BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. 012

Tesamorelin

A synthetic 44-residue analogue of human growth hormone-releasing hormone with a trans-3-hexenoyl group attached to the N-terminal tyrosine — a single targeted modification that confers resistance to dipeptidyl-peptidase-IV cleavage while preserving the full receptor pharmacology of native GHRH(1-44).

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
218949-48-5	BM-LYO-012	Synthetic peptide · 44 a.a. + N-terminal acylation	May 2026

Tesamorelin (development designation TH9507) is a synthetic 44-residue analogue of human growth hormone-releasing hormone (GHRH(1-44)) with a single targeted N-terminal modification: a trans-3-hexenoyl group (a C6 chain with a double bond at position 3) covalently attached to the N-terminal tyrosine residue. This hydrophobic acyl modification protects the N-terminus from cleavage by dipeptidyl-peptidase IV (DPP-IV), the principal plasma peptidase responsible for native GHRH degradation, while preserving receptor binding affinity to the GHRH receptor. The molecule was developed by Theratechnologies Inc. and represents the only GHRH analogue with a FDA-approved indication (HIV-associated lipodystrophy, Egrifta, approved November 2010) — chemistry context noted here for receptor-pharmacology purposes only. Tesamorelin retains the full 44-residue length of native GHRH (in contrast to the 29-residue sermorelin and Modified GRF 1-29 analogues), including the C-terminal extension whose function in receptor binding is auxiliary. ***This monograph summarises published preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	Tesamorelin · TH9507 · hexenoyl-GHRH(1-44)
PRIMARY SEQUENCE	trans-3-hexenoyl-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser-Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-NH_2
MODIFICATIONS VS. NATIVE GHRH(1-44)	trans-3-hexenoyl acylation on the N-terminal Tyr1 (DPP-IV protection); C-terminal amide; otherwise identical to native human GHRH
CAS REGISTRY	218949-48-5
MOLECULAR FORMULA	$C_{221}H_{366}N_{72}O_{67}S$
AVERAGE MOLECULAR MASS	5135.9 g · mol^{-1}
PRIMARY MOLECULAR TARGET	GHRH receptor (GHRHR), Class B GPCR — full agonist with affinity comparable to native GHRH[1]
PHYSICAL FORM	White lyophilised solid (typically supplied as the acetate salt)
SOLUBILITY (LAB RECONSTITUTION)	Soluble in sterile water for injection; the hexenoyl modification increases lipophilicity relative to native GHRH; reconstituted solutions are held cold and used promptly
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated, light-protected; reconstituted solution refrigerated 2–8 °C, used promptly; the internal Met27 remains oxidation-susceptible and warrants air-exposure minimisation
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

Tesamorelin was developed at Theratechnologies Inc. (Montréal, Canada) as a chemistry-engineered GHRH analogue addressing the principal limitation of native GHRH: its rapid plasma degradation, primarily through DPP-IV-mediated cleavage of the Tyr1-Ala2 bond at the N-terminus. The Theratechnologies approach was conceptually distinct from the residue-substitution strategy used for Modified GRF 1-29 (Monograph 015): rather than substituting D-Ala for L-Ala at position 2 to block DPP-IV, the tesamorelin design retains the native L-Ala but acylates the N-terminal Tyr with a trans-3-hexenoyl group — a six-carbon hydrophobic acyl chain with a double bond at position 3.[1]

The trans-3-hexenoyl modification serves three chemistry functions. First, it caps the N-terminus, preventing aminopeptidase recognition and DPP-IV cleavage that requires a free N-terminal α-amine. Second, the moderate lipophilicity it introduces alters the molecule's partitioning behaviour in plasma, contributing to in-vivo behaviour distinct from unmodified GHRH(1-44). Third, the acylation chemistry preserves receptor binding affinity at GHRHR; the receptor's binding pocket accommodates the modified N-terminus without loss of agonist potency. Unlike Modified GRF 1-29, tesamorelin retains the native amino acids at the internal positions (Asn8, Gly15, Met27) that the Mod GRF scaffold modifies — so the molecule retains the chemistry liabilities of native GHRH at those positions (deamidation, helical instability, methionine oxidation) while addressing only the DPP-IV cleavage vulnerability.[2]

