BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. 003

Cagrilintide + Semaglutide (Combined Preparation)

A two-component lyophilized research preparation combining a long-acting synthetic amylin analogue with a long-acting GLP-1 receptor agonist — engaging the amylin receptor complexes (AMY1R, AMY3R) and the GLP-1 receptor (GLP-1R) in a single preparation, with mechanistically complementary engagement of the amylin satiety axis and the GLP-1 incretin pathway.

CATALOG REFERENCE	FORM FACTOR	STRENGTH	DATE OF ISSUE
BM-LYO-003	Lyophilized vial	10 mg total (Cagrilintide 5 mg + Semaglutide 5 mg)	May 2026

*This research preparation is a two-component lyophilized combination of **Cagrilintide** (a long-acting synthetic amylin analogue developed at Novo Nordisk by Kruse and colleagues) and **Semaglutide** (a long-acting GLP-1 receptor agonist developed at Novo Nordisk by Knudsen and colleagues). The two compounds are co-lyophilized at 5 mg of each per 10 mg vial. The combination engages two mechanistically distinct receptor pathways that converge on metabolic homeostasis: Cagrilintide engages the amylin receptor complexes (AMY1R, AMY3R) and the parent calcitonin receptor (CTR), while Semaglutide engages the GLP-1 receptor (GLP-1R). Both molecules are acylated peptides that bind reversibly to serum albumin via long-chain fatty acid side chains — Cagrilintide through an N-terminally linked C20 diacid; Semaglutide through a Lys26 C18 diacid with a γGlu-2×OEG linker. **This monograph summarises published cellular pharmacology and preclinical findings for laboratory research reference only.***

01 Component Composition

COMPONENT A — CAGRILINTIDE	5 mg · 37-residue amylin analogue with C20 fatty diacid · CAS 1415456-99-3 · Novo Nordisk development code NN9838 / AM833
COMPONENT B — SEMAGLUTIDE	5 mg · 31-residue GLP-1(7-37) analogue with Aib8 and C18 diacid + γGlu-2×OEG linker at Lys26 · CAS 910463-68-2 · Novo Nordisk development code NN9535
TOTAL MASS PER VIAL	10 mg lyophilized solid
FORM FACTOR	Lyophilized vial · sterile water reconstitution
PHYSICAL FORM	White lyophilized solid co-lyophilizate
ANALYTICAL SPECIFICATION	Component-level ≥ 98 % purity by HPLC; composition verified by HPLC quantification (BIOMOD Labs internal release specification)

02 Rationale for Combined Composition

The amylin–GLP-1 dual-pathway preparation engages two mechanistically complementary receptor systems. **Cagrilintide** acts at the AMY1R and AMY3R amylin receptor complexes (heterodimers of the calcitonin receptor with RAMP1 or RAMP3 respectively) and at the parent calcitonin receptor (CTR), with downstream Gαs coupling and cAMP elevation. Carvas, Leuthardt, and colleagues (2025) demonstrated using genetic knockout models that Cagrilintide's body-weight effects in mice are mediated specifically through brain AMY1R and AMY3R receptors, with the hindbrain identified as a critical anatomical locus. **Semaglutide** acts as a full agonist at the glucagon-like peptide-1 receptor (GLP-1R), a Class B GPCR with extensive expression on pancreatic β-cells, gut enteroendocrine cells, vagal afferent neurons, hypothalamic populations, brainstem area postrema, vascular endothelium, and cardiomyocytes. The combination thereby engages both the amylin satiety axis (centrally, principally via hindbrain) and the GLP-1 axis (peripherally and centrally) in a single preparation.

For complete preclinical characterisation of each component, refer to the individual-compound research literature on Cagrilintide (Kruse et al. *J Med Chem.* 2021, PMID 34288673) and Semaglutide (Knudsen and Lau, *Front Endocrinol.* 2019, PMC6474072).

03 Critical Chemistry-Handling Notes for the Combined Preparation

MULTI-COMPONENT HANDLING CONSIDERATIONS

Both components are acylated peptides with extended plasma residence achieved through reversible albumin binding via long-chain fatty acid side chains. Three handling considerations apply to the combined lyophilizate. **First, Cagrilintide retains the Cys2-Cys7 disulfide of native amylin** — reducing agents (DTT, β-mercaptoethanol, TCEP) must be excluded from buffers, vehicles, and laboratory glassware to preserve the receptor-engaging conformation of Cagrilintide. **Second, Cagrilintide exhibits gelling behaviour on rapid reconstitution at high concentration** — slow reconstitution with gentle mixing is recommended, particularly given the 10 mg total mass in 10 mL of standard reconstitution volume. **Third, both molecules contain Trp residues** (Trp25 in Semaglutide's GLP-1 backbone; the amylin Cys2-Cys7 loop region in Cagrilintide) that are photo-oxidation susceptible; light protection during handling is recommended.

04 Laboratory Handling, Reconstitution, and Storage

Lyophilized solid storage at −18 °C, desiccated, light-protected. Reconstitution in sterile water for injection or bacteriostatic water at neutral pH; reconstitute slowly with gentle mixing rather than vortexing (Cagrilintide gelling behaviour). The acylated lipid side chains create surfactant-like behaviour at dilute concentrations; siliconized glass or polypropylene tubes are preferred. Reconstituted solutions held refrigerated 2–8 °C for short-term work; aliquoted long-term storage at −18 °C with strict minimisation of freeze–thaw. Reducing agents must be excluded throughout. Working concentrations are determined by the investigator's experimental design.

05 References

1. Kruse T, Hansen JL, Dahl K, Schäffer L, Sensfuss U, Poulsen C, Schlein M, Hansen AMK, Jeppesen CB, Dornonville de la Cour C, Clausen TR, Johansson E, Fulle S, Skyggebjerg RB, Raun K. Development of Cagrilintide, a Long-Acting Amylin Analogue. *J Med Chem.* 2021;64(15):11183–11194. PMID: 34288673
2. Lau J, Bloch P, Schäffer L, Pettersson I, Spetzler J, Kofoed J, Madsen K, Knudsen LB, McGuire J, Steensgaard DB, Strauss HM, Gram DX, Knudsen SM, Nielsen FS, Thygesen P, Reedtz-Runge S, Kruse T. Discovery of the once-weekly glucagon-like peptide-1 (GLP-1) analogue semaglutide. *J Med Chem.* 2015;58(18):7370–7380. PMID: 26308095
3. Knudsen LB, Lau J. The discovery and development of liraglutide and semaglutide. *Front Endocrinol (Lausanne).* 2019;10:155. PMC6474072
4. Carvas AO, Leuthardt A, Kulka P, Lommi G, Hassan S, Coester B, Lundh S, Pers T, Secher A, Raun K, Lutz TA, Le Foll C. Cagrilintide lowers bodyweight through brain amylin receptors 1 and 3. *EBioMedicine.* 2025;117:105836. PMC12270663