# Real-World Evaluation of the Natural History and Long-Term Clinical Effects of GLP-1 and GLP-1/GIP Therapies in US Adults Living With Obesity: REFLECT US

**First published:** 20/11/2026

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Study Planned

## Administrative details

**EU PAS number**

EUPAS1000001167

**Study ID**

1000001167

**DARWIN EU® study**

No

**Study countries**

United States

**Study description**

Unique Protocol ID: K9531-5101-US

**Study status**

Planned

# Contact details

**Study institution contact**

Kailera Therapeutics, Inc. info-clinicalstudies@kailera.com

**Study contact**

info-clinicalstudies@kailera.com

**Primary lead investigator**

Medical Director

**Primary lead investigator**

# Study timelines

**Date when funding contract was signed**

Actual: 31/10/2026

**Study start date**

Planned: 30/11/2026

**Date of final study report**

Planned: 31/03/2030

# Regulatory

**Was the study required by a regulatory body?**

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Methodological aspects

## Study type

## Study type list

**Study topic:**

Disease /health condition

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Disease epidemiology

Drug utilisation

Effectiveness study (incl. comparative)

Healthcare resource utilisation

Safety study (incl. comparative)

**Data collection methods:**

Secondary use of data

**Study design:**
K9531-5101-US is a retrospective observational cohort study designed to characterise the natural history, treatment patterns, clinical outcomes, and healthcare resource utilisation of adults living with obesity in the United States (US).

**Main study objective:**
K9531-5101-US will evaluate the natural history of obesity in the US using longitudinal real-world healthcare data. The study is intended to provide context regarding participant characteristics, disease burden, treatment patterns, clinical outcomes, and healthcare utilisation among adults living with obesity in routine clinical practice.

A random index date will be assigned to each qualifying participant from eligible visit dates, requiring at least 12 months of prior data to assess eligibility. Newly qualifying participants in subsequent years will receive an index date within their first year of eligibility. Baseline characteristics will be assessed at the index date, with follow-up to evaluate changes and prespecified outcomes.

The study will also provide real-world evidence on obesity and obesity management in routine clinical practice and support the design of 4 prospective cohorts intended to mirror the following three Phase 3 registrational, randomized, double-blinded, placebo-controlled trials that are currently investigating the effects of ribupatide compared with placebo and semaglutide: K9531-3103 (NCT07284875), K9531-3104 (NCT07284901), and K9531-3107 (NCT07284979).

Retrospective observational cohort studies of the natural history of obesity will also be conducted in the United Kingdon (UK) (K9531-5102-UK [REFLECT UK]) and in Spain (K9531-5103-ESP [REFLECT Spain]).

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Medicinal product name**

OZEMPIC

WEGOVY

RYBELSUS

MOUNJARO

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**Medicinal product name, other**

Semaglutide

Tirzepatide

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**Medical condition to be studied**

Obesity

## Population studied

**Short description of the study population**

Participants will be defined by body mass index (BMI), type 2 diabetes mellitus (T2DM), cardiometabolic comorbidities, and treatment with glucagon-like peptide-1 (GLP-1)/glucose-dependent insulinotropic polypeptide (GIP) at index.

Participants must meet protocol-defined inclusion and exclusion criteria during at least 1 outpatient visit that occurred between January 1, 2018, and June 30, 2024.

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**Age groups**

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

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**Estimated number of subjects**

8.780.022

## Study design details

**Setting**

Key Inclusion Criteria:

Cohort 1:

• BMI ≥30 kilograms/square metre (kg/m^2) on at least 2 visits or

• BMI ≥27 to <30 kg/m^2 on at least 2 visits and previously diagnosed with at

least 1 of the following the year before the second BMI ≥27 to <30 kg/m^2 visit: hypertension; dyslipidemia; obstructive sleep apnoea; ischemic cardiovascular disease

Cohort 2:

• BMI ≥27 kg/m^2 on at least 2 visits

• Diagnosis of T2DM the year before the second BMI ≥27 kg/m^2 visit

Cohort 3:

