



Corporate Overview

June 2021

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Disruptive therapies through unique approach to DNA Damage Response



STRONG MANAGEMENT & OPERATIONAL TEAM

Team of 30 ; experts in translational & clinical research ; experienced management & board with demonstrated track record ; SAB of leading experts

1ST-IN-CLASS CANDIDATES WITH DIFFERENTIATED MECHANISM OF ACTION



Diverting and hyper-activating (rather than inhibiting) key processes of tumor cells DNA repair: AsiDNA™ at clinical stage, OX401 preclinical



FROM BENCH TO PROOF-OF-CONCEPT

Creating value by bringing drug candidates from preclinical stage to proof-of concept in man, the best inflection points to monetize these assets and generate revenues.

SECURE FUNDING FOR CLINICAL EXPANSION



Support from core shareholders ; financial visibility at least until end 2022, beyond key clinical milestones of the strategic plan



An experienced management team and board of directors



JUDITH GRECIET (PHARM.D), CEO
(formerly Pharmacia, Wyeth, Eisai)



NICOLAS FELLMAN, CFO
(Pfizer, Ernst & Young)



OLIVIER DE BEAUMONT (MD), CMO
(Aventis, Quintiles, Stallergenes Greer)



PHILIPPE MAITRE, EVP, CBDO
(Aventis, PPD, mAbRx)



DANIÈLE GUYOT-CAPARROS
Chairwoman of the Board
Senior Advisor Deloitte Consulting



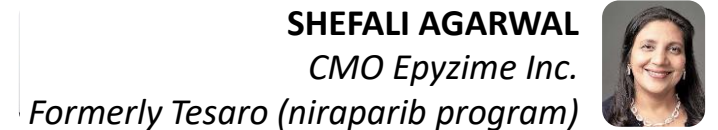
JUDITH GRECIET
CEO



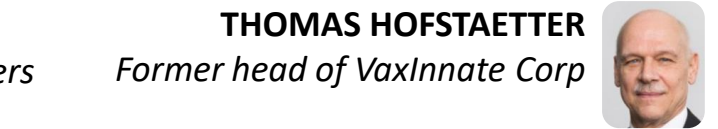
CHRISTINE GARNIER
Co-Founder of AEC Partners
Strategic consulting



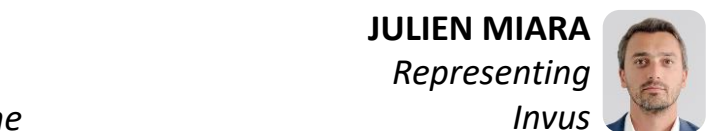
NICOLAS TREBOUTA
Representing
Financière de la Montagne



SHEFALI AGARWAL
CMO Epyzime Inc.
Formerly Tesaro (niraparib program)



THOMAS HOFSTAETTER
Former head of VaxInnate Corp



JULIEN MIARA
Representing
Invus

Demonstrated track record in product development
as well as business development



Newly formed committee of leading scientific experts to guide product design and clinical development



Gilbert Chu, MD, PHD

Stanford Medical School - USA



Core interests

DNA repair proteins, DNA breakers toxicity, cell biology under radio/chemotherapy



Gilles Favre, PHD

Oncopole Toulouse - France



Core interests

Cancer cell signalling, biomarkers, reversion of resistance to targeted therapies



Lorenzo Galluzzi, PHD

Weill Cornell New York - USA



Core interests

Tumor metabolism, adaptive stress response, tumor immune response



Ruth Plummer, MD, PhD

CRUK Newcastle Cancer Centre - UK



Core interests

DNA repair, early phase trial design for new therapeutics, PARPi, ATMi...



