Osteo-Metabolix Pharmaceuticals Inc.

Strategic Partnership Opportunity

Innovative Targeted Delivery of Bone Disease Therapies

December 2010

Introduction

Osteo-Metabolix (OMX) Pharmaceuticals Inc. presents a strategic partnership opportunity for development, formulation and pre-clinical evaluation of unique targeted therapies for bone disease.

The Problem

Loss of bone mineral density in osteoporosis, osteoarthritis, rheumatoid arthritis, bone cancer and Paget's disease is a real and significant clinical problem. The polypeptide hormone calcitonin (CT) is currently used as a treatment to inhibit the bone-resorptive actions of osteoclasts and decrease their numbers, thereby improving bone-mineral density. However, the half-life of unconjugated CT is short (43 minutes), the peptide concentration in bone is greatly reduced by systemic dilution, and its therapeutic effectiveness is reduced. Increasing CT dosage is limited by unwanted systemic side effects and organ toxicity.

The OMX Solution: Bisphosphonate-conjugated Calcitonin

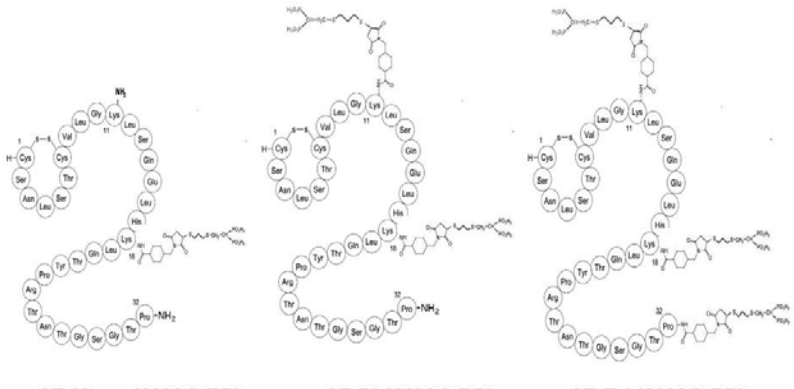
OMX Pharmaceuticals has developed and synthesized bone-seeking variants of calcitonin by conjugation of CT with a bisphosphonate under highly controlled reaction conditions. **BP-conjugated calcitonin (BP-CT) directly targets bone tissue** by its specific binding to hydroxyapatite, eliminating the problem of systemic drug dilution and side effects.

Our BP-CT conjugates currently have several formulations containing from one to three water-soluble bone targeting moieties.

Osteo-Metabolix Pharmaceuticals Inc.

- Biopharma technology start-up located in Edmonton, Alberta.
- Develops, formulates and evaluates bone-targeting therapeutics for bone cancer, osteoporosis, and osteoarthritis.
- Bisphosphonate conjugated calcitonin is unique to the company
- Very strong IP position on BP-CT – provisional patent filed Oct 2009, with full PCT filing in Oct 2010
- Fee-for-service bone mass and mineral density micro-CT services and high throughput bone toxicology cell culture assays
- Managed by highly experienced research team at the University of Alberta