• BMI ≥35 kg/m^2 on at least 2 visits

Cohort 4:

• BMI ≥35 kg/m^2 on at least 2 visits

• At least 1 filled semaglutide prescription

Key Exclusion Criteria:

Cohorts 1, 3, and 4:

• History of type 1 diabetes mellitus (T1DM) or T2DM

• One-year pre-index history of T1DM, T2DM, diabetic ketoacidosis or hyperosmolar state/coma

• One-year pre-index laboratory evidence of diabetes mellitus (DM) including haemoglobin A1c ≥6.5%, fasting glucose ≥126 milligrams/decilitre (mg/dL), or random glucose or 2-hour glucose measurement from a 2-hour oral glucose tolerance test ≥200 mg/dL

Cohort 2 (history of T2DM is inclusion criterion):

• One-year pre-index history of T1DM, DM due to underlying condition, drug or chemical induced DM, other specified, diabetic ketoacidosis or hyperosmolar

state/coma
• One-year pre-index history of T2DM with hypoglycaemia with coma or T2DM with hypoglycaemia without coma and use of hypoglycaemia treatment

All Cohorts:
• Three-month pre-index initiation of medications strongly associated with weight gain
• One-year chronic treatment with medications that strongly affect gastrointestinal motility
• One-year pre-index diagnosis of multiple endocrine neoplasia Type 2 or medullary thyroid cancer
• One-year pre-index diagnosis of chronic or acute pancreatitis
• One-year pre-index diagnosis of gastric-emptying abnormalities
• One-year pre-index diagnosis of severe major depressive disorder/episode and disruptive mood disorders

Note: Other protocol-specified criteria may apply.

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**Outcomes**

Primary Outcomes:
1. Percentage Change from Index Date in Body Weight

Secondary Outcomes:
2. Number of Participants with Obesity Per 1,000 Patient Years
3. Participant Age
4. Participant Sex
5. Participant Race
6. Participant Ethnicity
7. Participant Weight
8. Number of Participants Admitted to the Hospital

9. Length of Inpatient Hospital Stay (Days)
10. Number of Outpatient Visits
11. Annual Healthcare Cost
12. Change from Index Date in Body Weight
13. Change from Index Date in Systolic Blood Pressure and Diastolic Blood Pressure
14. Time from Index Date to Death (All Cause)
15. Number of Participants Admitted to the Hospital
16. Length of Inpatient Hospital Stay (Days)
17. Number of Outpatient Visits
18. Annual Healthcare Cost
19. Number of Participants Initiating GLP-1 or GLP-1/GIP by 6-month Intervals
20. Number of Participants Permanently Discontinuing GLP-1 or GLP-1/GIP by 6-month Intervals
21. Systolic Blood Pressure and Diastolic Blood Pressure in the Intention-to-treat (ITT) and Per-protocol (PP) Subgroups at Index
22. Percentage Change in Body Weight in ITT and PP Subgroups
23. Time from Index Date to Death (All Cause) for ITT and PP Subgroups
24. Number of Participants Admitted to the Hospital for ITT and PP Subgroups
25. Length of Inpatient Hospital Stay (Days) for ITT and PP Subgroups
26. Number of Outpatient Visits for ITT and PP Subgroups
27. Annual Healthcare Cost for ITT and PP Subgroups
28. Systolic Blood Pressure and Diastolic Blood Pressure in Age Subgroups
29. Percentage Change in Body Weight by Age Subgroups
30. Time From Index Date to Death (All Cause) in Age Subgroups
31. Number of Participants Admitted to the Hospital for Age Subgroups
32. Length of Inpatient Hospital Stay (Days) for Age Subgroups
33. Number of Outpatient Visits for Age Subgroups
34. Annual Healthcare Cost for Age Subgroups

## Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s), other**

Truveta Data

**Data sources (types)**

Electronic healthcare records (EHR)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Yes

**Check completeness**

Yes

**Check stability**

Yes

**Check logical consistency**

Yes

# Data characterisation

**Data characterisation conducted**

Yes