



## SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

### 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, nanomedicine,



## 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 lipidantisense (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)



## TARGET POPULATION

Prostate cancer, cancers and other disease



## TARGET PROFILE

New Chemical Entities (NCE)



## STRENGTHS & 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)
- Possibility of coformulations in combination with anti-cancer drugs
- Important activity in vitro and activity in vivo
- 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:**

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



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

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