



# ANNUAL GENERAL MEETING JUNE 10, 2021

## MANAGEMENT PRESENTATION

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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

## **1<sup>ST</sup>-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



## **CLEAR STRATEGY & BUSINESS MODEL**

Create 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



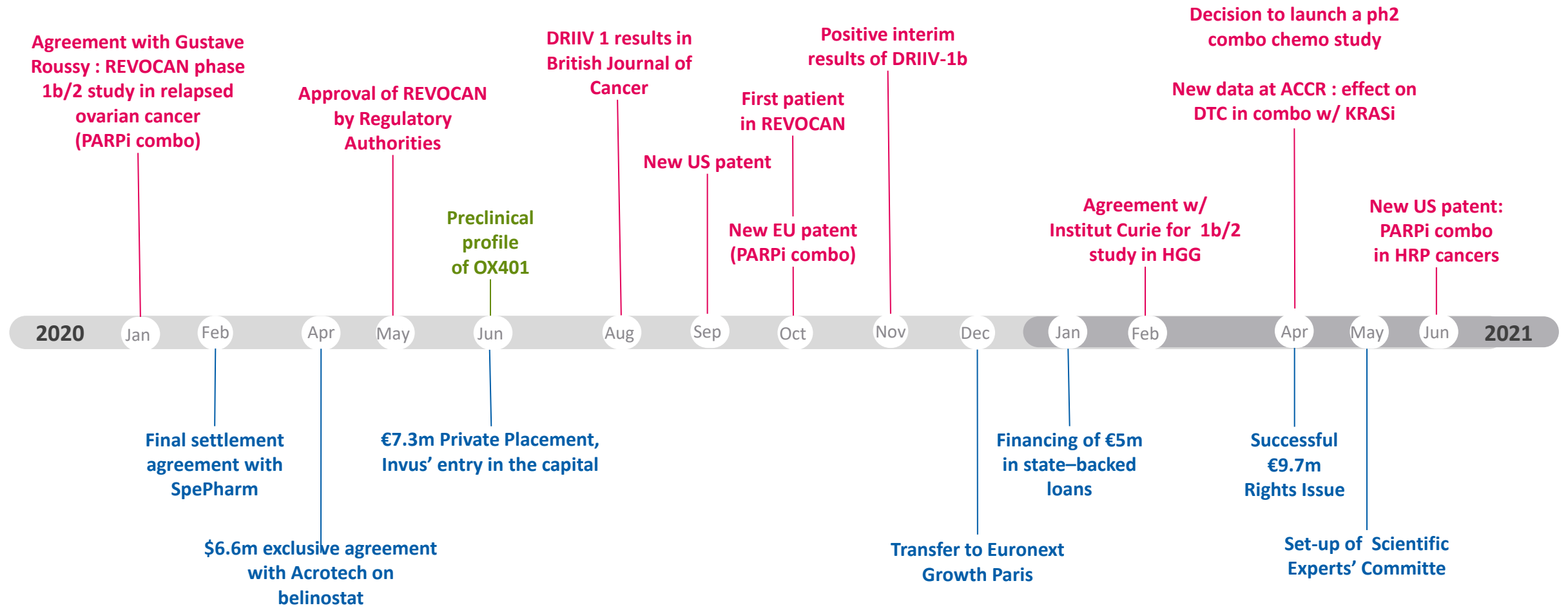
# Expanding development pipeline focused on efficacy synergy and effect on resistance in combination

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

 Completed
  Ongoing
  Starting in 2021



# Significant achievements in 2020 & YTD: strong progress in R&D, extended cash horizon, strengthened shareholding structure



AsidNA™ OX400 Corporate



# FY 2020 Financial highlights



## The Acrotech deal: a transaction with significant impacts on the 2020 IFRS accounts

- Transaction grants Acrotech full and worldwide rights to belinostat in all territories and allows complete focus of Onxeo on its DDR assets
- All future revenues from the belinostat franchise to revert to Acrotech after full repayment of the bond debt from SWK
- Deal considered as an asset sale under IFRS with the following impacts:
  - Transaction price of \$6.6m (€6.1m) and royalties received after deal date are booked as non-current operating income
  - Future royalties are crystallized in the 2020 accounts
  - R&D assets related to Beleodaq®/ belinostat are written-off