Caroline Robert, MD, PhD

Gustave Roussy - France



Core interests

Translational research on immunotherapy and targeted therapy, novel biomarkers



platON™, game-changing platform technology fueling the pipeline with first-in-class therapeutics

Creating “decoy-agonists“ of the DDR

1 Active component

Double-stranded DNA fragment (oligonucleotide) of variable sequence and length



2

Linker

Tethered loop to prevent dissociation



3

Vector

When appropriate, to facilitate tumoral & nuclear uptake



Same mechanism of action and core benefits

- Turning tumor cell biology against itself by sending misleading signals
- Hijacking (**decoy**) and hyper-activating (**agonist**) selected DDR proteins
- Interfering with tumor cell functions, **without inducing resistance**



Differentiated targets and properties

- **Targeting specific proteins, optimized binding & activation**
- 2 candidates to date, more in discovery

AsiDNA™ (clinical stage)




Targeting multiple proteins incl. DNA-PK: hindering both NHEJ and HR (drug-driven synthetic lethality), acting on pharmacotolerant cells causing resistance to treatment

OX401 (preclinical)

Potent agonist of PARP, with effect on tumor cell metabolism ; activation of the innate immune response via the STING pathway



Expanding development pipeline focused on efficacy synergy and effect on resistance in combination

Programs	PRÉCLINIQUE	PHASE I	PHASE Ib	PHASE II	WITH
AsiDNA™ +/- chemotherapy <i>All solid advanced tumors, all lines</i>		DRIIV mono	DRIIV -1b combo		
AsiDNA™ + chemotherapy <i>mNSCLC/ other solid tumors</i>				Randomized phase 2	
AsiDNA™ + radiotherapy <i>Recurrent High Grade Glioma (children)</i>			AsiDNA™ Children		
AsiDNA™ + PARPi <i>Relapsed Ovarian Cancer</i>			REVOCAN		
AsiDNA™ + other targeted therapies <i>Other indications</i>	In vivo				
OX401 <i>PARP agonist + STING pathway activation</i>	In vivo				



Completed



Ongoing



Starting in 2021



AsiDNA™

*Unique Decoy-Agonist Mechanism
of Action in DNA Damage Response*



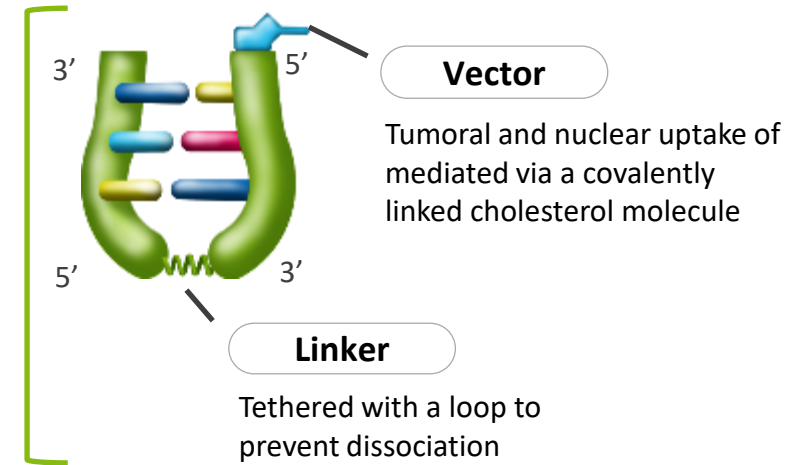
AsiDNA™, the first decoy agonist in DNA Damage Response (DDR)

Purposed-built oligonucleotide designed to interfere with repair pathways through a mechanism of capture and hyperactivation of key DDR proteins, notably DNA-PK



Strong and broad IP up to 2040

Active 32 bp DNA duplex





AsiDNA™, a first-in-class DDR pan-inhibitor

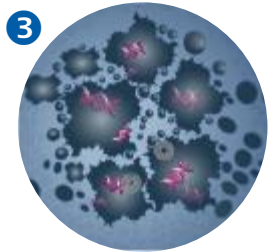
How it works



1 AsiDNA™ mimics DNA breaks in the tumor cell and saturates it with false alarm signals (**decoy**) and then traps and hyperactivates (**agonist**) key DDR proteins responding to this false alarm – notably DNA-PK



2 This prolonged signaling, trapping and overactivation **depletes** the DDR and hinders both HR and NHEJ, making any resistance impossible



3 Actual lesions are not repaired and accumulate, cancer cells die when they divide with damaged DNA.

Competitive advantages

Good tolerance

Specific to cancer cells, translating in outstanding safety profile in man, a clear asset in combination

Absence of resistance

Turning tumor DDR against itself and leaving no escape repair pathways, in contrast with targeted therapies

