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(21) International Application Number: PCT/US98/07438 (22) International Filing Date: 13 April 1998 (13.04.98) (30) Priority Data: 08/837,042 11 April 1997 (11.04.97) US (71) Applicant (for all designated States except US): FERRING B.V. [NL/NL]; Marsstraat 9, P.O. Box 3129, NL-2130 KC Hoofddorp (NL). (72) Inventors; and (75) Inventors/Applicants (for US only): SEMPLE, Graeme [GB/GB]; 2 Station Road, Romsey, Hampshire SO51 8DP (GB). JIANG, Guangcheng [CN/US]; Apartment #39, 8020 Avenida Navidad, San Diego, CA 92122 (US). (74) Agents: SAMPLES, Kenneth, H. et al.; Fitch, Even, Tabin & Flannery, Room 900, 135 S. LaSalle, Chicago, IL 60603 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: GnRH ANTAGONISTS BEING MODIFIED IN POSITIONS 5 AND 6		
(57) Abstract Peptides are provided which have improved duration of GnRH antagonistic properties. These antagonists may be used to regulate fertility and to treat steroid-dependent tumors and for other short-term and long-term treatment indications. These antagonists have a derivative of aminoPhe or its equivalent in the 5- or the 5- and 6- positions. This derivative is modified so as to contain a carbamoyl group or heterocycle, including a urea moiety in its side chain. Particularly effective decapeptides, which continue to exhibit very substantial suppression of LH secretion at 96 hours following injection, have the formulae: Ac-D-2Nal-D-4Cpa-D-3Pal-Ser-4Aph(L-hydroorotyl)-D-4Aph(acetyl)-Leu-Lys(isopropyl)-Pro-D-Ala-NH₂, and Ac-D-2Nal-D-4Cpa-D-3Pal-Ser-4Aph(L-hydroorotyl)-D-4Amf(Q₂)-Leu-Lys(isopropyl)-Pro-Xaa₁₀, wherein Q₂ is Cbm or MeCbm and Xaa₁₀ is D-Ala-NH₂, D-Ala-ol or Ala-ol.		