# Consolidated P&L account

<i>In € thousands</i>	12/31/2020	12/31/2019
Recurring revenue from licensing agreements	1,077	3,455
Non-recurring revenue from licensing agreements	699	833
<b>TOTAL REVENUES</b>	<b>1,776</b>	<b>4,289</b>
Purchases	(347)	(350)
Personnel expenses	(4,265)	(4,808)
External expenses	(3,882)	(7,857)
Taxes and duties	(176)	(127)
Net depreciation, amortization and provisions	(618)	(671)
Other current operating expenses	(515)	(365)
<b>OPERATING EXPENSES</b>	<b>(9,803)</b>	<b>(14,178)</b>
Other current operating income	213	95
<b>CURRENT OPERATING INCOME (LOSS)</b>	<b>(7,814)</b>	<b>(9,794)</b>
Other operating income and expenses	10,008	(24,543)
Share of profit from equity affiliates	-	(39)
<b>OPERATING LOSS AFTER SHARE OF PROFIT FROM EQUITY AFFILIATES</b>	<b>2,194</b>	<b>(34,376)</b>
Income from cash and cash equivalents	-	19
Gross cost of financial debt	(958)	(1,037)
Other financial income and expenses	611	(659)
<b>FINANCIAL INCOME (LOSS)</b>	<b>(347)</b>	<b>(1,677)</b>
Income tax expense	(757)	2,324
- of which deferred taxes	(415)	2,330
<b>CONSOLIDATED NET INCOME (LOSS)</b>	<b>1,089</b>	<b>(33,728)</b>

Decrease in recurring revenue due to the transfer of commercial rights on Beleodaq to Acrotech

Lower R&D expenses, reflecting notably the finalisation of manufacturing operations of AsiDNA™ for clinical trials

### Impacts of the Acrotech deal:

- + €5.7m from direct transaction income
- + €7.1m for the expected post-signature royalties
- €2.8m related to the R&D NAV under IFRS disposal contract

Cost of bond financing with SWK Holdings Corporation

Danish tax on current and future revenues from Beleodaq





## Consolidated balance sheet - Assets

<i>Assets in € thousands</i>	12/31/2020	12/31/2019
<b>Non-current assets</b>		
Intangible assets	20,534	23,358
Tangible assets	83	109
Right-of-use assets	2,479	2,718
Investments in equity-accounted companies	-	20
Other financial fixed assets	233	141
<b>TOTAL NON-CURRENT ASSETS</b>	<b>23,329</b>	<b>26,345</b>
<b>Current assets</b>		
Stocks and work in progress	-	64
Accounts receivable and related accounts	6,654	3,353
Other receivables	2,000	2,159
Cash and Cash equivalent	14,523	5,708
<b>TOTAL CURRENT ASSETS</b>	<b>23,177</b>	<b>11,284</b>
<b>TOTAL ASSETS</b>	<b>46,506</b>	<b>37,629</b>

Derecognition of belinostat-related R&D assets -€2.8m

Rights of use relating to leases in the scope of IFRS 16

Royalties receivable on sales of belinostat from Acrotech until full repayment of the SWK bond loan



# Consolidated balance sheet - Liabilities

Liabilities and Shareholders' Equity in € thousands	12/31/2020	12/31/2019
<b>Shareholders' equity</b>		
Share capital	19,579	15,329
Minus: treasury shares	(182)	(189)
Share premium	18,577	44,924
Reserves	(10,024)	(9,139)
Earnings	1,089	(33,728)
<b>TOTAL EQUITY</b>	<b>29,036</b>	<b>17,197</b>
<b>Non-current liabilities</b>		
Deferred tax liabilities	415	
Provisions	1,640	6,821
Non-current financial and other liabilities	9,367	7,412
<b>TOTAL NON-CURRENT LIABILITIES</b>	<b>11,423</b>	<b>14,233</b>
<b>Current liabilities</b>		
Short-term borrowings and financial debts	1,979	1,170
Trade payables and related accounts	2,762	3,672
Other liabilities	1,306	1,358
<b>TOTAL CURRENT LIABILITIES</b>	<b>6,047</b>	<b>6,199</b>
<b>TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY</b>	<b>46,506</b>	<b>37,629</b>

