MATWIN
MATURATION & ACCELERATING TRANSLATION **WITH INDUSTRY**

TECHNOLOGY OFFER

SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

THERAPY

TCTP-NALCaP

TCTP INHIBITION USING HYBRID NUCLEIC ACID-LIPIDS AS A NEW THERAPEUTIC STRATEGY TO RESTORE HORMONE- AND CHEMO-SENSITIVITY FOR THE TREATMENT OF CASTRATION-RESISTANT PROSTATE CANCER AND OTHER CANCERS

CONTEXT & BACKGROUND

The development of a reliable antisense-based therapy for in vivo implementation is still hampered in many cases by the **poor cellular uptake of highly negatively charged antisense molecules**. To improve the cellular internalization of oligonucleotides a covalent tethering of a Lipophilic (L) group(s) to the oligonucleotide antisense (ASO) is realized in this technology.
This self-drug delivery strategy (SDDS) based on LASO supramolecular systems is applied for a new therapeutic approach in castration resistant prostate cancer (CRPC).

This novel therapeutic approach involves ASO targeting translationally controlled tumor protein (TCTP), which has been demonstrated to be highly over-expressed in CRPC.
The goal of this project is to continue to develop a second generation of TCTP-ASO (TCTP-LASO) using lipid-oligonucleotides modifications and/or co-formulating hybrid molecules such as nucleolipids in order to improve stability, biodisponibility and delivery of TCTP-ASO. Importantly, in addition to the delivery of the ASO sequence, the LASO supramolecular systems and formulations can be used as a cargo for a second anti cancer drug such as docetaxel or gonadotrophin analogues.

INNOVATIVE COMPONENT & TECHNOLOGY

Target Product Profile (LASO) will be a New Chemical Entity (NCE). The new TPP expected will be an improvement of the worldwide patented first generation of TCTP oligonucleotide antisense (ASO) targeting TCTP (PCT10306447.3, 2010).

Self delivery of ASOs:
- LASOs address the stability, biodisponibility and delivery issues
- LASOs increase the cellular uptake (no need of transfecting reagent)

OBJECTIVES

The objective of this project is to develop lipid-conjugated oligonucleotides formulations in order to improve their stability, biodisponibility and delivery. Additive effect with current chemotherapy will be evaluated.

SCOPE

New specific anti-cancer drugs (Oligonucleotides) based on lipid-antisenses conjugates (LASOs).

KEYWORDS

Cancer, oligonucleotides, drug delivery, prostate cancer, chemotherapy

DEVELOPMENT & MATURATION STAGE

POC in vitro and in vivo for antisense (ASO) sequences targeting resistant Prostate cancer and POC **in vitro and in vivo for lipid-antisense** (LASOs). The anticancer activities of ASOs are improved by the LASOs technology.
The LASOs technology is under development through an international platform (POC on several biological targets).

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

ASOs and L-ASO against TCTP and other cancers are protected with 3 patents

TARGET POPULATION

Prostate cancer, cancers and other disease

TARGET PROFILE

New Chemical Entities (NCE)

STRENGHTS & COMPETITIVE ADVANTAGES

- Strong know-how in cancer and nucleic acid chemistry (Team is leader in the field of hybrid nucleic acids for formulations and the development of new API derived from nucleic acids)
- Important activities both in vitro and in vivo
- Possibility to extend the technology to other targets, including small cell lung cancer or colorectal cancer, for example
- Possibility of coformulations in combination with anti-cancer drugs
- Important medical needs in targeted diseases
- Possibility to extend the system in combination with anticancer drugs already on the market (docetaxel etc) or in clinical trials
- Clear regulatory path (antisenses in human, i. e. OGX 427…)
- first project using LASO on CRCP

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

242,000 new cases of prostate cancer (PC) were diagnosed in the **U.S. in 2012 with 28,000 men dying from it.**
Total PC market value is expected to reach **$50.3 billion in 2017** after increasing at a five-year compound annual growth rate (CAGR) of 11.4%.
3 main segments:

1. diagnosis and screening, ($12.1 billion in 2012 and **$17.4 billion in 2017**, a CAGR of 7.5%
2. surgical and radiation therapy, ($9 billion in 2012 and nearly **$14.3 billion in 2017**, a CAGR of 9.7%)
3. drug therapeutics. ($8.1 billion in 2012 and nearly **$18.6 billion in 2017**, a CAGR of 18%)

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