Bone Therapeutics reports initial efficacy results from its PREOB® Phase IIA trial in severe osteoporosis

Positive effects on pain and bone turnover markers in first patient cohort

Gosselies, Belgium, 29 March 2016 – BONE THERAPEUTICS (Euronext Brussels and Paris: BOTHE), the bone cell therapy company addressing high unmet medical needs in the field of bone fracture repair, fracture prevention and spinal fusion, today announces the 12-month efficacy results from the first cohort of seven[1] patients treated with PREOB® in its Phase IIA severe osteoporosis trial. These initial data demonstrate positive effects on pain and osteoporosis blood markers of a single administration of PREOB®.

Osteoporosis is a condition characterized by an excessive loss of bone mass due to impaired bone turnover. The natural balance between bone formation and bone resorption is disturbed, leading to bone fragility and increased fracture risk. The ongoing Phase IIA trial has been designed to evaluate a single intravenous administration of PREOB® in patients with severe osteoporosis, defined as those who no longer respond to anti-osteoporotic therapy. In total, 20 patients will be enrolled in the study and followed up over 12 months. The primary endpoints of the study are safety and biodistribution of PREOB® cells. In addition, effects on clinical symptoms (i.e., pain and general health status[2]) and serum markers of bone turnover are being evaluated.

In this first cohort, patients experienced a pronounced and clinically relevant decrease in pain (of more than 40%), reaching a maximum at six months post-treatment. In a similar patient population, six-month daily subcutaneous administration of the bone anabolic agent[3] teriparatide only achieved a 30% decrease in pain[4]. A same positive trend was also observed on the general health status of PREOB®-treated patients.

Moreover, analysis of the profile of bone markers in the blood shows a surprising dual trend: (i) in an early phase of the 12-month follow-up, a decrease (of more than 25%) of bone resorption (bone breakdown) markers[5] was observed, while bone formation markers[6] were either unaffected or even slightly increased and (ii) in a later phase of the 12-month follow-up, a continuous increase in bone formation markers was observed with a moderate increase in bone resorption markers. The unexpected early decrease in bone resorption markers is especially remarkable, as studies[7] have shown that in a comparable population of severe osteoporosis patients, where bone turnover is totally suppressed, antiresorptive drugs have no additional effect on bone resorption.

These preliminary results thus seem to indicate that a single administration of PREOB® progressively stimulates bone remodelling, with a bone formation-to-resorption ratio more favourable than that generally reported with other anti-osteoporotic agents in the same patient population. Indeed, by comparison, while bone anabolic treatments in general show stronger effects on bone formation markers, their bone formation-to-resorption ratio is less favourable, with bone resorption twice as highly increased as bone formation[8]. Therefore, this surprising effect of PREOB® on bone turnover suggests a different – potentially more favourable – mechanism-of-action compared to existing therapies.

Enrico Bastianelli, CEO of Bone Therapeutics, commented: *"These initial 12-month results are encouraging as they show that a single intravenous administration of PREOB®, through a different mechanism-of-action, could have beneficial effects on pain and bone turnover in treatment-resistant osteoporosis patients. We look forward to reporting additional results on this innovative approach."*

[1] In total, nine patients were enrolled in the study, of which seven have received PREOB®. In such a small number of patients, the relevance of statistical analysis is limited.
[2] Pain is measured using a validated scale (100mm-Visual Analogue Scale) completed by the patient. Pain relief is considered as clinically relevant when it reaches a change of at least 10mm on the scale (in accordance with literature). General health status is measured using a validated questionnaire (SF-36).
[3] Unlike standard antiresorptive agents, anabolic (bone-forming) agents aim to stimulate bone formation.
[4] Jakob *et al*. European Journal of Endocrinology (2012)87–97.
[5] Carboxy-terminal crosslinked telopeptide of type 1 collagen (CTX) is considered as the standard bone resorption marker. It is a degradation product of collagen produced during bone matrix resorption.
[6] Bone-specific alkaline phosphatase (B-ALP) and osteocalcin (OC) are considered as standard bone formation markers. They are produced by bone-forming cells (osteoblasts) and are a measure of their number and activity.

[7] Black *et al*. Journal of Bone and Mineral Research (2012)243-254; Miller *et al*. Osteoporosis Int (2012)1747-1756: the extension or switch of an initial treatment by an anti-resorptive agent to the anti-resorptive zoledronic acid (Black *et al.*) or ibandronate (Miller *et al.*), after an initial treatment period, had no or limited impact (10% decrease) on the resorption markers CTX within the first 12 months, and either stabilize or increase during the following 3 years (HORIZON-PFT and MOBILE studies).
[8] Keel *et al.* J Bone Miner Metab (2010)68–76: Following therapy switch from bisphosphonate to daily teriparatide treatment, the bone formation marker B-ALP increased by 50% while the bone resorption marker CTX increased by 100% at 12 months. Middleton *et al*. Journal of Bone and Mineral Research (2010) 455–462: Following therapy switch from bisphosphonate to strontium ranelate, the bone formation marker B-ALP increased by 46% while the bone resorption marker CTX increased by 61% at 12 months.

About PREOB®

PREOB® is Bone Therapeutics' first-in-class autologous osteoblastic cell product. Based on promising results of the proof-of-concept Phase II studies, which have shown statistically significant and clinically relevant benefits, PREOB® is currently in two pivotal trials in Europe: a Phase III trial for the treatment of hip osteonecrosis and a Phase IIB/III trial for the treatment of long bone non-union fractures. For these indications, PREOB® is administered percutaneously via a minimally invasive approach, avoiding the need for open surgery. Additionally, PREOB® is being evaluated in a proof-of-concept Phase IIA clinical trial for the treatment of severe osteoporosis, where it is administered intravenously.

About severe osteoporosis

Osteoporosis is a condition characterized by an excessive loss of bone mass, leading to bone fragility and increased fracture risk. Osteoporosis is considered a serious public health concern and ageing demographics continue to increase the affected population. Current treatments for osteoporosis predominantly inhibit bone resorption (by altering osteoclast activity and lifespan) but do not actively stimulate bone formation, and up to one third of patients under treatment are still losing bone mass or experiencing fractures. With PREOB®, Bone Therapeutics aims to offer a new mechanism of action to improve bone mass based on the administration of differentiated bone-forming cells that provide osteogenic, osteoclastic and angiogenic properties.

About Bone Therapeutics

Bone Therapeutics is a leading biotechnology company specializing in the development of cell therapy products intended for bone fracture repair and fracture prevention. The current standard-of-care in this field involves major surgeries and long recovery periods. To overcome these problems, Bone Therapeutics is developing a range of innovative regenerative products containing osteoblastic/bone-forming cells, administrable via a minimally invasive percutaneous technique; a unique proposition in the market.

PREOB®, Bone Therapeutics' autologous bone cell product, is currently in pivotal Phase IIB/III clinical studies for two indications: osteonecrosis and non-union fractures, and in Phase II for severe osteoporosis. ALLOB®, its allogeneic "off-the-shelf" bone cell product, is in Phase II for the treatment of delayed-union fractures and lumbar fusion for degenerative disease of the spine, including a minimally invasive therapy for failed spinal fusions. The Company also runs preclinical research programs and develops novel product candidates.

Founded in 2006, Bone Therapeutics is headquartered in Gosselies (South of Brussels, Belgium). Bone Therapeutics' regenerative products are manufactured to the highest GMP standards and are protected by a rich IP estate covering 11 patent families. Further information is available at: www.bonetherapeutics.com.

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