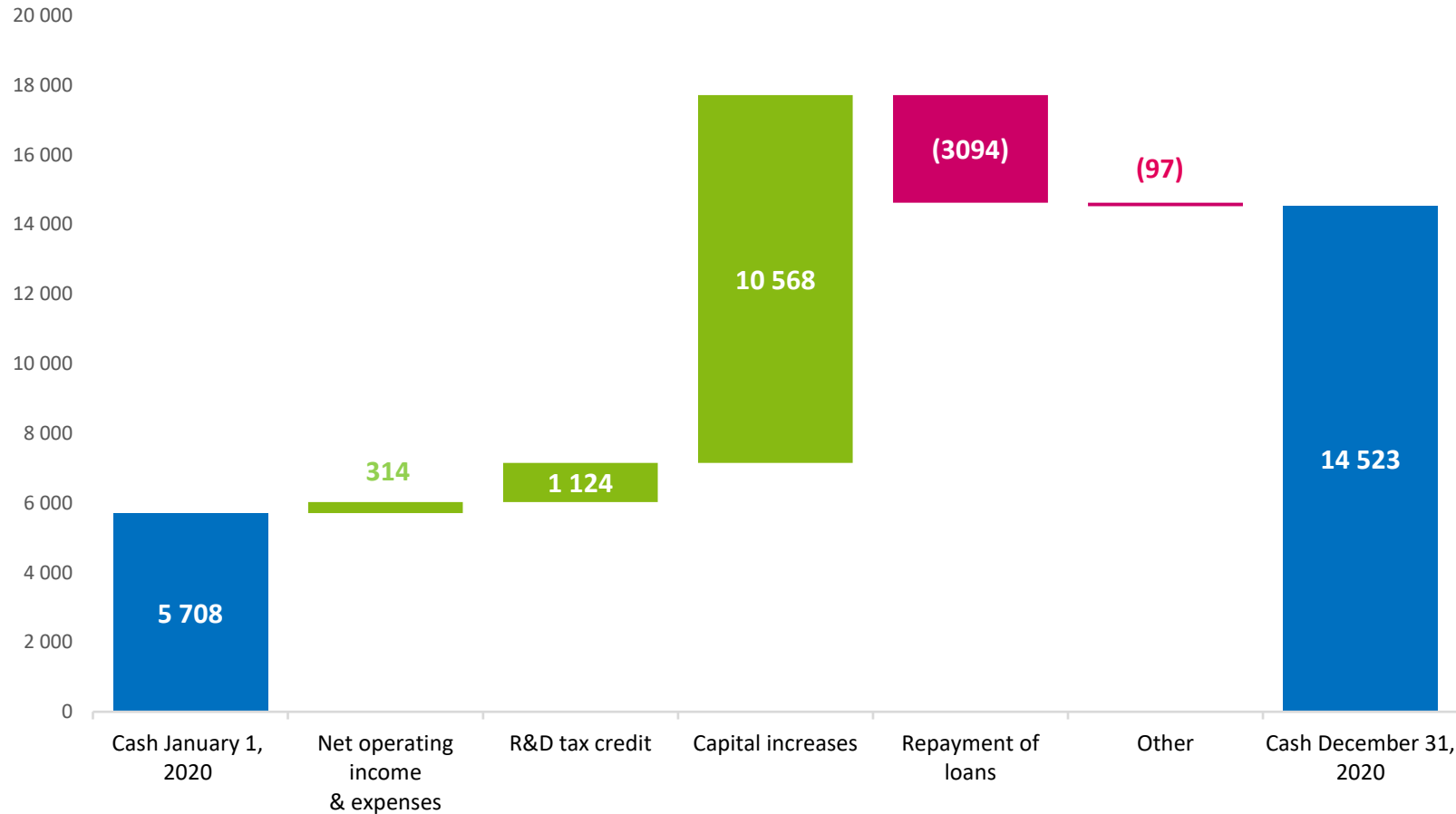
Capital increase from equity line + private placement (€10.7m) + offset of share premium with prior years' losses

