MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

THERAPY

12b80

HBP-bound doxorubicin: development of a new bone-targeting anticancer therapy to cure primary bone cancer and secondary bone metastases Telomium

CONTEXT & BACKGROUND

Primary bone cancer, which includes **osteosarcoma,** chondrosarcoma and Ewing's sarcoma, is a rare type of cancer accounting for less than 0.2% of all cancer. Though it is the most common primary bone tumor, osteosarcoma represents less than 1000 and 1500 patients diagnosed each year in USA and EU respectively, which makes it an ultra-orphan disease. Osteosarcoma can arise at any age but shows higher incidence in patients below 24 years (with a peak during pubertal growth between 15 and 19)
and accounts for about **3% of cancers that happen in children and youths**. There is another high incidence of osteosarcoma above 60 years. Standard treatment for osteosarcoma includes limb salvage surgery, neoadjuvant and adjuvant chemotherapy (combination of doxorubicin, cisplatin and high-dose methotrexate) and heavy pain management. Despite impressive efforts, no improvement have been made over the past decade in the treatment primary osteosarcoma and relapsed disease is still considered as noncurable, denoting **unmet needs** for rapid progress beyond current medical care. **Atlanthera** is a clinical stage small pharmaceutical company expert in the **bone targeting and delivery** of chemical drugs through custom-made **bisphosphonate vectors**.
Since osteosarcoma responds to chemotherapy, the rationale of **12b80 project** is to develop a new antineoplastic drug candidate to get a cure for osteosarcoma patients. Atlanthera is focused on osteosarcoma related issues that are treating both localized tumor, unresectable tumor, lung metastasis and tumor associated bone resorption.

INNOVATIVE COMPONENT & TECHNOLOGY

The idea behind 12b80 is simple: **Decrease doxorubicin systemic distribution and associated cardiotoxicity through targeting of bone tissue and specific release in a tumor microenvironment-dependent manner.** Our drug candidate 12b80 is a patented bifunctional molecule, which is composed of three blocks: the **gold standard doxorubicin** (which still has the best response rate as monotherapy in osteosarcoma), a custom synthetized bone targeting **new hydroxy-bisphosphonate (HBP) vector** and the core of the innovation, a **pH-sensitive linker** that we designed to take advantage of tumor associated acidity to trigger doxorubicin release. Atlanthera has fulfilled the preclinical development of 12b80 molecule by demonstrating the proof of concept on various experimental rodent models of bone cancer and in a veterinary dose escalation study in osteosarcoma bearing companion dogs

SCOPE

A new Small Molecule Drug Conjugate : Targeting bone to cure primary bone cancer and secondary bone metastases

KEYWORDS

Bone cancer, bisphosphonate, doxorubicin, vectorization, bone-targeted drug delivery, chemotherapy, antineoplastic

OBJECTIVES

The primary objective for Atlanthera is to start a coupled **phase I/IIa** multicentered trial in France with up to five investigator centers in collaboration with our medical board.
Our second objective is to build subsequently **a partnership with large pharmaceutical companies** to negotiate a licence transfer to get 12b80 marketed.
Our third objective is to **develop,** in parallel of 12b80, **new vectorised compounds** with other promising active molecules.

DEVELOPMENT & MATURATION STAGE

12b80 is under preclinical regulatory toxicity study. Phase I/IIa will start in Q2 2018

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

Derives hydroxybisphosphoniques hydrosolubles de la doxorubicine.
PCT/EP2015/077279

TARGET POPULATION

Young adults and adults with primary and metastatic osteosarcoma.

TARGET PROFILE

12b80 will be conditioned as sterile powder, reconstituted in NaCl 0.9%, delivered by slow intravenous infusion through intermittent cycles with three weeks break.
The first indication of 12b80 compound will be the neoadjuvant and adjuvant treatment for primary and metastatic osteosarcoma. The clinical trial with 12b80 will be first as salvage monotherapy in phase I in patients with metastatic or unresectable bone tumors, including osteosarcoma, chondrosarcoma, Ewing's sarcoma or patients with uncurable metastases derived from breast and prostate cancer. Phase I will be coupled to a phase II with an extended minimum cohort of 15 patients with osteosarcoma and 15 patient with breast/prostate-derived bone-only metastases.
Even we have obtained a vast amount of data demonstrating the efficacy of 12b80 in monotherapy, final clinical use of 12b80 will certainly be in combination therapy with cisplatin, high-dose methotrexate or with the most advanced drugs such as targeted therapy or immunotherapy.

STRENGHTS & COMPETITIVE ADVANTAGES

12b80 is a new compound with low and reversible toxicity, specific bone tumor environment targeting, prevention of tumor associated bone remodeling, strong antitumor effects on primary bone tumor, osteosarcoma derived lung metastasis and secondary bone metastasis, potent therapeutic effect in companion dogs and with a strong IP.
By targeting osteosarcoma, we expect to get an **orphan drug designation** for 12b80 in USA and EU, which will give substantial advantages (such as tax credit of the clinical drug testing cost, waiver of NDA/BLA application fees, seven year USA and ten years EU exclusivity after approval of marketing) to maximize the probability of a successful outcome at the marketing authorization stage.

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

12b80 compound fulfills a currently unmet medical need in osteosarcoma. Incidence of osteosarcoma is less than 1000 patients diagnosed each year in USA and less than 1500 in EU. A fair estimate of the cost of a new drug, especially in the context of price regulation in EU, would depend on its cost-effectiveness ratio based on the cost of additional quality-adjusted life years (QALYs) they provide. While we cannot predict yet the gain of life quality with 12b80 treatment, since half of the patients will be youths, 12b80 gain of QALY will be an important criteria to impact its economic value.
Primary targeted market of 12b80 molecule is osteosarcoma, yet there could be a possible extension of indication to bone metastases, which represents the opportunity to cure a larger population of patients.
The art of chemically binding any chemical compound to a HBP vector makes Atlanthera a unique pharmaceutical company: experience from 12b80 development will give us the opportunity to develop other bone targeting therapies for other bone related diseases such as inflammation, infection and pain.
Moreover, we aim to build a strong partnership with large pharmaceutical companies to improve their marketed products by getting new indications, patent possibilities and give a second chance to products that have been rejected for adverse toxicity or tissue distribution issue.

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