MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

# TECHNOLOGY OFFER

**SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY**

THERAPY

## GS168

CD9P1 as a novel biomarker and therapeutic target for advanced and metastatic solid tumours

## CONTEXT & BACKGROUND

Immunotherapy with Immune Checkpoint Inhibitors (ICIs) has emerged as the most promising treatment of diverse advanced and metastatic cancers. Anti-PD1 or anti-PDL1 are now becoming the new standard of care for patients with advanced non-small-cell lung cancer. Most patients, however, remain non-responders or become non-responders by developing resistance, making research of alternative immunotherapy strategies a priority.

The tumour microenvironment (TME) is known to direct resistance to various therapies. Tumour-associated macrophages (TAMs), especially the immunosuppressive M2 macrophage subset, actively contribute to tumour progression, metastasis, chemo-resistance and immunosuppression. Targeting M2 macrophages to drive them toward the M1 killer phenotype and prevent tumour progression and metastasis would be a therapeutic advance in cancer. To this aim, we propose to target CD9P-1. We identified this novel target in our discovery platform conceived to discover new targets aiming at preventing tumour growth through starvation. In the in vivo screening and validation process, we discovered that CD9P-1 was overexpressed in M2 macrophages. We then observed that CD9P-1+ M2 macrophages invaded the TME of advanced and metastatic human lung tumour samples. We developed drug candidates, a peptide (GS168P3) preventing the interaction of CD9P-1 to its partners, and a monoclonal antibody (9bF4mAb) neutralizing CD9P-1. GS168P3 specifically induced the repolarization of M2 macrophages into anti-tumour M1 macrophages with tumoricidal activity, and significantly inhibited tumour growth in mouse models of human and murine cancers, synergizing with cisplatin. The anti-tumour effects of GS168P3 correlated with an increased M1/M2 ratio in the TME, and with cytotoxic lymphocyte infiltration in the tumour core. These data provide the impetus for identifying CD9P1+ patients and target CD9P 1 in combination therapy with current best standard of care in oncology.

Our provisional work plan aims at deepening our understanding of the CD9P-1 pathway in promoting the M2 phenotype. We plan to identify the best drug candidate (peptide or monoclonal antibody) for clinical development; this would include providing additional proof of concept for treatment of advanced and metastatic tumours with high expression of CD9P-1 in combination with chemotherapy or immunotherapy. Finally, we want to establish CD9P-1 as a biomarker of efficacy of immunosuppression on M2 macrophages.

We expect that increasing the M1/M2 ratio would stimulate cytotoxic lymphocyte infiltration and slow tumour and metastasis progression. Our project aims at demonstrating the clinical relevance of the inactivation of the CD9P1 pathway in advanced lung cancer treatment, as a first step.

## INNOVATIVE COMPONENT & TECHNOLOGY

New target in immune-modulation to enrich the tumour environment in M2 macrophages.

## OBJECTIVES

Optimize and develop an inhibitor of CD9P1 to deliver a biologic as clinical candidate.


## KEYWORDS

Immunosuppression, M2 Macrophage repolarization, advanced and metastatic cancers, immunotherapy, cold tumour, targeted therapy, Non-small cell lung cancer

## DEVELOPMENT & MATURATION STAGE

Pre-clinical stage with two selected products to be optimized. Companion diagnostics developed in parallel.

## INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

Two patents owned by the company

## TARGET POPULATION

Patients with solid tumours CD9P1 positive

## TARGET PROFILE

- CD9P-1 expression is associated with cancer cells and tumour-associated M2 macrophages (TAM) in advanced lung cancers
- CD9P-1 over-expression was observed in different types of tumours
- High level of CD9P-1 expression in more than 50% of cases in lung epidermoid carcinoma and mesothelioma with a strong expression on the tumour cell surface
- After chemotherapy in patients with metastasis, CD9P-1 over-expression is maintained at a high level. In these cases, a strong CD9P-1 expression was observed in macrophages in tumour environment correlating with CD163 expression, M2 macrophage marker
- Inhibition of CD9P-1 is associated with cancer cell apoptosis and conversion of M2 to M1 macrophages promoting cytotoxic T lymphocyte infiltration into the tumour core leading to tumour growth inhibition in vivo (immune-competent pre-clinical model).

## STRENGHTS & COMPETITIVE ADVANTAGES

First in class and novel mechanism of action triggering conversion of M2 pro-tumour macrophages to M1 killer macrophages, stimulating of cytotoxic T lymphocyte infiltration in the tumour core. Potential to increase ICIs efficacy.

## INDUSTRIAL APPLICATIONS & OPPORTUNITIES

Oncology, treatment of solid tumours expressing CD9P1 with or without metastases, alone or in combination with ICIs.

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