Transfer to other non-current liabilities of the additional amounts due to SpePharm

Bond debt to SWK Holdings + debt to SpePharm



# Consolidated cash outlook



## Post-closing information

- **€5.0m secured in the form of State-Backed Loans on Jan. 28, 2021**
- **€9.7m raised in the rights issue finalized on April 12, 2021**

**Financial visibility extended to the end of 2022**

**Strengthened capital structure with over 30% held by reference shareholders**

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# Activities & Perspectives

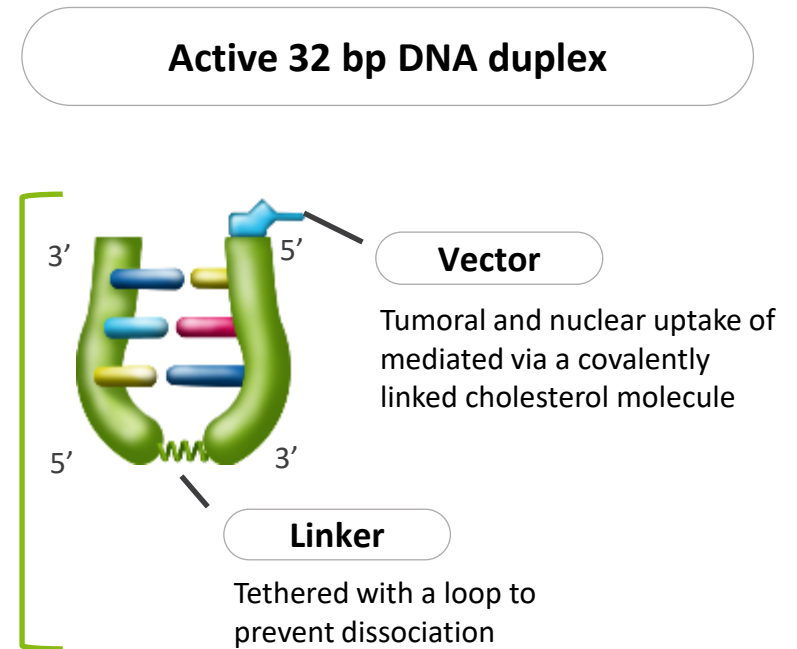


# AsiDNA™, the first decoy agonist in DNA Damage Response (DDR)

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





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

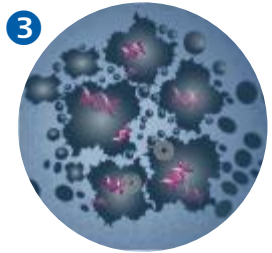
## How it works



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

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



# 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)	
<b>Cohort 1</b> 3 pts ∨	<b>+ carboplatin</b>	TNBC	6 <sup>th</sup> line	5.5 months	<b>Stable Disease</b>	<ul style="list-style-type: none"> <li>• No DLT and very good tolerance of the combination</li> <li>• In 2/3 patients, disease controlled for significantly longer than with any of the prior lines</li> </ul>
		NSCLC (Epidermoid)	3 <sup>rd</sup> line	8.5 months	<b>Stable Disease</b>	
<b>Cohort 2</b> (5 pts)	<b>+ carboplatin</b> <b>+ paclitaxel</b>	NSCLC (Adenocarcinoma)	4 <sup>th</sup> line	3 months	<b>Partial Response -40%</b>	<ul style="list-style-type: none"> <li>• No DLT and very good tolerance of the combination</li> <li>• Disease controlled for significantly longer than w/ any of the prior lines</li> </ul>
		NSCLC (Adenocarcinoma)	2 <sup>nd</sup> line	11 months	<b>Stable Disease</b>	

