AsiDNA™

A FIRST-IN-CLASS, HIGHLY DIFFERENTIATED MOLECULE INHIBITING TUMOR DNA DAMAGE RESPONSE (DDR)

Interim results of DRIIV-1 study

Conference Call
November 5, 2018

ONXEO

LISTED
EURONEXT | Paris
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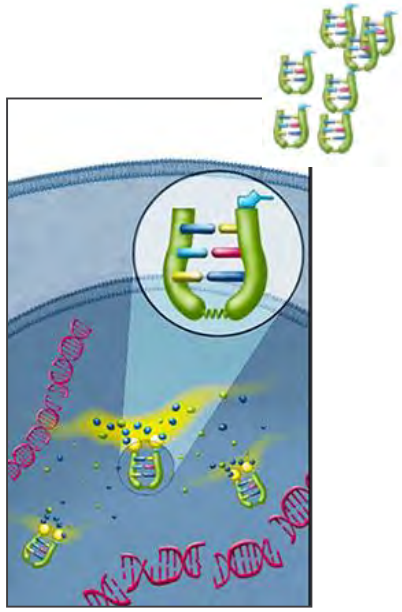
AsiDNA™: The only agonist in development that disrupts and exhausts the ability of a tumor cell to repair its damaged DNA

- AsiDNA™ is a fragment of double-strand DNA (oligonucleotide) acting as a **decoy** and an **agonist** of the DDR
- It **mimics** DNA breaks in the tumor cell, **hyperactivates** and then **binds** the DDR cascade of cellular events (sensing, signaling and repairing), **diverting** DDR proteins **away** from the true damage. [1,2,3]

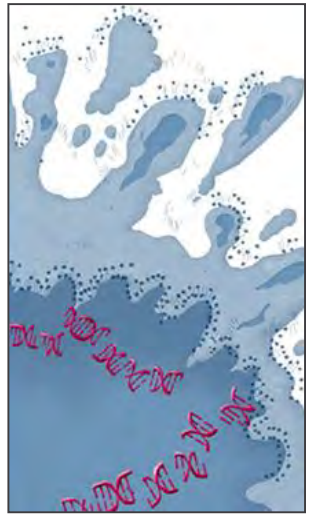
1 AsiDNA™ **sends false alarms** throughout the tumor cell nucleus and then **activates and binds** key components of the DNA Damage Response.

2 This **sustained** artificial DNA damage signaling (**agonist effect**) leads to **exhaustion** of the tumor DNA repair machinery



3 Actual tumor DNA damage is not repaired and accumulates : **cancer cells die** when dividing with a damaged DNA.

However, AsiDNA™ is safe for healthy cells which stop dividing until the false alarm disappears.



AsiDNA™ acting upstream of the DDR cascade, interferes with multiple DNA repair pathways

1. Quanz M, et al. Clin Cancer Res 2009 15:1308-1316;
2. Quanz M, et al. PLoS ONE. 2009 4(7), doi: 10.1371/ journal.pone.0006298;
3. Jdey W, et al. Oin Can Res. 2016;22:DOI: 10.1158/ 1078-0432.CCR-16-1193

DRIIV-1 study – Design & Cohort Status

DNA Repair Inhibitor administered IntraVenously in patients with advanced solid tumors

