Addressing beta-cell depletion in diabetes with icovamenib

Progressive decline in beta-cell function in T2D	Characterized by a decrease in beta-cell mass and function over time
Role of menin in glucose homeostasis	Menin is a scaffold protein that regulates glucose homeostasis
	Inhibiting menin promotes beta-cell proliferation thereby enhancing insulin secretion
Icovamenib: an oral covalent small molecule menin inhibitor	Currently in clinical development for T2D and T1D
COVALENT-111: Multiple Ascending Dose	Participants with T2D maintained glycemic control up to 22 weeks after 4 weeks of daily icovamenib
COVALENT-111: Phase 2 Expansion	Design and methods of the trial (NCT05731544)

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COVALENT-111 Expansion: Study Overview

Study Design

- 52-week randomized, double-blind, placebo-controlled study
- First major data readout at Week 26
- Ongoing study in US and Canada

COVALENT-111 Expansion Study

Key Eligibility Criteria

- Age 18-65
- Diagnosed with T2D duration ≤ 7 years
- HbA1c 7-10.5%
- BMI 25-40 kg/m^2
- Treated with diet/exercise ± up to 3 antidiabetic medications (insulin secretagogues and insulin excluded)
- At least 75% treated with lifestyle intervention ± MET

Treatment Groups

- Dosing: 8-12 weeks of icovamenib with follow up until Week 52
- Targeting 72 patients in each arm (54 active: 18 placebo)

Group 1: 100mg QD for 8 weeks, then placebo for 4 weeks (redosing at Week 22 for 4 weeks, if necessary)

Group 2: 100mg QD for 12 weeks

Group 3: 100mg QD for 8 weeks, then 100mg BID for 4 weeks

Endpoints

Primary Objective

- Assess the effect on HbA1c at Week 26

Secondary Objective

- Assess safety and tolerability
- Assess the effect on fasting plasma glucose

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COVALENT-111: Advancing diabetes treatment with icovamenib

Icovamenib targets the root cause of T2D

- Addresses progressive decline in beta-cell function

COVALENT-111 study overview

- Once-daily orally-dosed icovamenib therapy
- Assesses long-term efficacy and safety
- Duration:
  - Short-term therapy: Up to 12 weeks
  - Long-term assessment: Follow-up until 52 weeks

Potentially addresses unmet need in T2D treatment

Aligns with FDA's 2023 guidance on the necessity for new therapies to address the unmet medical needs in diabetes

FDA. Draft Guidance for Industry: Diabetes Mellitus—Developing Drugs and Therapeutic Biologics for Treatment and Prevention. 2023.

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