CLOSER LOOK

MEMORANDUM

BI/Zealand's survodutide, dual GLP-1/glucagon RA, conferred ~17% weight loss in people with overweight or obesity at Week 76 – April 28, 2026

Topline SYNCHRONIZE-1 results showed improved cardiometabolic risk; full results to be presented at ADA 2026

Boehringer Ingelheim (BI) announced this morning positive topline results of the phase 3 SYNCHRONIZE-1 trial (n=725), which evaluated survodutide (dual GLP-1/glucagon RA) in people with overweight or obesity, but not diabetes.

In the trial, survodutide conferred 16.6% weight loss, compared to 3.2% with placebo, at 76 weeks, according to the efficacy estimand (assuming full treatment adherence). Moreover, 85% of the survodutide group (vs. 39% with placebo) achieved ≥5% weight loss at 76 weeks. Moreover, survodutide led to significant reductions in fat mass and waist circumference. Full results of the trial will be presented at ADA 2026.

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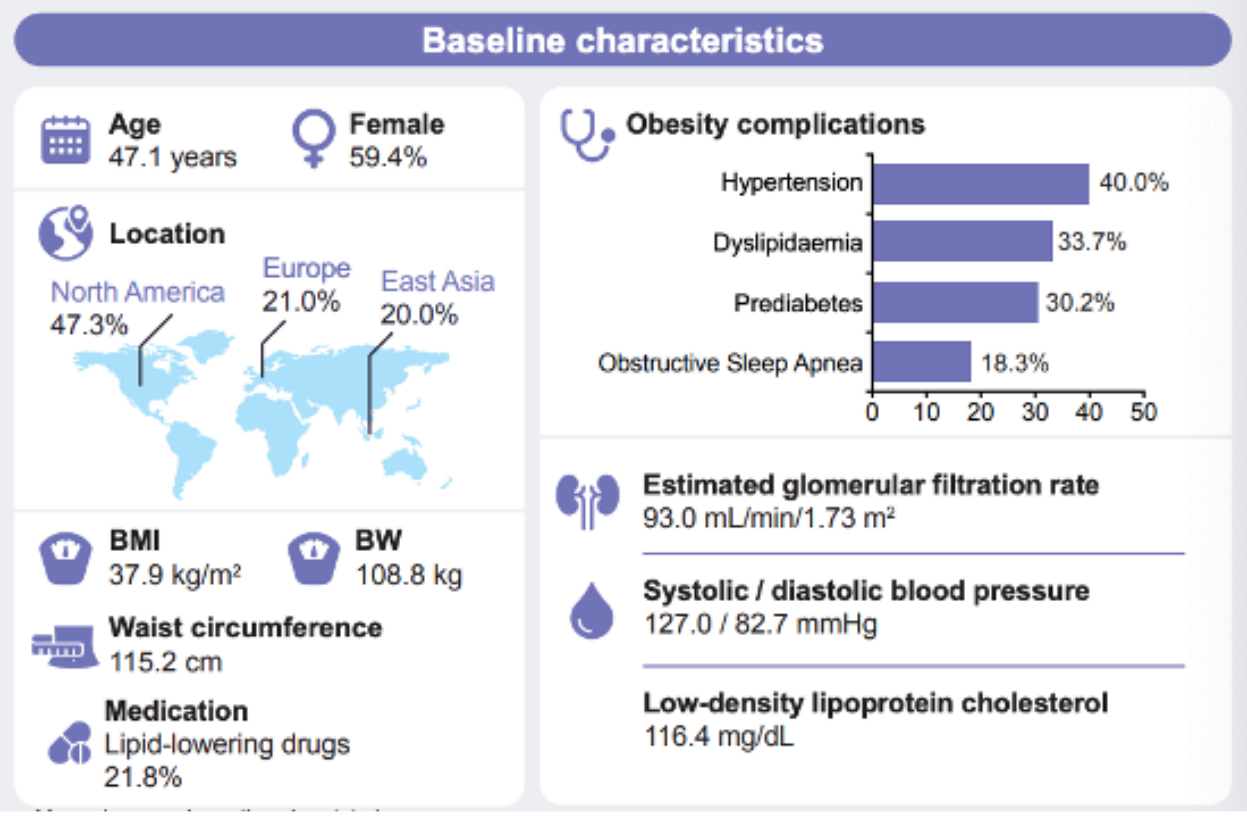
Baseline characteristics: Participants had mean body weight of 240 lbs and waist circumference of 45 inches

Baseline characteristics were published in *Diabetes, Obesity, and Metabolism* in November 2025 (see figure below). Participants (n=725) were 47 years old, with the majority (59%) female. As a global study conducted across 14 countries, 47% were from North America, 21% from Europe, and 20% from East Asia.