Several of our BP-conjugated Calcitonin variants



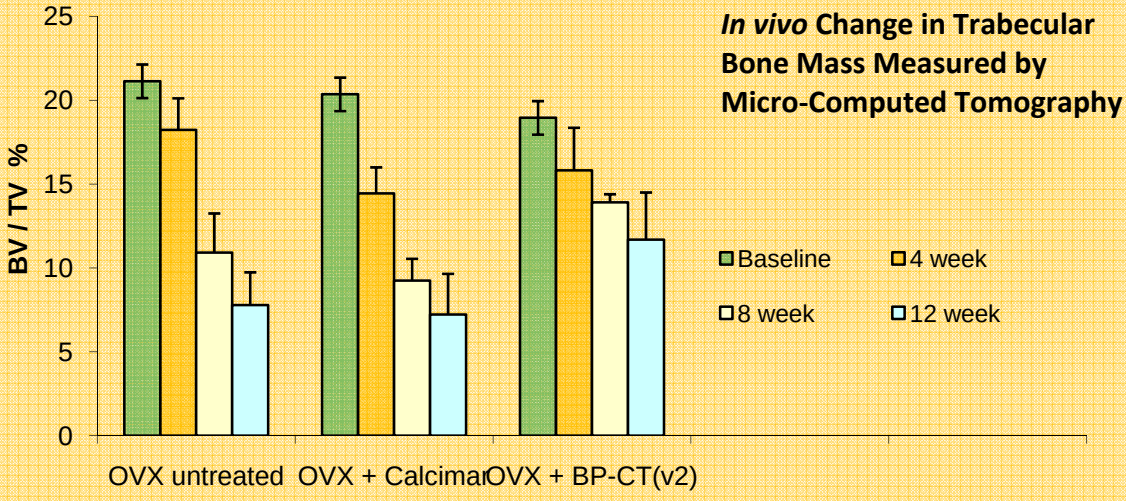
sCT-Mono (SMCC-BP) sCT-DI (SMCC-BP) sCT-Tri (SMCC-BP)

These compounds have been characterized extensively by analytical techniques (NMR spectroscopy, MALDI-TOF, SDS-PAGE) to prove that BP-CT has a greatly increased affinity for bone than unconjugated CT. We have used hydroxyapatite binding studies to show that BP-CT has increased affinity for bone mineral, and an *in vitro* cAMP binding assay to show calcitonin receptor activation. BP-CT conjugates reduce serum calcium levels in rats to the same degree as unconjugated CT.

BP-CT Outperforms Commercially Available Calcitonin *In Vivo*

We tested the pre-clinical antiresorptive efficacy of BP-CT versus unmodified calcitonin in a rat model of osteoporosis secondary to ovariectomy (OVX). We measured the bone mass in groups of 4 rats by micro- computed tomography at 0, 4, 8 and 12 weeks after OVX surgery.

Rats that received BP-CT showed significantly greater bone mineral density than untreated rats, or those that received commercially purchased calcitonin (Calcimar, sanofi-aventis).



This preliminary study clearly shows compelling evidence for the antiresorptive efficacy and potency of our BP conjugated calcitonin formulation.

The Business Opportunity

BP-conjugated calcitonin is unique to OMX Pharmaceuticals. While there is significant activity in the area of BP-conjugated protein drugs in general, **no other research groups are currently investigating BP-CT as a targeted anti-resorptive therapy.** This means that BP-CT is highly marketable as a significantly improved treatment for a wide range of diseases where there is low bone mass, including osteoporosis.

This puts OMX Pharmaceuticals in a very strong IP position, and based on this we successfully filed a US provisional patent in October of 2009 (application serial number 61/251,472), with full PCT protection currently under way. In the patent application we provide details of and make claims for our BP-CT conjugates, functional bioassays and methods for applying the new drugs for treatment of osteoporosis and other bone diseases.

Why Partner with OMX?

OMX is looking to partner with industry for mutual benefit. We have an already-developed product with patent protection and great market potential that follows on well from the synthetic calcitonin program at PHARMA. In pre-clinical testing, we have proven that BP-CT would be a superior product to other calcitonin formulations already on the market, and oral formulations under development.

The company that partners with OMX will gain world-wide exclusive rights to market this product, along with improved patent protection. OMX will also provide in-depth expertise in bone biology and related animal models, and access to specialized assays for bone mass and mineral density measurement and bone-targeted drug toxicity testing (see Appendix).

Partnering with PHARMA would allow us to proceed with optimization of BP-CT for pharmaceutical formulation through characterization of its pharmacokinetic and pharmacodynamic properties (see sidebar). We have already established animal models of osteoporosis and osteoarthritis to be used in this testing.

Partnership with OMX will fast-track the long lead times for new product development, providing a novel drug with multiple applications for diseases affecting large patient populations. These include osteoporosis, osteoarthritis, rheumatoid arthritis, bone cancer and Paget's disease.

