BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. 007

PT-141 / Bremelanotide

A cyclic heptapeptide melanocortin receptor agonist derived from the Melanotan-II scaffold by metabolic conversion or chemical engineering — characterised as a non-selective agonist at MC3R and MC4R with preserved activity at MC1R, developed at Palatin Technologies as the lead asset of a structure–activity programme targeting melanocortin signalling.

CAS REGISTRY	CATALOG REFERENCE	CLASS	DATE OF ISSUE
189691-06-3	BM-LYO-007	Synthetic cyclic peptide · 7 a.a.	May 2026

PT-141 (INN: bremelanotide) is a cyclic heptapeptide melanocortin receptor agonist with sequence Ac-Nle-cyclo(Asp-His-D-Phe-Arg-Trp-Lys)-OH, developed at Palatin Technologies (USA) from the Melanotan-II (Monograph 054) scaffold. The molecule represents a structure–activity refinement of MT-II — sharing the same cyclic-lactam core but lacking the C-terminal -Pro-Val-NH_2 tail that contributes to MT-II's strong MC1R pigmentation activity. PT-141 retains potent agonist activity at MC3R and MC4R (the melanocortin receptors most implicated in central nervous system and sexual-function pathways) while exhibiting reduced MC1R engagement compared with the parent Melanotan-II. Like MT-II, PT-141 is built around the canonical melanocortin pharmacophore His-D-Phe-Arg-Trp (positions 6-9 of α-MSH), cyclised through a Lys-to-Asp lactam bridge that locks the bioactive turn conformation. ***This monograph summarises published cellular pharmacology and preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	PT-141 · Bremelanotide
PRIMARY SEQUENCE	Ac-Nle-cyclo(Asp-His-D-Phe-Arg-Trp-Lys)-OH (where Nle = norleucine)
CYCLISATION	Lactam bridge between the Asp side chain and the Lys ε-amine; locks the His-D-Phe-Arg-Trp pharmacophore in a defined turn conformation
CAS REGISTRY	189691-06-3
MOLECULAR FORMULA	$C_{50}H_{68}N_{14}O_{10}$
AVERAGE MOLECULAR MASS	1025.18 g · mol^{-1}
PRIMARY MOLECULAR TARGETS	Melanocortin receptor 4 (MC4R) — principal target for central nervous system and sexual-function effects; Melanocortin receptor 3 (MC3R) — secondary target; lower-affinity engagement at MC1R compared with Melanotan-II[1]
RECEPTOR SELECTIVITY VS. MT-II	Reduced MC1R activity (less pigmentation chemistry) and preserved MC3R/MC4R activity — the principal pharmacological distinction from Melanotan-II[2]
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Water-soluble; the cyclic-lactam architecture confers structural rigidity that does not impede aqueous solubility
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated, light-protected (Trp7 photo-oxidation susceptibility); reconstituted solution refrigerated 2–8 °C; long-term aliquots at −18 °C
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

PT-141 emerged from structure–activity work at Palatin Technologies on the Melanotan-II scaffold. The parent MT-II is a cyclic heptapeptide (Ac-Nle-cyclo(Asp-His-D-Phe-Arg-Trp-Lys)-NH_2) with C-terminal amidation and broad melanocortin-receptor activity including substantial MC1R engagement (producing the pigmentation effects of the parent compound). The Palatin programme observed that metabolic conversion of MT-II through deamidation of the C-terminal amide produces a molecule with reduced MC1R activity while preserving

MC3R/MC4R activity — and developed PT-141 (the C-terminal free-acid form) as the lead asset of this lineage. The structure–activity rationale builds on the canonical melanocortin pharmacophore work of Hruby, Sawyer, and colleagues from the 1980s and 1990s, which established the His-D-Phe-Arg-Trp core sequence as the receptor-binding determinant of α-MSH and related melanocortin peptides.[1]

