiovascular burden. Targeting menin with icovamenib represents a fundamentally new therapeutic approach in diabetes. Rather than simply replacing insulin, it seeks to improve endogenous beta cell function. The early results we are seeing in Type 1 diabetes are highly encouraging.
I am excited to explore longer dosing periods to fully assess the potential of enabling patients to regain their own beta cell–mediated glucose control which is something no current therapy has been able to achieve. If this approach is confirmed, this could represent a meaningful step towards allowing patients to live their daily lives with greater physiological stability and far less constant fear of their disease.

Ralph DeFronzo, M.D.

ENDOCRINOLOGIST, PROFESSOR OF MEDICINE UTHSCSA

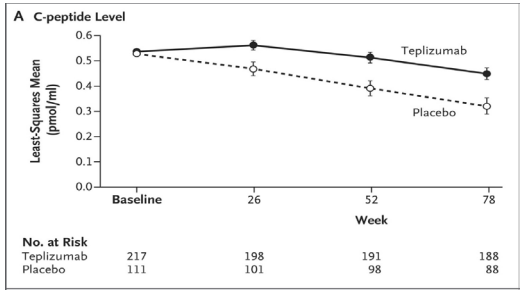
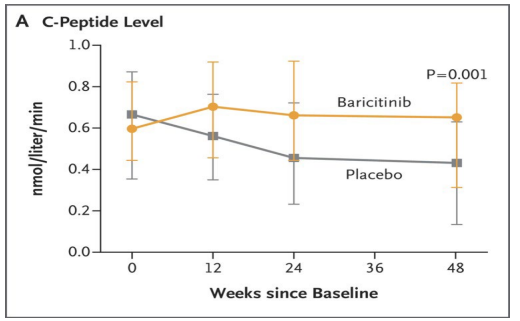
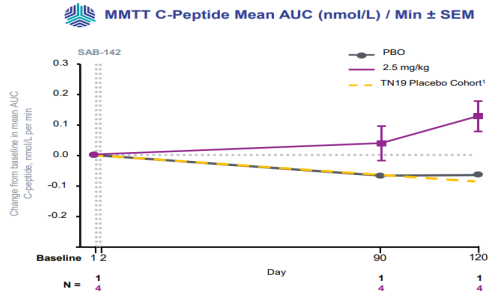
Type 1 diabetes (stage 3) therapies in development - beta cell protection

biomea FUSION

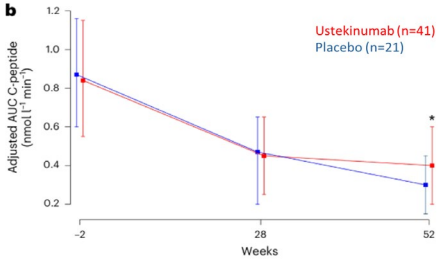
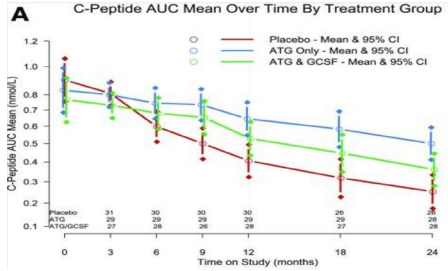
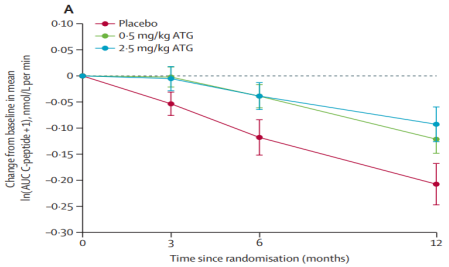
DRUG	MOA	ROUTE & DOSING	N	AGE (YRS)	TIME SINCE TID DX	PHASE	C-PEPTIDE AUC (~WEEK 52)	SAFETY	C-PEPTIDE AUC VS PLACEBO
Verapamil	Beta cell protection	Oral daily	88	7–17	≤31 days	2	**~30–35% less decline** vs placebo *(inferred; near-stable vs decline)*	Well-tolerated	
	Nature. 2018 Aug;24(8):1108-1112								
Rituximab	Anti-CD20 monoclonal antibody; B-cell depletion	IV, 4 weekly infusions	87	8–40	≤100 days	2	**~20–25% preservation** vs placebo	Mainly infusion-related AEs; broader class risks include infection and late neutropenia	
	NEJM. 2009 361:2143–2152								

Type 1 diabetes (stage 3) therapies in development - immunomodulation / suppression

biomea FUSION

DRUG	MOA	ROUTE & DOSING	N	AGE (YRS)	TIME SINCE T1D DX	PHASE	C-PEPTIDE AUC (~WEEK 52)	SAFETY	C-PEPTIDE AUC VS PLACEBO
Teplizumab (Tzield)	Anti-CD3	IV (12d × 2 cycles)	328	8–17	≤6 weeks	3	**~59% less decline** vs placebo *(Week 78 proxy)*	CRS, lymphopenia-rash	
	ESPE Yearbook of Paediatric Endocrinology (2024) 21 10.2								
Baricitinib	JAK1/2 inhibitor	Oral dail	91	Adult	≤100 days	2	**~40–50% less decline** vs placebo *(inferred from 0.65 vs 0.43)*	Chronic immuno-suppression risk	
	N Engl J Med 2023;389:2140-2150								
SAB-142	Human anti-thymocyte Ig	IV (2-day + 6 mo)	4	5–40	3.3 years	2b	**C-peptide increase** vs baseline at ~120 days	Favorable safety	
	SAB Bio website corporate presentation (March 10, 2026) https://www.sab.bio/								

Type 1 diabetes (stage 3) therapies in development - immunomodulation / suppression

DRUG	MOA	ROUTE & DOSING	N	AGE (YRS)	TIME SINCE T1D DX	PHASE	C-PEPTIDE AUC (~WEEK 52)	SAFETY	C-PEPTIDE AUC VS PLACEBO
Ustekinumab	IL-12/23	SC (1x every 12 weeks)	72	12–18	≤100 days	2	**~30–40% less decline** vs placebo	Well-tolerated	
	Nature Medicine 2024 vol 30, 2657–2666								
ATG (TrialNet)	T-cell depletion	IV (1x over 2 days)	89	12–45	≤100 days	2	~**50–60% less decline** vs placebo	CRS, serum sickness	
	Diabetes Care 2018 Jul 16;41(9):1917–1925								
MELD-ATG	Optimized ATG	IV (1x over 2 day)	114-117	5–25	≤100 days	2	**~25–35% less decline** vs placebo	CRS, serum sickness	
	Lancet 2025 Sep 27;406(10510):1375-1388								

*Ladarixin and Diamyd, both Immune modulating, not mentioned here as they demonstrated no meaningful difference compared to placebo