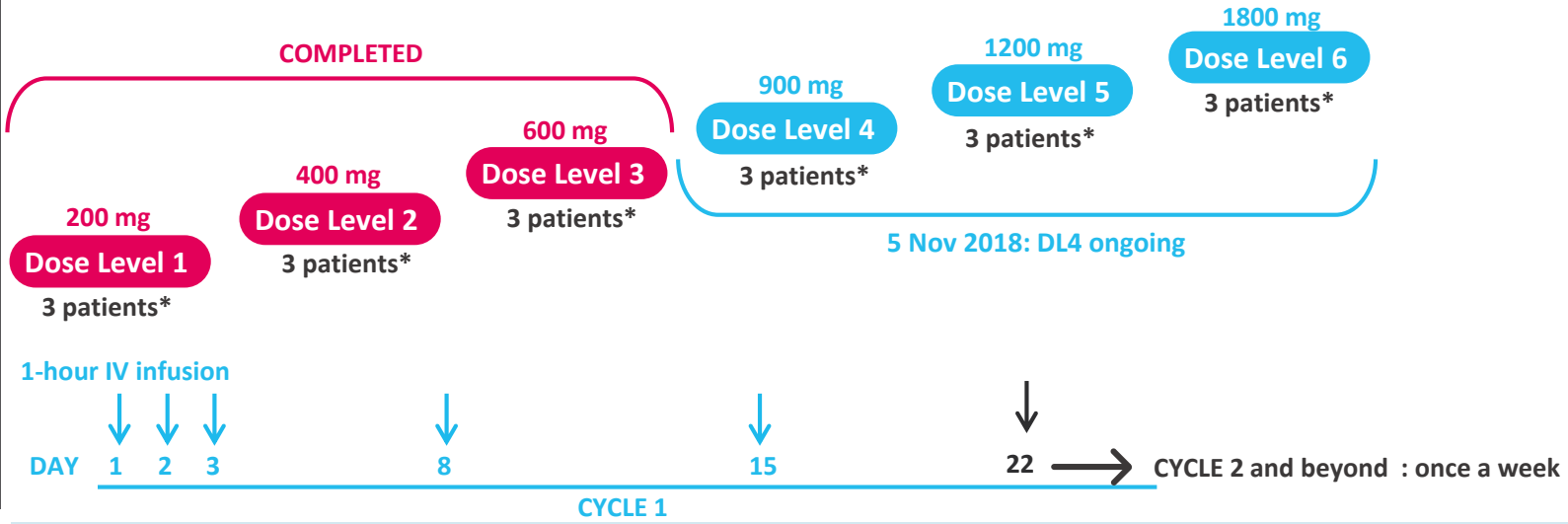
PHASE I

- Open-label, dose escalation, phase I study
- Max. 36 patients
- 2 European countries: FR, BE
- 5 centers: Paris(2),Toulouse, Lyon, Brussels
- Study coordinator: Pr. C. Le Tourneau (Institut Curie)
- DSMB

APRIL 2018
FPI

Q4 2018 – PRELIMINARY RESULTS
TOLERANCE, PK/PD, ACTIVE DOSE FINDING (TARGET ENGAGEMENT)

H1 2019 – FINAL RESULTS



TREATMENT SCHEDULE

- 1-hour I.V. infusion ; cycle 1 : loading dose (day 1, day 2, day 3) then weekly dosing day 8 and day 15; cycle 2 & beyond : weekly dosing; 21-day cycles

OBJECTIVE - To assess the safety, pharmacokinetics and pharmacodynamics of AsiDNA™

- To determine **dose-limiting toxicities** (DLTs) and the **maximum tolerated dose** (MTD)
- To evaluate the **pharmacokinetics/pharmacodynamics** (PK/PD) **effects** of AsiDNA™ based on **biomarkers of activity** in blood and in tumor tissue (MN, γH2AX, pHsp90, PARP activation)
- To assess the **preliminary efficacy** of AsiDNA™

** 3 additional patients if a dose limiting toxicity is found*

→ Compelling safety & activity results as early as dose 2

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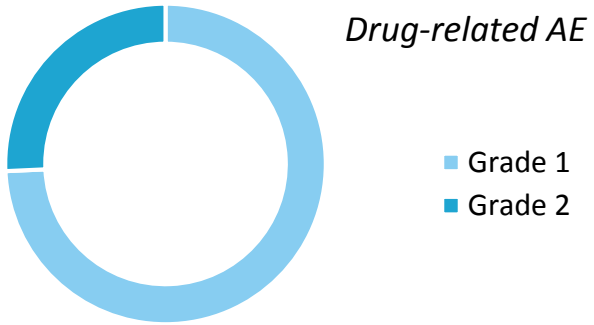
Mid-study results of DRIIV-1 : Favorable safety profile

(November 5, 2018)

In DRIIV-1 ongoing study
10 patients - 200mg, 400 mg & 600 mg

- Dose proportionality for both Cmax and AUC

- **No drug-related serious adverse events**
- No dose-limiting toxicity
- Maximum tolerated dose not reached
- Only grade 1 & 2 drug-related adverse events



Favorable safety profile confirms positive regulatory toxicity studies

- No in-vitro genotoxicity
- Positive repeated in-vivo regulatory toxicity studies, incl. 4-week study in animal
- Maximum tolerated dose not reached