Determining the Value of Bone-Targeting Calcitonin

- **Pharmacokinetics**: Injection of ^{125}I-BP-CT into animal models via s.c. and i.v. routes
- **Determination of dosage**: toxicity and efficacy testing in animal models
- **Testing vs. conventional CT therapy:** FDA-designed preclinical efficacy trial in established rat model of osteoporosis

Summary

OMX Pharmaceuticals Inc. specializes in the development of novel bone-targeted therapies with a broad spectrum of applications in bone disease. Bisphosphonate conjugated calcitonin is unique to OMX, putting us in a very strong IP position with excellent market potential. BP-CT has improved therapeutic efficacy in increasing bone density and reduced systemic side-effects versus conventional, unconjugated calcitonin.

Strategic partnership with OMX will provide the partnering company with shortened product development times, improved patent position, natural follow on from existing drug development programs, and access to specialized expertise and testing methodologies for drugs acting on bone cells.

Contact Information

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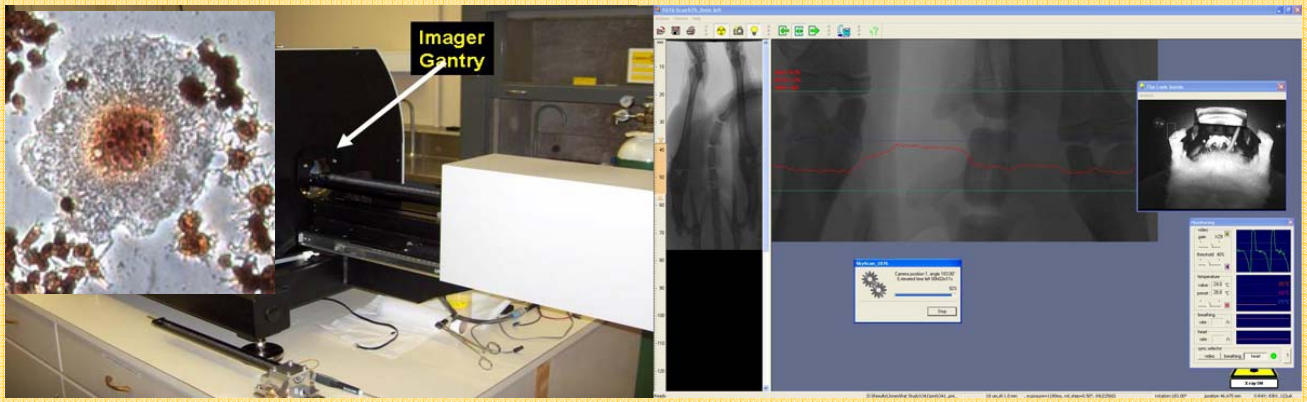
Appendix: OMX Advanced Laboratory Services

OMX offers unique advanced bone mass, mineral density and bone toxicology assays on a fee-for-service basis.

1. High Resolution Micro-Computed Tomography Imaging of Bone
OMX is equipped with an in vivo micro-CT unit, for the non-invasive quantification of bone and mineral adaptations after pharmaceutical, orthopaedic, orthodontic and biomedical interventions in experimental laboratory animals.

2. *In vitro* Bone Toxicology: High-Throughput Cell Culture Assays
We have established state of the art osteoclast and osteoblast culture systems, in order to conduct bone cell assays under GLP conditions. These allow us to test novel drug or environmental chemical compounds for effects on bone cell stimulation, inhibition, and/or toxicity.

Skyscan 1076 *in vivo* Micro-CT



Bone Cell Toxicology Assays

- **Osteoclast Cultures**: testing of drug antiresorptive activity (RANK receptor activation, TRAP activity assay, densitometric mineral resorption, MTT-based cytotoxicity assay, calcitonin receptor binding affinity, ELISA assay of bone turnover markers NTX-I, CTX-I, TRAP5b)

- **Osteoblast Cultures:** testing of drug stimulatory and/or toxic activity (RT-PCR for collagen type I gene expression, ELISA assay of bone turnover markers, MTT-based cytotoxicity assay)