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Introduction
Various effective therapies are available for the treatment of human osteoporosis including traditional anti-catabolic and modern anabolic treatments. In clinical practice, anabolic agents available include recombinant human parathyroid hormone (PTH) analog (1–34) [nPT31–34, teriparatide, FORTEO/FRORTEO], recombinant human intact PTH (1–84) [nPTP1–84, PREO/PROCTACT], and recombinant human PTH related peptide analog (1–34) [nPTP11–34, alaboparatide, TYMOLO]. PF708 is a 34 amino acid recombinant analog of human PTH that has the same route of administration, dosage form, formulation, and delivery device functionality as the branded reference product FORTEO. PF708 is being developed as a therapeutic equivalent in the U.S. and as a biosimilar outside the U.S. to provide an option for the reference product.

Aim of the Study
The purpose of this study was to compare the nonclinical efficacy of PF708 to FORTEO in the treatment of established osteoporosis in the rat ovarectomy (OVX) model of human postmenopausal osteoporosis.

Materials and Methods
Animal experimentation. The study was conducted using Sprague-Dawley rats (BioPorto, Denmark). All animal experiments were reviewed and approved by the animal ethics committee of the University of Turku. Rats were housed in a temperature and humidity-controlled environment with a 12-hour light/dark cycle. All experiments were performed in accordance with the Guide for the Care and Use of Laboratory Animals, the ARRIVE guidelines 2.0, and the Animal Welfare Act, and were conducted in accordance with the principles of the Animal Welfare Act, the Guide for the Care and Use of Laboratory Animals, and the ARRIVE guidelines 2.0. The development of OVX-induced osteoporosis was confirmed by UCT in rats after 6 post-surgery weeks. UCT values were calculated by dividing the bone weight obtained at the beginning and end of treatment by body weight obtained before surgical operation. Relative change in BMD (B) was calculated by dividing the values obtained before the start and at the end of treatment period by values obtained before surgical operation. Relative change in BMD (B) was calculated by dividing the values obtained at the end of treatment period by values obtained before the start of treatment period (end/start). One-way ANOVA indicated a statistically significant difference from OVX control group treated with vehicle alone and from vehicle + PF708. Other statistical treatments were performed as described in the methods section. The authors are grateful to Mircea Auranen, Pia Tiirikko, Anilolu Lusinde, Jukka Lehto, Jochen Zippouna, Pfint Allmannia, Laura Jakobson, Rasu Kyrysh, Ingemar Seggert, and Yenesis Rokos for their expert technical assistance.

Body and Uterine Weight

Tibial Diaphysis

Summary
In body and uterine weight, there were no significant differences between adult OVX rats treated with PF708 and FORTEO at 8 µg/kg/d each (Fig. 1).
In the tibial metaphysis of adult OVX rats, both PF708 and FORTEO treatments at 8 µg/kg/d were increased bone BMD compared with vehicle and the other treatments. Absolute change in BMD (B) was calculated by dividing the bone weight obtained before the start and at the end of treatment period by values obtained before surgical operation. Relative change in BMD (B) was calculated by dividing the values obtained at the end of treatment period by values obtained before the start of treatment period (end/start). One-way ANOVA indicated a statistically significant difference from OVX control group treated with vehicle alone and from vehicle + PF708. Other statistical treatments were performed as described in the methods section. The authors are grateful to Mircea Auranen, Pia Tiirikko, Anilolu Lusinde, Jukka Lehto, Jochen Zippouna, Pfint Allmannia, Laura Jakobson, Rasu Kyrysh, Ingemar Seggert, and Yenesis Rokos for their expert technical assistance.

Conclusions
This study demonstrated that the nonclinical efficacy of PF708 is equivalent to FORTEO in the treatment of established osteoporosis in the rat ovarectomy (OVX) model of human postmenopausal osteoporosis.

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