

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

PHOST'IN

A NEW CLASS OF BIOACTIVE MOLECULES TARGETING CANCER (FIRST THERAPEUTIC INDICATION: GLIOBLASTOMA)

2012_Bakalara

SCOPE

PHOST'IN develops a **new class of anti-cancer drugs, targeting glycosylation with an innovative MoA**. A first lead has been qualified on various indications including our first targeted pathology, **Glioblastoma (GBM)**. First-in-Human is planned in 2017

KEYWORDS

Oncology, glioblastoma, glycomimetics, aggressive solid tumors

CONTEXT & BACKGROUND

PHOST'IN is the result of a collaborative work between biologists, chemists and world-class clinicians specialized in GBM care. This triple vision has structured the project around a precise clinical need: **the development of a treatment that is both anti-tumor and anti-invasive**, targeting tumor progression. In this context, the PHOST'IN team has focused on **the selective disruption of GBM cell glycosylation**. Using its expertise on phosphorus chemistry, 400 original glycomimetics have been selected and synthesized, Phostines™, to select the lead compound PST 3.1a.

INNOVATIVE COMPONENT & TECHNOLOGY

PHOST'IN has demonstrated, **for GBM and other cancers, *in vitro* effects of PST 3.1a on tumor proliferation and migration. *In vivo* studies show a strong reduction of tumor volume, invasiveness (up to 90% in GBM orthotopic model), and metastasis formation in various orthotopic and subcutaneous models. Median survival time is significantly increased.** Deciphering the MoA, **which involves intrinsic cytotoxic effects combined with activation of an inhibited immune response (NK)**, has highlighted predictive response markers and opened the way to new indications.

Beyond the specific results achieved with PST3.1a, more than 100 new compounds can be generated per year, based on the Phostines™ scaffold. Anti-proliferation, anti-invasive, anti-migratory effects have already been demonstrated *in vitro* / *in vivo* with other Phostines™, confirming the family's potential.

OBJECTIVES

Our ambition is to develop new chemical entities that can ameliorate suffering of people affected with rare and invasive cancers. Phost'In begins with a first qualified Lead that targets various aggressive solid tumors, including the rare disease Glioblastoma (currently no effective curative therapy available), but also Squamous Cell Carcinoma (SCC), NSCLL, resistant breast Cancers, etc.

TARGET POPULATION

PHOST'IN focuses on strongly invasive cancers, many of them lacking a satisfying curative treatment at this time, such as GBM, (53,000 cases / year around the world), squamous cancers (>900,000 cases), pancreas cancer (338,000 cases), resistant breast cancers, etc.

TARGET PROFILE

Each of these segments could represent a potential €1 billion market. In September 2011, the direct GBM market which was evaluated to 370m\$ was supposed to reach 450m\$ in 2018. This apparently niche market can be explained by the short time overall survival and to the supply failure: Temodal patent expiration, new generic compound and low efficacy of new entries. The potential market was estimated to **750 m\$ (US) or 450 m\$ (EU)**.

DEVELOPMENT & MATURATION STAGE

Qualified *in vivo* on subcutaneous and intracranial mouse models, **our lead compound passes through the blood-brain-barrier. It has demonstrated strong antitumoral activity, associated with no toxic effects.** Its MoA involves **intrinsic cytotoxic effects combined with activation of an immune response. Furthermore, it inhibits the metastatic process**, extending the potential application of the overall family. Ours next goals are:

1. To achieve IMPD by the end of the year and to carry out Phase I/II in 2017/2018

2. To enlarge the family of compounds

INTELLECTUAL PROPERTY & PATENT CO-OWNER(S)

The company PHOST'IN has an international exclusive license from 2 academic patents (2009 & 2013) that are protecting the whole family and its therapeutic indications. A new patent application is on-going.

STRENGTHS & COMPETITIVE ADVANTAGES

With respect to our first targeted indication, GBM, many clinical studies are in progress, for the most part corresponding to old compounds screened on other cancerous pathologies. However, no sound results can be observed regarding overall survival. Hope focuses on very innovative treatments (gene therapy, antibodies, vaccines), but they are much more expensive and risky in terms of R&D and industrial development.

In comparison, PHOST'IN brings:

- (i) **An innovative compound family.**
- (ii) **Small molecules**, with low costs **for research and production.**
- (iii) Compounds that can **inhibit metastatic processes** and target secondary cancer.

Specifically for the lead candidate / GBM indication:

- (iv) **A new target** (whose therapeutic potential is strongly highlighted in recent literature) and **original Mode of Action.**
- (v) In vivo anti-proliferation and anti-invasive effects, **correlated with strong improvement of median survival time.**
- (vi) Classical administration and **ability to pass through the blood-brain-barrier (BBB).**
- (vii) **Initial screening directly carried out on cell lines and primary cultures of human GBM.**

INDUSTRIAL APPLICATIONS & PARTNERSHIP OPPORTUNITIES

PHOST'IN's objectives are bringing to the Pharmaceutical Industry a new class of anti-tumoral compounds first on GBM and to extend their uses to other cancers. Our current goal is to obtain an industrial co-development agreement regarding the first Lead molecule.

CONTACT

PHOST'IN : Karine Chorro & Ludovic Clarion, contact@phostin.com

Inventor & co-founder Phost'In : Norbert Bakalara (academic inventor) norbert.bakalara@enscm.fr

MATWIN : Lucia Robert, lucia.robert@matwin.fr