Promising data support launch of randomized phase 2 end 2021\*

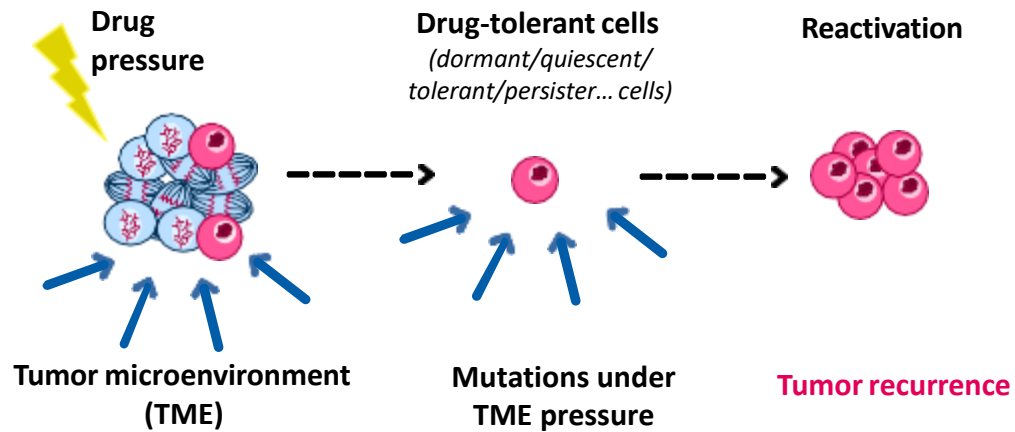




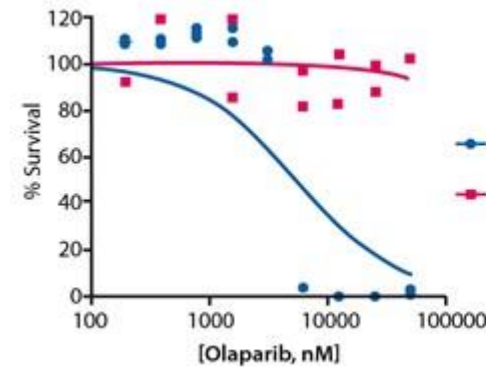
# Acquired resistance to targeted therapies evolves from drug-tolerant cells (DTC) vulnerable to AsiDNA™

DTC: an established cause<sup>1</sup> of resistance to TKI\*

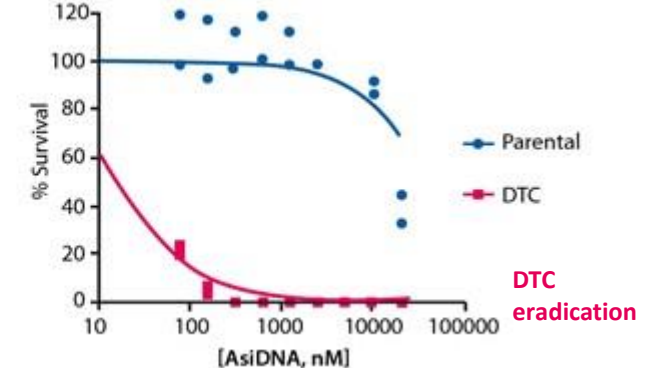
Onxeo showed that resistance to **PARPi** and **KRAsi** also evolves from drug-tolerant cells<sup>2</sup>