Chemically, the cyclic-lactam structure is the defining feature: the Asp side-chain carboxyl forms an amide bond with the Lys ε-amine, producing a 23-atom macrocyclic ring that constrains the His-D-Phe-Arg-Trp pharmacophore in the β-turn conformation required for melanocortin receptor binding. The D-Phe at position 4 of the cycle is critical — replacement with L-Phe substantially reduces receptor activity. The N-terminal Nle (norleucine) replaces the native Met of α-MSH and confers protease resistance.[3]

03 Molecular Targets and Cellular Signalling

PT-141 IS A FULL AGONIST AT MELANOCORTIN RECEPTORS MC3R AND MC4R, WITH REDUCED BUT NON-ZERO activity at MC1R. The melanocortin receptors are Class A G-protein-coupled receptors coupled principally to Gαs, with downstream adenylyl cyclase activation, cAMP elevation, and PKA-mediated signalling. The CNS distribution of MC3R and MC4R — particularly the dense MC4R expression in hypothalamic appetite-regulating populations and in the medial preoptic area — has motivated the use of PT-141 in preclinical studies of central appetite regulation, sexual function, and additional CNS-mediated outcomes.[2] PRECLINICAL · RAT

04 Preclinical Findings

SYSTEM	ANIMAL MODEL / PREPARATION	REPORTED OBSERVATION	REF.
Receptor activation	MC1R, MC3R, MC4R-transfected cell lines	Full agonism at MC3R and MC4R; reduced MC1R activity vs. Melanotan-II	1
Central sexual-function pathways	Rat preparations of sexual behaviour	MC4R-mediated activation of central sexual-function pathways	2
Pigmentation chemistry	Cell-culture melanocyte preparations	Reduced melanin synthesis activity vs. Melanotan-II at equivalent doses	1
Appetite regulation	Rodent food-intake preparations	MC4R agonism-mediated appetite reduction at higher concentrations	2

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

PT-141 has a well-characterised receptor pharmacology in the published literature, with its primary distinction from Melanotan-II being the reduced MC1R activity. For researchers working with melanocortin-receptor-targeted compounds, the principal experimental considerations are (a) the cyclic-lactam structure must be preserved; harsh hydrolytic conditions can open the lactam ring and destroy activity; (b) the Trp7 of the cycle is photo-oxidation susceptible; light protection is recommended; and (c) careful selection between PT-141 and Melanotan-II depends on the specific receptor-subtype targets of the experiment — PT-141 is appropriate for studies focused on MC3R/MC4R-mediated central nervous system effects, while Melanotan-II is appropriate for studies requiring all melanocortin-receptor engagement including MC1R-mediated pigmentation chemistry.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised PT-141 is supplied under research-use specifications. The cyclic-lactam molecule is water-soluble. **The Trp7 residue is photo-oxidation susceptible** — light protection is recommended throughout. Lyophilised storage at −18 °C, desiccated, light-protected; reconstituted solutions held refrigerated 2–8 °C; aliquoted long-term storage at −18 °C with minimised freeze–thaw. Working concentrations are determined by the investigator's experimental design.

07 References

1. Molinoff PB, Shadiack AM, Earle D, Diamond LE, Quon CY. PT-141: a melanocortin agonist for the treatment of sexual dysfunction. *Ann N Y Acad Sci.* 2003;994:96–102. pubmed.ncbi.nlm.nih.gov/12851303
2. Pfaus JG, Shadiack A, Van Soest T, Tse M, Molinoff P. Selective facilitation of sexual solicitation in the female rat by a melanocortin receptor agonist. *Proc Natl Acad Sci USA.* 2004;101(27):10201–10204. pubmed.ncbi.nlm.nih.gov/15226502
3. Hruby VJ, Cai M, Cain JP, Mayorov AV, Dedek MM, Trivedi D. Design, synthesis and biological evaluation of conformationally constrained analogues of the melanocyte-stimulating hormone (α-MSH) related peptides (chemistry context). *Curr Top Med Chem.* 2007;7(11):1107–1119. pubmed.ncbi.nlm.nih.gov/17584132
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