03 Molecular Target and Cellular Signalling

Tesamorelin is a full agonist at the growth hormone-releasing hormone receptor (GHRHR), the Class B G-protein-coupled receptor expressed on pituitary somatotrophs. Receptor pharmacology in cell-line transfection systems and rat pituitary preparations is comparable to native GHRH(1-44); the hexenoyl modification does not interfere with receptor engagement. Cellular signalling follows the canonical Class B GPCR architecture: Gαs coupling, adenylyl cyclase activation, cAMP elevation, PKA activation, and CREB phosphorylation. In pituitary somatotroph cell culture, tesamorelin produces dose-dependent exocytotic GH release with potency equivalent to native GHRH.[1,3] PRECLINICAL · RAT

04 Preclinical Findings

SYSTEM	PREPARATION	REPORTED OBSERVATION	REF.
Receptor activation	GHRHR-transfected cell lines & rat pituitary	Full GHRHR agonism with potency comparable to native GHRH	1
DPP-IV resistance	Plasma stability studies in animal models	Resistance to deactivation by DPP-IV; extended plasma signal vs. unmodified GHRH	2
Cellular signalling	Pituitary somatotroph cell culture	Gαs → ↑ cAMP → PKA / CREB → GH gene transcription & granule exocytosis	3
Markedly elevated plasma GH/IGF-1	Rat preclinical dose-ranging	Once-daily dosing produces sustained GH and IGF-1 elevation	2
Visceral adipose effects	Animal lipodystrophy models	Reduction in visceral fat markers; preservation of lean tissue markers in preclinical comparisons	2

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

Tesamorelin is one of the better-characterised GHRH-analogue compounds in the published literature, with substantial preclinical data on receptor activation, DPP-IV resistance, and animal-model lipodystrophy outcomes. Researchers should be aware that (a) the molecule retains native Asn8, Gly15, and Met27, so chemistry liabilities at those positions remain present — handling considerations are closer to native GHRH than to Modified GRF 1-29; (b) the trans-3-hexenoyl modification confers DPP-IV resistance specifically, and other plasma peptidase pathways are not addressed by the modification; and (c) the 44-residue length of tesamorelin distinguishes it from the 29-residue sermorelin and Mod GRF analogues, retaining the C-terminal extension whose contribution to receptor pharmacology is documented in the GHRH structure–activity literature.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised tesamorelin (typically supplied as the acetate salt) is held at −18 °C, desiccated, and light-protected. Reconstitution in sterile water for injection is the standard practice in cited methodology. **The internal Met27 residue is oxidation-susceptible** — air exposure of reconstituted solutions should be minimised, and antioxidant excipients or sealed-vial handling are common practice. Reconstituted solutions are held refrigerated 2–8 °C for short-term work; long-term aliquoted storage at −18 °C with strict minimisation of freeze–thaw. Working concentrations are determined by the investigator's experimental design.

07 References

1. Falutz J, Mamputu JC, Potvin D, Moyle G, Soulban G, Loughrey H, Marsolais C, Turner R, Grinspoon S. Effects of tesamorelin (TH9507), a growth hormone-releasing factor analog, in human immunodeficiency virus-infected patients with excess abdominal fat: a pooled analysis of two multicenter, double-blind placebo-controlled phase 3 trials with safety extension data. *J Clin Endocrinol Metab.* 2010;95(9):4291–4304. pubmed.ncbi.nlm.nih.gov/20554713
2. Stanley TL, Falutz J, Mamputu JC, Soulban G, Potvin D, Grinspoon SK. Effects of tesamorelin on inflammatory markers in HIV patients with excess abdominal fat: relationship with visceral adipose reduction. *AIDS.* 2011;25(10):1281–1288. pubmed.ncbi.nlm.nih.gov/21516030
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