Independence from the genetic context

Active regardless of genetic context, unlike most targeted therapies



Exploring AsiDNA™ through extensive preclinical & clinical POC programs



In vitro



In vivo



Clinical studies

SYNERGY

RESISTANCE

Favorable safety	✓ Specific to cancer cells	✓ Safe in monkey tox. study	✓ Confirmed in man (DRIIM, DRIIV, DRIIV-1b)
No resistance observed	✓ Multiple cell lines	✓ Multiple models	✓ Confirmed in man (DRIIM, DRIIV, DRIIV-1b)
Efficacy synergy with chemo	✓ Multiple cell lines	✓ Increases efficacy & survival	✓ Signals of efficacy in DRIIV-1b ✓ Randomized phase 2 to start end 2021
Efficacy synergy with radio	✓ Multiple cell lines	✓ Sensitizes to radiation	✓ Signals of efficacy in DRIM (IT – melanoma) ✓ Phase 1b/2 to start in 2021 (HGG - pediatric)
Efficacy synergy with PARPi	✓ Sensitive & resistant lines ✓ No need for genetic context	✓ Increases survival & responders ✓ Induces transient HRD	TBD
Abrogate resistance to PARPi	✓ Multiple cell lines	✓ Stops acquired resistance	✓ REVOCAN phase 1b/2 (advanced OC) started in 2020
Abrogate/prevent resistance to other targeted therapies	TKI, KRASi, ...	Ongoing	TBD



AsiDNA™ combined with chemo: favorable safety and efficacy signals

DRIIV-1b

- Patients eligible to carboplatin +/- paclitaxel, phase 1b, open label 3+3 cohorts
- Heavily pre-treated patients with advanced metastatic tumors, progressing at inclusion
- Objectives: AsiDNA™ safety profile in combination and signals of efficacy (RECIST)

AsiDNA™ 600mg	Tumor	Treatment line	Treatment duration	Response	Preliminary safety overview and best responses (4/7 evaluable patients to date)	
Cohort 1 3 pts ∨	+ carboplatin	TNBC	6 th line	5.5 months	Stable Disease	<ul style="list-style-type: none"> • No DLT and very good tolerance of the combination • In 2/3 patients, disease controlled for significantly longer than with any of the prior lines
		NSCLC (Epidermoid)	3 rd line	8.5 months	Stable Disease	
Cohort 2 (5 pts)	+ carboplatin + paclitaxel	NSCLC (Adenocarcinoma)	4 th line	3 months	Partial Response -40%	<ul style="list-style-type: none"> • No DLT and very good tolerance of the combination • Disease controlled for significantly longer than w/ any of the prior lines
		NSCLC (Adenocarcinoma)	2 nd line	11 months	Stable Disease	

Promising data support launch of randomized phase 2 end 2021*

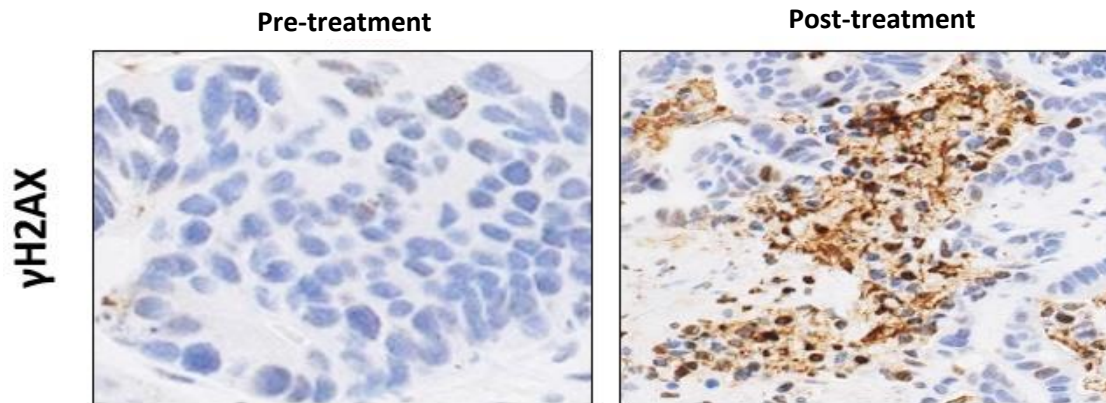


Safety and activity of AsiDNA™ established in dose-finding phase 1

- DRIIV-1**
- Open-label, 3+3 dose escalation
 - n =22; 5 doses (200mg -1300mg)

