# Survodutide

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| **Cat. No.:** | HY-P4146 |
| **CAS No.:** | 2805997-46-8 |
| **Molecular Formula:** | $C_{192}H_{289}N_{47}O_{61}$ |
| **Molecular Weight:** | 4231.62 |
| **Sequence Shortening:** | H-{1-amino-1-cyclobutanecarboxylic acid}-QGTFTSDYSKYLDERAAKDFIK-{GGSGSG-γE-C18 di-acid)}-WLESA-NH2 |
| **Target:** | GLP Receptor; GCGR |
| **Pathway:** | GPCR/G Protein |
| **Storage:** | Sealed storage, away from moisture and light<br>Powder -80°C 2 years<br>-20°C 1 year<br>* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light) |

Survodutide

## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (23.63 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 0.2363 mL | 1.1816 mL | 2.3632 mL |
| | 5 mM | 0.0473 mL | 0.2363 mL | 0.4726 mL |
| | 10 mM | 0.0236 mL | 0.1182 mL | 0.2363 mL |

Please refer to the solubility information to select the appropriate solvent.

## BIOLOGICAL ACTIVITY

**Description**

Survodutide (BI 456906) is a potent, selective glucagon receptor/GLP-1 receptor (GCGR/GLP-1R) dual agonist with $EC_{50}$s of 0.52 nM and 0.33 nM in CHO-K1 cells, respectively. Survodutide, a 29-amino-acid peptide, is a potent acylated peptide containing a C18 fatty acid. Survodutide has robust anti-obesity efficacy achieved by increasing energy expenditure and decreasing food intake[1].

**In Vitro**

The $EC_{50}$ is 0.36 nM for Survodutide (BI 456906) in the endogenous mouse GLP-1R in the insulinoma cell line MIN6, and the $EC_{50}$ is 60 pM for GLP-1. In 0.5% human and mouse plasma, Survodutide shows a similar potency to that of endogenous GLP-1. For the GCGR, in 0.5% human and mouse plasma, Survodutide is 6-fold less potent (0.29 and 0.17 nM, respectively) in relation to endogenous glucagon (47 and 30 pM, respectively)[1].

Proteolytic stability of Survodutide is helped by C-terminal amidation and the introduction of a non-coded amino acid 1-aminocyclobutane-1-carboxylic acid (Ac4c) in position 2, well established as the site of proteolytic activity for dipeptidyl peptidase-4. The desired extended terminal half-life of Survodutide is achieved by the introduction of a glycine–serine linker

in position 24, carrying a C18 di-acid[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**In Vivo**

Survodutide (BI 456906; 3, 10, 20, 30 nmol/kg; SC; daily; 30 days) achieves a greater bodyweight-lowering efficacy in diet-induced obese mice compared with maximally effective doses of Semaglutide (HY-114118; 20, 100 nmol/kg). Survodutide dose-dependently reduces plasma glucagon[1].

Survodutide (1, 3, 10, 30, 100 nmol/kg; SC; single dose) dose-dependently reducesacute food intake in WT but not in GLP-1R KO mice (Three-week-old, male, lean NMRI outbred mice)[1].

Survodutide (1, 3, 10, 30, 100 nmol/kg; SC; single dose) engages the glucagon receptor in vivo upon single dosing, increases liver nicotinamide N-methyltransferase mRNA, and reduces plasma serine and glutamine[1].

Survodutide (SC injection) causes mean residence times of 44 and 140 h and $T_{max}$ values of 7 and 51 h obtained in mice and dogs, respectively[1].

Pharmacokinetic Parameters of Survodutide (BI 456906) in mice and dogs[1].

| | Mice (20 nmol/kg; SC) | Dogs (10 nmol/kg; SC) |
|---|---|---|
| $T_{max}$ (h) | 7 | 50.7 |
| $C_{max}$ (nM) | 84.9 | 62.0 |
| $AUC_{0-\infty}$ (nM⊠h) | 4640 | 9540 |

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| Animal Model: | Male C57BL6/J mice pre-fed with a 60% HFD (22 weeks)[1] |
| Dosage: | 3, 10, 20, 30 nmol/kg |
| Administration: | SC; daily; 30 days |
| Result: | Dose-dependently reduced bodyweight from baseline by up to 32% at Day 28 at a dose of 30 nmol/kg. |

## REFERENCES

[1]. Tina Zimmermann, et al. BI 456906: Discovery and preclinical pharmacology of a novel GCGR/GLP-1R dual agonist with robust anti-obesity efficacy. Mol Metab. 2022 Dec:66:101633.



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