

RESEARCH MONOGRAPH . COMPOUND PROFILE

Survodutide

A long-acting GLP-1 and glucagon receptor dual agonist developed by Boehringer Ingelheim and Zealand Pharma, advanced through Phase 3 in obesity and MASH.

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AUTHOR	Kodiac bioLabs Research
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ABSTRACT

Survodutide (BI 456906; SAR-441255; CAS 2403761-22-2 mass) is a long-acting GLP-1 receptor and glucagon receptor dual agonist developed by Boehringer Ingelheim in collaboration with Zealand Pharma. The compound is a 39-residue lipidated peptide based on the glucagon and GLP-1 sequences, with selective potency approximately equivalent at the two receptors and with a fatty acid chain modification enabling once-weekly subcutaneous administration through serum albumin binding (the same pharmacokinetic strategy used by semaglutide, liraglutide, and tirzepatide). The dual-agonist mechanism produces synergistic effects on body weight: GLP-1 receptor agonism reduces appetite and slows gastric emptying through hypothalamic and brainstem pathways (the dominant mechanism shared with semaglutide and other GLP-1 monoagonists), while glucagon receptor agonism increases hepatic fatty acid oxidation and energy expenditure, mobilizing hepatic and visceral fat in a manner not achieved by GLP-1 monoagonism. Phase 2 obesity results published in 2024 reported up to approximately 19 percent body weight reduction at 46 weeks at the highest dose, similar to the magnitude observed with tirzepatide and substantially greater than semaglutide. The compound is in active Phase 3 development in obesity (SYNCHRONIZE program) and MASH (SYNCHRONIZE-2; metabolic dysfunction-associated steatohepatitis) with anticipated regulatory submissions in 2026 to 2027. Side effect profile parallels other GLP-1-class agents (nausea, vomiting, diarrhea, occasional gastroparesis) with the additional consideration of glucagon-related effects (modest heart rate elevation, occasional hypoglycemia masked by reduced insulin

sensitivity, and consideration of bilirubin elevation). Survodutide is distinct from retatrutide (Eli Lilly's triple GLP-1/GIP/glucagon agonist) in lacking GIP receptor agonism and from cotadutide (AstraZeneca's GLP-1/glucagon dual) in pharmacokinetic profile and clinical positioning.

1. Compound Identification

Survodutide is described as glp-1 and glucagon receptor dual agonist. A long-acting GLP-1 and glucagon receptor dual agonist developed by Boehringer Ingelheim and Zealand Pharma, advanced through Phase 3 in obesity and MASH.

1.1 Class summary

GLP-1 and glucagon receptor dual agonist

1.2 Subtitle

A long-acting GLP-1 and glucagon receptor dual agonist developed by Boehringer Ingelheim and Zealand Pharma, advanced through Phase 3 in obesity and MASH.

2. Abstract

Survodutide (BI 456906; SAR-441255; CAS 2403761-22-2 mass) is a long-acting GLP-1 receptor and glucagon receptor dual agonist developed by Boehringer Ingelheim in collaboration with Zealand Pharma. The compound is a 39-residue lipidated peptide based on the glucagon and GLP-1 sequences, with selective potency approximately equivalent at the two receptors and with a fatty acid chain modification enabling once-weekly subcutaneous administration through serum albumin binding (the same pharmacokinetic strategy used by semaglutide, liraglutide, and tirzepatide). The dual-agonist mechanism produces synergistic effects on body weight: GLP-1 receptor agonism reduces appetite and slows gastric emptying through hypothalamic and brainstem pathways (the dominant mechanism shared with semaglutide and other GLP-1 monoagonists), while glucagon receptor agonism increases hepatic fatty acid oxidation and energy expenditure, mobilizing hepatic and visceral fat in a manner not achieved by GLP-1 monoagonism. Phase 2 obesity results published in 2024 reported up to approximately 19 percent body weight reduction at 46 weeks at the highest dose, similar to the magnitude observed with tirzepatide and substantially greater than semaglutide. The compound is in active Phase 3 development in obesity (SYNCHRONIZE program) and MASH (SYNCHRONIZE-2; metabolic dysfunction-associated steatohepatitis) with anticipated regulatory submissions in 2026 to 2027. Side effect profile parallels other GLP-1-class agents (nausea, vomiting, diarrhea, occasional gastroparesis) with the additional consideration of glucagon-related effects (modest heart rate elevation, occasional hypoglycemia masked by reduced insulin sensitivity, and consideration of bilirubin elevation). Survodutide is distinct from retatrutide (Eli Lilly's triple GLP-1/GIP/glucagon agonist) in lacking GIP receptor agonism and from cotadutide (AstraZeneca's GLP-1/glucagon dual) in pharmacokinetic profile and clinical positioning.

3. Mechanism of Action

Co-agonism at GLP-1 and glucagon receptors with similar potency. GLP-1 reduces appetite and slows gastric emptying; glucagon increases hepatic fatty acid oxidation and energy expenditure. Synergistic body weight reduction and hepatic lipid mobilization.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Phase 2 obesity 0.6 to 4.8 mg subcutaneous once weekly. Phase 3 dosing similar with titration over 16 weeks.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Le Roux CW, et al. Survodutide for obesity: a phase 2 randomized trial. Lancet 2024.
2. Boehringer Ingelheim. SYNCHRONIZE Phase 3 obesity and MASH trials. Pipeline disclosure 2024.
3. Knerr PJ, et al. Selection and progression of unimolecular agonists at GLP-1 and glucagon receptors. Mol Metab 2022.

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