MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

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

CONTEXT & BACKGROUND

RAS/RAF/MEK/ERK pathway plays an essential role in cell proliferation and survival. It is now known that those proteins are over-activated in many cancers. Thus, proteins of this pathway represent targets of interest for cancers treatment. During the last decades, pharmaceutical industries have developed therapies which inhibit protein kinases of this pathway. RAF protein kinase and RAS GTPase are two major oncogenes that lead to cancer when mutated. RAF-dependent cancers correspond to 7% of all cancers and are now becoming rapidly resistant to current treatments (chemotherapies, targeted therapies such as Vemurafenib, a RAF inhibitor). RAS-dependent 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 for the treatment of metastatic melanoma, and in combination with chemotherapies or other targeted therapies to treat pancreatic cancers.

INNOVATIVE COMPONENT & TECHNOLOGY

A new original series of small molecules (“NCE” New Chemical Entity) has been identified, that inhibit ERK kinase activity by using a Fragment-Based approach. After a chemical optimization through the company AGV Discovery, the team obtained selective ERK inhibitors with very high affinities for their target. Studies revealed very high anti-proliferative activities in RAF and RAS cell lines. An in vivo proof of concept has also been obtained and showed a promising efficacy profile with no apparent toxicity. Good synergies were also achieved with different targeted therapies and chemotherapies in several in vitro cancer models.

SCOPE

New treatment for metastatic melanoma and pancreatic cancers

KEYWORDS

S Preclinical development, cancer, therapeutic innovation, drug candidate, kinase inhibitors, ERK2

OBJECTIVES

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

DEVELOPMENT & MATURATION STAGE

Preclinical stage.

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. Patients that correspond to these genotypes will be targeted.

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

European patent filed in November 2015.
IP shared by AGV Discovery, Inserm, CNRS and University of Montpellier.
Exclusive license conceded to AGV Discovery

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.
- High efficacy in RAF and RAS mutated cancer cell lines.
- High in vitro therapeutic index.
- High synergies with current treatments in several cancers.
- In vivo POC in a RAF melanoma xenograft mouse model.

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

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

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