Clinically, participants had a mean body weight of 240 lbs (108.8 kg), BMI of 37.9 kg/m^2, and waist circumference of 45 inches (115 cm). Furthermore, mean A1c was 5.5%, eGFR was 93 mL/min/1.73 m^2, systolic blood pressure was 127 mmHg, diastolic blood pressure was 83 mmHg, and LDL-cholesterol was 116 mg/dL. Comorbidities were common, including hypertension (40% of participants), dyslipidemia (34%), prediabetes (30%), and obstructive sleep apnea (18%). T2D was considered as an exclusion criterion for SYNCHRONIZE-1.

Figure 1. Baseline characteristics of SYNCHRONIZE-1 participants



Source: Prof. Carel le Roux et al., *Diabetes, Obesity and Metabolism*, 2025.

Survodutide led to nearly 17% weight loss in people with overweight or obesity, similar to semaglutide

The trial met both of its co-primary endpoints. Survodutide conferred a 16.6% weight loss (vs. 3.2% with placebo) at 76 weeks, assuming full treatment adherence. Moreover, 85% of adults on survodutide (vs. 39% of the placebo group) achieved ≥5% weight loss.

Further analyses showed that survodutide significantly lowered waist circumference. Fat mass loss is predicted to drive weight loss in these participants.

While difficult to compare across trials, the results are comparable to semaglutide, which conferred 17.4% weight loss (vs. 5% with placebo) at Week 68 from a baseline of 236 lbs (107 kg), regardless of treatment adherence. Tirzepatide reported a stronger efficacy, conferring 21% weight loss (vs. 3% with placebo) from a baseline body weight of 231 lbs (105 kg), regardless of treatment adherence.

Survodutide is evaluated in phase 3 programs for weight management, as well as liver health

Survodutide is evaluated in phase 3 programs for obesity, following the phase 2 results, in which survodutide demonstrated 19% weight loss in people with obesity and overweight. In addition to the SYNCHRONIZE-1 trial (n=725), several other trials in the program have recently completed or are underway:

- **SYNCHRONIZE-2** (n=755), evaluating survodutide for overweight and obesity with T2D, was completed in March 2026.
- **SYNCHRONIZE-MASLD** (n=218), evaluating survodutide for overweight and obesity with MASH, was completed in December 2025.
- **SYNCHRONIZE-CVOT** (n=5,533), assessing CV outcomes in people with obesity and established cardiovascular disease (CVD) or chronic kidney disease (CKD) or risk factors for CVD, is expected to be

completed in June 2026.

- **SYNCHRONIZE-JP** (n=274) and **SYNCHRONIZE-CN** (n=307), studying survodutide in people with obesity in Japan and China, respectively, have been completed in December 2025 and January 2026.

Key phase 3 data are expected in 2026, after which BI plans to file for approval for survodutide in 2027.

Survodutide is also investigated for MASH in the LIVERAGE program:

- **LIVERAGE** (n=1,800) trial of survodutide in MASH with moderate or advanced fibrosis (stage 2 or 3), expected to complete in December 2031; and
- **LIVERAGE-Cirrhosis** (n=1,590) trial of survodutide in MASH with compensated cirrhosis (stage 4 fibrosis), expected to complete in June 2029.

As background, BI obtained an exclusive global license for survodutide from Zealand in 2011. BI holds responsibility for global development and commercialization. Zealand is eligible to receive up to €315 million (~$367 million) and high-single to low-double-digit percentage royalties on global sales.

BI advances cardiometabolic pipeline for weight management and liver health

BI has a broad cardiovascular-renal-metabolic pipeline for diabetes, obesity, and cardiorenal diseases.

- Vicadrostat/empagliflozin (aldosterone synthase inhibitor/SGLT-2 inhibitor) is evaluated in a phase 3 program for CVD, CKD, and heart failure.
- Triple GLP-1/GIP/NPY2 RA will enter phase 2 in the middle of this year.

Close Concerns' Questions

1. When are SYNCHRONIZE-2 topline results expected?
2. What factors might account for the differences between the phase 2 and phase 3 weight loss (16.6% vs. 19%)?
3. Who is the ideal candidate to use a therapy like survodutide?
4. What is the safety and tolerability profile of survodutide in the SYNCHRONIZE-1 trial?

-- by Kat Moon, Monica Oxenreiter, and Kelly Close