Proof of mechanism

AsiDNA™ doing what it was meant to do :
hyper-activation of DNA-PK at cell level



γH2AX (DNA-PK biomarker) readout in tumor biopsies

Favorable safety outcome

- No drug-related SAE < 900mg
- No DLT < 900mg
- 89% of TEAE were grade 1 or 2
- MTD was not reached

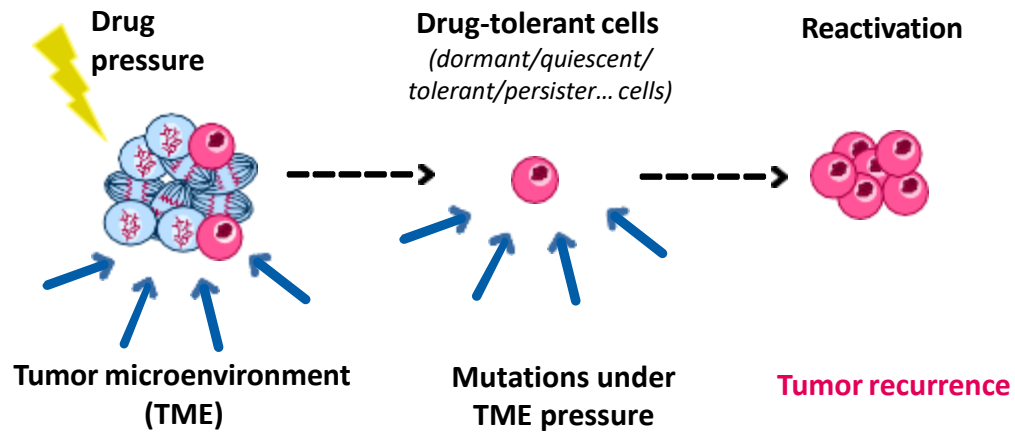
600 mg dose selected for current clinical development in combos



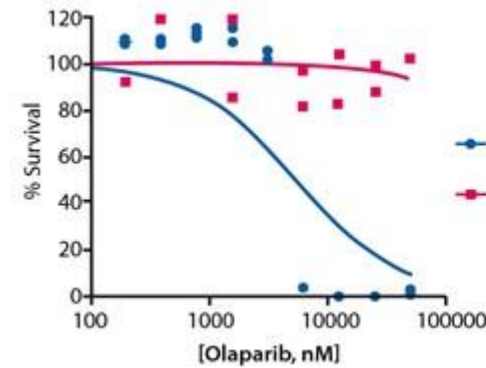
Acquired resistance to targeted therapies evolves from drug-tolerant cells (DTC) vulnerable to AsiDNA™

DTC: an established cause¹ of resistance to TKI*

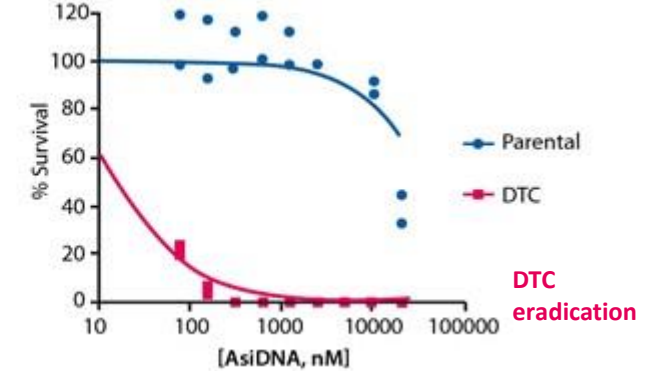
Onxeo showed that resistance to **PARPi** and **KRAsi** also evolves from drug-tolerant cells²



AsiDNA™ prevents resistance to PARPi by acting on DTC²



IC50 olaparib – parental cells: 5µM



IC50 AsiDNA™ – DTC: 17nM



TNBC model BC227 BRCA2 mut

AsiDNA™ could effectively counter DTC-driven resistance to a wide range of targeted therapies