AsiDNA™ prevents resistance to PARPi by acting on DTC<sup>2</sup>



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

<sup>1</sup> Sharma VS et al. Cell, 2010, 141-1:69-80

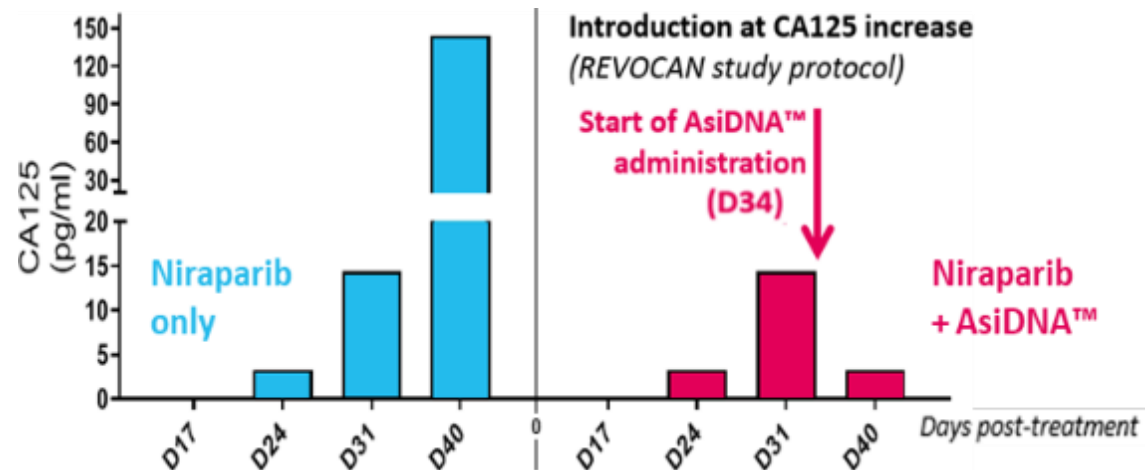
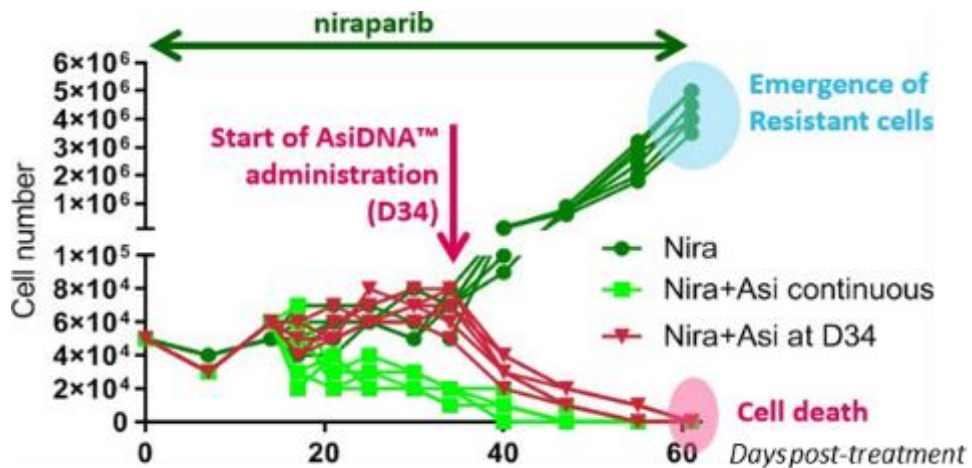
<sup>2</sup> AACR 2020 - [Acquired resistance to PARP inhibitors evolves from drug-tolerant persister cells vulnerable to AsiDNA™](#)

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<sup>null</sup>)



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-Gineco<sup>1</sup>*

### DESIGN

Multicenter, open-label phase 1b/2

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

Platinum-sensitive relapsed ovarian cancer under 2<sup>nd</sup> 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



# 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



# Significant value catalysts expected for AsiDNA™\*

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



# Onxeo in 2021: building for success



## UNIQUE MOA IN DDR

Differentiated approach to address major challenges in oncology



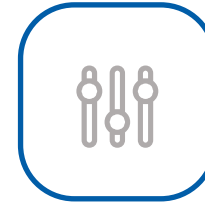
## PORTFOLIO OF FIRST-IN-CLASS CANDIDATES

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!**

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ONXEO