MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

THERAPY

Oncolytic virus Myb34.5 for pancreatic adenocarcinoma

CONTEXT & BACKGROUND

We are a biopharmaceutical company which develops oncolytic virus Myb34.5. Worldwide exclusive rights on human and veterinary uses were licensed from Massachusetts General Hospital (Harvard University). Our initial focus is on a severe indication in high medical need: advanced pancreatic ductal adenocarcinoma.

Pancreatic cancer is one of the deadliest cancer types and remains one of the most difficult cancers to treat despite recent moderate therapeutic improvements. Median survival is only six to 11 months. Gemcitabin has been for many years and remains the main standard of care. Combination of gemcitabin with other chemotherapies (oxaliplatin, erlotinib) has shown no or only limited survival prolongation. FOLFIRINOX regimen and the combination of gemcitabin and nab-paclitaxel have shown moderate survival improvements and have become new standards of care. The medical need is still very high.

Myb34.5 is derived from Herpes Simplex Virus type-1 (HSV-1) through targeted genetic engineering. Intratumoral injection of Myb34.5 strongly inhibited tumour progression in an orthotopic xenograft model of pancreatic adenocarcinoma. Combining gemcitabine and Myb34.5 resulted in a significant higher inhibition of tumour growth than either treatment alone. Myb34.5 replication correlated well with expression of b-myb and other markers in pancreatic adenocarcinoma, which will be evaluated as possible biomarkers for patients' selection in clinical trials, and thus as companion diagnostic.

INNOVATIVE COMPONENT & TECHNOLOGY

Myb34.5 is derived from HSV-1 through targeted genetic engineering. Key mutation is insertion of cellular transcription factor b-myb as promoter sequence retargeting expression of virulence gene gamma34.5. Replication of Myb34.5 is conditioned by expression of b-myb, which is dysregulated (amplified and/or highly expressed) in almost all cancer types, and is also over-expressed in pancreatic adenocarcinoma. as a result, Myb34.5 selectively replicates in cancer cells, resulting in cancer cell death, while sparing normal surrounding tissues.

Most recently approved or currently developed targeted therapies (kinase inhibitors, monoclonal antibodies, ...) are more a cytostatic than a cytolytic approach in nature. These agents are aimed at reducing more specifically, but also more progressively, the tumour burden by preventing or slowing tumour growth rather than by directly lysing the cells and thus shrinking the tumour. By contrast, most classical cytotoxic chemotherapeutic agents were aimed at completely destroying the tumour burden. These compounds were often rather efficient against the cancer cells. However, their limited specificity for cancer cells resulted in fairly high (and often fatal) toxicities or side effects.

Oncolytic virus Myb34.5 is a cytolytic agent aimed at selectively and specifically lysing cancer cells, but with limited side effects or toxicity, because of its selectivity for those cancer cells.

SCOPE

Develop HSV-1 derived oncolytic virus Myb34.5 initially for pancreatic adenocarcinoma, in combination with immune therapy.

KEYWORDS

HSV-1, oncolytic virus, pancreatic adenocarcinoma, biomarker

OBJECTIVES

Develop Myb34.5 initially for pancreatic adenocarcinoma, in combination with immune therapy (checkpoint inhibitor).

DEVELOPMENT & MATURATION STAGE

Myb34.5 is at preclinical development stage, with proof of concept established in vitro and in vivo in various cancer types, including pancreatic adenocarcinoma.

TARGET POPULATION

Patients with metastatic or advanced pancreatic ductal adenocarcinoma.

TARGET PROFILE

First-line therapy for metastatic or advanced pancreatic adenocarcinoma, in combination with standard of care and/or immune therapy.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

Startup licensed from the General Hospital Corporation (Massachusetts General Hospital, Harvard University, Boston, MA) worldwide exclusive rights to develop and commercialise Myb34.5 for human as well as veterinary uses.

Patent "Cell-specific and/or tumor-specific promoter retargeting of herpes gamma 34.5 gene expression" was filed by inventors E. Antonio Chiocca and Richard Y Chung, and patent co-owner the General Hospital Corporation, in August 2000, with PTC extension.

Startup expands Industrial Property through strategic focus on rare cancers. We were granted orphan designations for the treatment of pancreatic cancer in the US (December 2014) and in the EU (January 2015). Major benefit of orphan designations is the market exclusivity once the product is approved: seven years in the US and 10 years in the EU. In parallel, Karcinolys will be exploring possibilities of patenting part or all of the manufacturing process.

STRENGHTS & COMPETITIVE ADVANTAGES

Direct competitors are other oncolytic viruses derived from HSV-1, reovirus or vaccinia virus. Most claim an immunogenic more than a cytolytic potential. Competitive advantage is a more potent oncolytic activity, while still being non-toxic.

Association of a potent cytolytic virus such as Myb34.5 with effective immunotherapies, such as anti-PD-1 or PDL-1 or CTLA4 monoclonal antibodies, thus offers a strong combination of complementary mechanisms of action.

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

Further to the positive data in an aggressive pancreatic cancer model, we are looking for additional funds in order to conduct preclinical and phase I/II clinical trials programmes. The funds will be used for manufacturing activities, additional pharmacology studies, required toxicology studies, and early phase clinical trials.

We are also seeking collaboration with industrial partners commercialising or developing immune therapies (e.g., checkpoint inhibitors), to evaluate in your models the combination with Myb34.5.

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