* TKI : tyrosine kinase inhibitors - ** Parental cell: primary tumor cell

¹ Sharma VS et al. Cell, 2010, 141-1:69-80

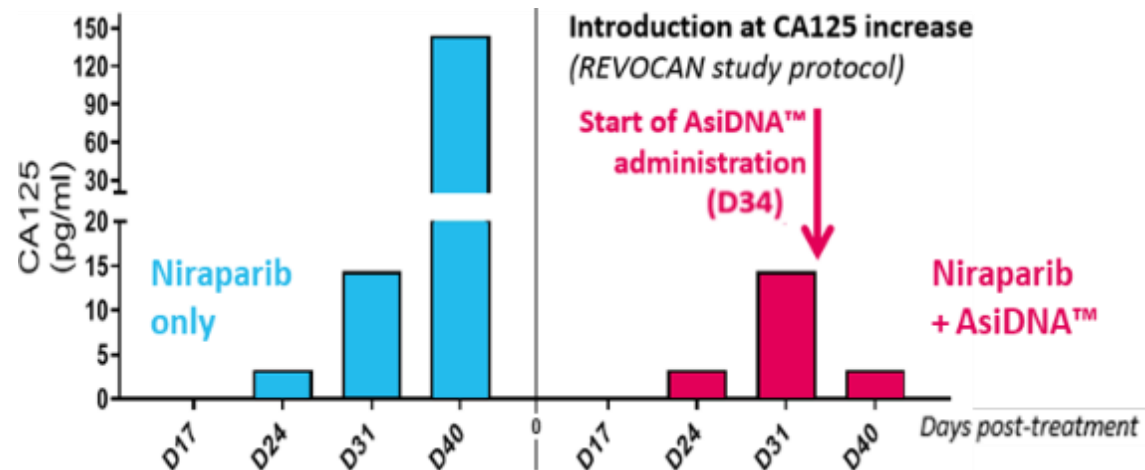
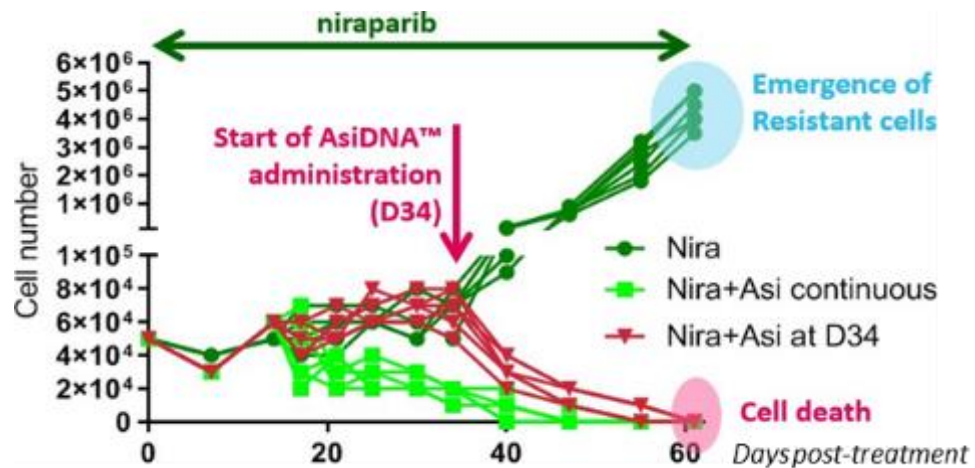
² AACR 2020 - [Acquired resistance to PARP inhibitors evolves from drug-tolerant persister cells vulnerable to AsiDNA™](#)

AACR 2021 - [Acquired resistance to KRAS inhibitors evolves from drug-tolerant persister cells vulnerable to AsiDNA™](#)



AsiDNA™ eradicates PARPi-resistant cells

UWB1.289 (Ovarian cancer model – BRCA1^{null})



Adding AsiDNA™ significantly decreases CA 125

Preclinical rationale supporting the REVOCAN study



POC study to assess reversion of resistance by adding AsiDNA™ to PARPi

REVOCAN REVersion of resistance in Ovarian Cancer with AsiDNA™ & Niraparib

Clinical Research Agreement with Gustave Roussy - Supported by Arcagy-Gineco¹

DESIGN

Multicenter, open-label phase 1b/2

Part 1b: 6 patients – part 2: up to 20 patients

Platinum-sensitive relapsed ovarian cancer under 2nd line of maintenance with PARPi > 6 months

