MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

THERAPY

EIR2
ERK INHIBITORS FOR THE TREATMENT OF RAF AND RAS MUTATED CANCERS

CONTEXT & BACKGROUND

RAS/RAF/MEK/ERK signaling pathway (also known as MAPK pathway) plays an essential role in cell proliferation and survival. It was demonstrated that MAPK pathway is over-activated in more than 30% of all human cancers. Indeed, RAF protein kinase and RAS GTPase are two major oncogenes that lead to cancer when mutated.

Thus, MAPK proteins represent targets of interest for cancers treatment. During the last decades, pharmaceutical industries have developed targeted therapies which inhibit protein kinases of this pathway such as RAF inhibitors (Vemurafenib, Dabrafenib) and MEK inhibitors (Trametinib, Cobimetinib). RAF-mutated cancers correspond to 7% of all cancers and are now becoming rapidly resistant to current treatments.

RAS-mutated cancers represent 25% of all cancers, are among the most aggressive ones and do not yet receive effective treatment. There is an urgent need for the development of new therapeutic strategies to cure those cancers. Thus, the aim of this project is to develop an ERK inhibitor that would be used as a single agent or in combination with current therapies (chemotherapies, targeted therapies, immunotherapies) for the treatment of MAPK-dependent cancers such as colorectal cancers.

INNOVATIVE COMPONENT & TECHNOLOGY

The team identified a new original series of small molecules (“NCE” New Chemical Entity) that inhibit ERK kinase activity by using a Fragment-Based approach. After a chemical optimization through a Biotech company, the team obtained a selective ERK inhibitor with strong affinity for its target.

Studies revealed a high efficacy and selectivity in MAPK-dependent cell lines. An oral efficacy with a dose-response effect has also been obtained in a KRAS colorectal cancer xenograft model which shows a promising efficacy profile with no apparent toxicity. Good synergies were also achieved with different targeted therapies and chemotherapies in several cancer models (colorectal cell lines among others). The lead optimization is currently in progress.

SCOPE

New treatment for colorectal cancers

KEYWORDS

Preclinical development, cancer, therapeutic innovation, drug candidate, kinase inhibitors, ERK2, colorectal cancers, resistance

OBJECTIVES

The company will continue pharmaceutical development until clinical phase I and is looking for a partner to pursue development.

DEVELOPMENT & MATURATION STAGE

Preclinical stage.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

European and US patents filed in May 2018.
IP shared by the company, Inserm, CNRS and University of Montpellier.
Exclusive license conceded to company.

TARGET POPULATION

Selective ERK inhibitors, to be used as a single agent or in combination, will be dedicated for the treatment of RAF and RAS dependent cancers, particularly in colorectal cancers. Patients that correspond to these genotypes will be targeted.

TARGET PROFILE

ERK protein is a kinase from MAPK pathway with key roles in metabolism, protein synthesis, cell proliferation and survival. This kinase is responsible for the phosphorylation of hundreds of substrates.

STRENGHTS & COMPETITIVE ADVANTAGES

- High affinity and selectivity for ERK.
- A potent and orally bioavailable inhibitor with prolonged efficacy
- A broad range of indications
- Synergy with different therapies in several cancers
- No cytotoxicity
- Intellectual property

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

New therapeutic option for cancers with high medical need such as colorectal cancers.
Possibility to be used in combination with current treatments in resistant cancers.
Co-development or licensing opportunities.

CONTACT | MATWIN : contact@matwin.fr