MATWIN
MATURATION & ACCELERATING TRANSLATION WITH INDUSTRY

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

An autophagy inhibitor with anti-tumoral properties

THERAPY

CONTEXT & BACKGROUND

The company is a clinical-stage company focusing on autophagy, which is mainly used by cancer cells to grow.
Autophagy modulators have been extensively studied in cancer, but none has reached sufficient exposure & efficacy in clinical trials until now.
The product; the first in class autophagy blocker, is the most advanced compound, and could orchestrate a genuine paradigm shift in this therapeutic area.
It was shown that, due to its lysosomotropic properties, the product could inhibit its in vitro target PPT-1, resulting in lysosomal accumulation of unbound Zn2+, impairment of cathepsin activity, blokckade of autophagic flux, altered location of mTOR, lysosomal membrane permeabilization, caspase activation and ultimately cell death.

KEYWORDS

Autophagy, Cancer, Immuno-oncology, New Chemical Entity, Synergy of action

The innovation here stands into the strong anti-tumoral activity on its own and in its capacity to favour the immune tumoral environment. The product displays in vitro many immunogenic properties. These properties lead us to think that the product could help fight immune evasion and thus act as a sensitizer for immunotherapies (anti-PD1, anti CTLA-4), resulting in synergistic activity.
Recently, more than 3 groups confirmed that autophagy in tumours allows cancer cells evasion from the body's immune system (Amaravadi's group in JCI insights 2020, Perera's & Kimmelman's groups in Nature 2020).

This perspective is evaluated by the company in vitro and vivo, with a confirmed activity in patient derived xenograft organoids (PDXO).

The product displayed a good PPT1 expression and a high distribution in liver that lead us to evaluate in vivo The product's potency in three hepatocarcinoma (HCC) models.

The product is safe in clinic and has an acceptable pharmacokinetic profile. It represents a promising new drug candidate and a hopeful therapeutic strategy in cancer treatment.

With an estimated 782,000 deaths in 2018, hepatocellular carcinoma stands as the most common primary liver cancer and constitutes the fourth leading cause of cancer-related death worldwide. New standard of care have been recently approved, including immune check point inhibitors. Autophagy-related lysosomal cell death, either alone or in connection with several other cell death pathways, has been recognized as a major target for cancer therapy.

The objectives is to bring in a 1st intent into liver cancers 2nd line and 1st line in combination with immunotherapies.

Our provisional work will consist of trying to evaluate potential biomarkers associated with autophagy inhibition and developing threshold to assess the product activity in each patient and identify sub-populations.

INNOVATIVE COMPONENT & TECHNOLOGY

The product is a new chemical entity, a quinoline derivative demonstrating high inhibition of autophagy through inhibition of the lysosomal enzyme PPT-1, leading to cancer cell death.

OBJECTIVES

To find partnerships and collaborations to pursue phase II clinical development of the molecule towards commercialization in both Hepatocarcinoma (HCC) and intrahepatic Cholangiocarcinoma (iCCA) indications.

DEVELOPMENT & MATURATION STAGE

Phase Ib completed, looking for opportunities to pursue clinical development (phase II & III)

TARGET POPULATION

Primary liver cancer patients (HCC, iCCA)

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S

1 composition of matter patent

TARGET PROFILE

Oral drug, administered in 28-day cycles, in combination with immunotherapy, in patients with locally advanced, metastatic and/or unresectable liver cancer
Follow-up of treatment through dosing of a biomarker associated with autophagy inhibition

STRENHGTS & COMPTETITIVE ADVANTAGES

Existing targeted therapies in the area cause problems of resistance (there is a cross-talk in cancer signaling pathways), targeting autophagy (as the product does) helps overcome this problem of resistance and position the product as a potential game-changer in the treatment of these pathologies.

Great potential for combination with immunotherapies, which turns competition into market opportunities to find new partnerships to finance onerous clinical development.

The product is a first in class compound, which could operate a unique revolution in hepato-oncology.

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

Liver cancers are a high unmet need in oncology with potential big markets not yet covered: $727M in 2021 for iCCA with a CAGR of 12.5% in the 2021-2030 time frame.
And $1 Bn in 2019 with a CAGR of 17.8% in the 2019-2027 time frame in Hepatocarcinoma.
The product would be an oral drug with ISO certified, cGMP compliant manufacturing techniques.

CONTACT

MATWIN : contact@matwin.fr