Favorable safety profile at active doses providing a comfortable therapeutic window

Mid-study results of DRIIV-1: Proof-of-Mechanism in man

(November 5, 2018)

- **Analysis of the first 3 dose levels out of 6 planned**
- **10 patients**
- **4 biopsies available at baseline and end of cycle 2**

Activity

Target engagement confirmed by significant increase of activity biomarkers from dose level 2 and 3 = Proof-of-Mechanism of AsiDNA™ in man

		Activity biomarkers	
DL2 : 400mg	**γH2AX**	**pHSP90**
Patient 0106	→	↑↑↑
Patient 0109	↑	↑↑

		Activity biomarkers	
DL3 : 600mg	**γH2AX**	**pHSP90**
Patient 0202	↑↑	↑
Patient 0301	↑↑↑	↑↑↑

Significant increase after treatment with AsiDNA™

Major increase after treatment with AsiDNA™

Tumor status

Decrease or stabilization of tumor proliferation rate from dose level 2 and 3

	Tumor proliferation biomarker		Tumor proliferation biomarker
DL2 : 400mg	**KI67**	**DL3 : 600mg**	**KI67**
Patient 0106	↓	Patient 0202	↓↓
Patient 0109	↓	Patient 0301	→

Robust target engagement in patients' tumors demonstrates AsiDNA™ activity via IV route

AsiDNA™ IV route: Validated for clinical program expansion

- **Favorable safety profile**
- **Proof-of-mechanism and activity in man**
- **Preclinical package* indicating unique properties of AsiDNA™ alone and in combination**
  - **Repeated treatment with AsiDNA™ leads to sensitization to AsiDNA™ and does not generate resistance**
  - **Resistance to PARPi is prevented by co-treatment with AsiDNA™**
  - **Strong synergy of AsiDNA™ in combination with PARPi**
  - **Strong synergy of AsiDNA™ in combination with carboplatin**

*Data submitted for publication to peer-reviewed journals

All our studies to date support AsiDNA™ potential in broad indications* and combinations

with PARP inhibitors

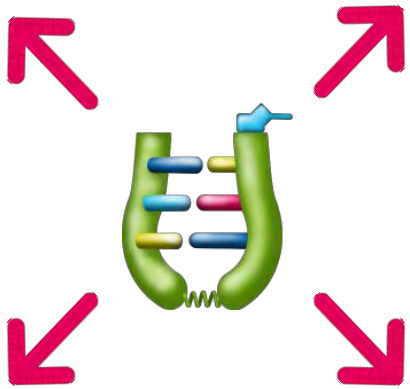
- Synergistic efficacy observed in vivo, including in HR proficient tumors
- Potential indications: OC, TNBC, SCLC *
- Strong rationale for use as maintenance

≈ 130,000 patients US + UE

as a monotherapy

- Selection of the best responding patients with stratification biomarkers

≈ 26,000 patients US + UE



with DNA-damaging chemotherapies

- 10 to 20% of all cancer patients are treated with platin-based chemotherapies
- Potential indication: SCLC* (ODD)

≈ 700,000 patients US + UE

with radiotherapy

- 50-60% of cancer patients treated with radiation therapy during the course of their disease
- DRIIM phase 1 study clinical signals of efficacy

≈ 2.3 Million patients US + UE

Unique mechanism of action positions AsiDNA™ at the heart of DDR strategies in oncology

** Targeted Population Company's Estimate – HR: Homologous recombination - OC : Ovarian cancer – TBNC : Triple negative breast cancer – SCLC : Small cell lung cancer – HCC : Liver cancer – mCRPC : Metastatic castration-resistant prostate cancer – mCRC : Metastatic colorectal cancer – ODD: Orphan Drug Designation*

AsiDNA™: a highly differentiated molecule with promising prospects for development

- AsiDNA™: a **unique mechanism of action** enabling a new approach to cancer treatment
- Exhaustive and **robust preclinical package** indicating product wide potential
- **Established proof-of-mechanism in man,** strong activity, favorable safety

Ready for expanded clinical development in combination

H1 2019 — **Initiation of Phase 1b/2 in combination with PARP inhibitors an/or DNA-damaging agents (chemotherapies)**

H2 2019 — **Initiation of IND filing in the US**

Thank you for your attention

We welcome your questions

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