Inclusion at CA 125 increase

OBJECTIVES

Primary

Safety run & CA125 decrease (GCIG criteria)

Secondary

Efficacy - PFS (RECIST criteria) – OS



Outlook



Significant value catalysts expected for AsiDNA™*

Study	Objectives	Timeline		
		S2 2021	2022	2023
DRIIV-1b + chemotherapy	Tolerance Efficacy signals	Full data set		
Randomized Phase 2 + chemotherapy mNSCLC / other solid tumors	Tolerance Efficacy – PFS/OS		1 st patient EU Potential US IND	Preliminary read-out
AsiDNA™ CHILDREN 1b/2 + radiotherapy High-grade glioma (pediatric)	Tolerance – effect on Rx dose - PFS/OS	1 st patient		Preliminary read-out
REVOCAN 1b/2 + PARP inhibitor Ovarian cancer	Tolérance Réversion de la résistance		1 st data read-out (part 1)	Topline data
<i>Pilot / Exploratory study + olaparib</i> mBC, HER2-, HRP	<i>Drug-induced synthetic lethality</i>			Regulatory filing



Financial resources in line with key development milestones objectives

Cash position of €14,5m at 12/31/2020

+ €5m from state-guaranteed loans in 01/2021

+ €9.7m from right issue in 04/2021



Cash runway to **end 2022** covering

- Expanded development programs
- Major milestones within 18 months

Sustained liquidity

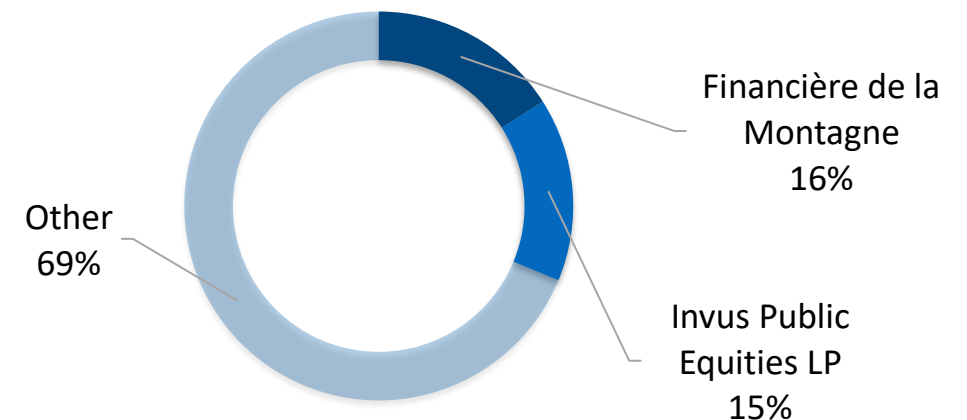
EURONEXT GROWTH | Paris - EPA: **ALONX**
FIRST NORTH | Copenhagen - EPA: **ONXEO**

ISIN: FR0010095596

Average Daily Volume > 336,207 shares

12 months at 03/31/2021

Strong support from two core shareholders



At 04/12/2021



Onxeo in 2021: building for success



UNIQUE MOA IN DDR

Differentiated approach to address major challenges in oncology



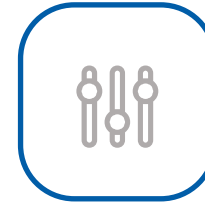
PORTFOLIO OF FIRST-IN-CLASS CANDIDATES

platON platform™ as innovation engine
AsiDNA™ in clinical studies
OX401, preclinical asset



STRONG & BROAD INTELLECTUAL PROPERTY

Platform and candidates protected by several patent families in key territories until at least 2040



SHORT-TERM CLINICAL MILESTONES

Data from two studies and initiation of two new trials in 2021



SIGNIFICANT MARKET POTENTIAL

In combination in multiple cancer indications with high unmet needs



WELL-FINANCED UNTIL END 2022

Beyond major value inflection points in the next 18 months

**Thank you for
your attention!**

The logo for ONXEO is centered within a white circle. The text "ONXEO" is written in a blue, sans-serif font. The letter "X" is stylized, with a pink vertical bar on its left side and a green vertical bar on its right side. The background of the slide features four overlapping, rounded rectangular shapes in pink, green, yellow, and blue, arranged in a cross-like pattern.

ONXEO