

Recombinant Human Parathyroid Hormone

Recombinant human parathyroid hormone (1-84) as an anabolic therapy for osteoporosis

Summary

Indication:

Osteoporosis

Development Stage:

Phase I and II clinical studies completed in USA, UK and Germany

Intellectual Property:

Several patents covering the proprietary method of production of *hPTH* filed in countries including US and EU.

Partnering Interests:

Co-development, Licensing out

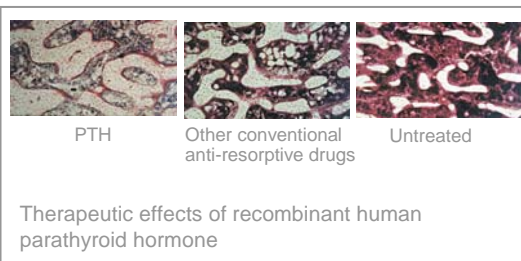
Introduction

PTH is a peptide of 84 amino acid residues that is synthesized in and secreted from the parathyroid gland. It is a major regulator of calcium and skeletal homeostasis, acting primarily through its receptor on target cells in bone and kidney. Unlike its physiological role as a catabolic molecule, the intermittent administration of PTH mediates anabolic increase of bone mass as has been demonstrated in numerous animal and human studies. This unusual property of PTH is being exploited by several drug companies, including Eli Lilly and NPS Pharmaceuticals, to develop it as a therapeutic drug for the metabolic disease, osteoporosis. Forteo, a short version of *hPTH*, has been launched by E. Lilly in the US and European markets.

PTH, as a therapy for osteoporosis, is unique in that it is anabolic in bone, as compared to currently available therapies such as estrogen, calcitonin and bisphosphonates which are all antiresorptives.

restoration of bone in terms of both amount and strength. Preclinical toxicity studies using mice, rats and cynomolgus monkeys were carried out to determine the maximum tolerable dose and the no toxic effect dose, which subsequently proved the safety of recombinant *hPTH* for clinical use. Both preclinical studies were carried out in the UK.

An IND was filed with the US FDA and two phase I clinical studies were conducted in the UK and USA. A phase IA clinical study (UK) with healthy volunteers was completed in a single-blind and dose escalation mode, demonstrating tolerability of the drug in human. The phase IB study (USA) was a randomized, double-blind, multidose (daily dosing for 7 days) study evaluating the safety and tolerability of recombinant *hPTH* in healthy postmenopausal women. The drug was well tolerated and showed expected physiological activities, demonstrating its suitability for further development. A phase II randomized and double-blind study (Germany) has been carried out with a total of 200 patients for investigating the efficacy and safety of *hPTH* on postmenopausal osteoporosis patients. The results obtained for the primary target parameter (intra-individual percentage change of the bone mineral density of the lumbar spine L2-L4, DXA-method) demonstrated a statistically significant increase in the patients treated with medium (75 µg) and high (100 µg) dose PTH (6.4% and 7.5% respectively) as compared to the patients treated with low (50 µg) dose PTH or placebo (3.4% and 1.5% respectively).



Development Summary

We have developed an efficient and novel process for the large-scale production of recombinant *hPTH* using an inducible expression system of *E. coli*. A proprietary fusion expression system and a site-specific proteolytic cleavage method have also been developed. Preclinical studies with recombinant *hPTH* using ovariectomized, and thus osteopenic rats demonstrated that it was effective in the

Potential Benefits

- Specific for bone cells with minimal side effects
- Proprietary expression and production systems
- Pilot scale production for clinical studies

Interested in this technology?
Ask for more information.

Contact:

Tel: +82 31 260 9877

Fax: +82 31 260 9808

Email: mogam@mogam.re.kr

Web: www.mogam.re.kr