Developing Novel DNA Decoy Therapeutics For Precision DDR Oncology Therapeutics

Corporate Presentation

4Q 2023

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A First-In-Class DDR, DNA Decoy Therapeutics Company

DNA Damage Repair Is Critical For Genomic Stability And Tumor Survival

DNA damage response (DDR) is a rapidly developing field in oncology, with approved PARP inhibitors and other clinically validated DDR targets including ATR and WEE1 inhibitors

First-In-Class DNA Decoy Therapeutics Mimicking DNA Damage And Trapping DNA Repair Proteins

*PlatON™ platform **mimics DNA damage and traps intracellular DNA binding targets with a unique MoA** - proteins in charge of detecting and signaling. ValerioTX has a clinical-stage pipeline of first-in-class DNA decoy drugs protected by several patent families in key territories until at least 2040*

DNA Decoys Are Superior To Current DDR Inhibitors & Has Applicability Beyond DDR

*ValerioTX's **DNA decoys do not rely on enzymatic active sites, thereby relieving evolutionary pressure** and the rapid development of resistance mutations. The DNA decoy therapeutics toolbox is being further expanded to include additional targeting moieties such as bispecific antibodies and aptamers to target transcriptional activation and epigenetic factors*

VIO-01 Is A Pan-DDR Decoy Targeting Multiple Proteins & Repair Pathways

***VIO-01 is a validated monotherapy with efficacy in late-stage IND-enabling studies.** Favorable safety and a high anti-tumor activity*

Strong Capabilities In End-to-end Product Development

*Management team with proven track record and **20+ years of experience in Pharma/Biotech, including deep oncology drug expertise**, experience working with FDA and regulatory agencies, network of KOLs and partners including Gustave Roussy, Institut Curie & USO*

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Agenda

Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

Summary

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Innovative Pipeline Of DNA Decoy Therapeutics

PlatON™	Program (Route Of Admin)	Target	Target Indication	Discovery	IND-Enabling	Phase 1/2	Phase 3	Partner(s)	Next Milestone
1st Generation	AsiDNA™ 1.0 (IV)	DNA-PK	*Recurrent **ovarian, breast, prostate** cancer (combination with PARPi)*	US Clinical Trial					FPI U.S. trial Mar-23
			*Maintenance for **ovarian** cancer with rising CA-125 (combination with PARPi)*	REVOCAN				GUSTAVE ROUSSY	Readout in 1Q24
			*Pediatric and adolescent **glioma** (combination with radiotherapy)*	GLIOMA				institut Curie	Readout in 1Q24
2nd Generation	**VIO-01 (IV)**	**PARP1, MRN, KU70/80**	***mHRR or HRD+ solid tumors** (monotherapy)*						**IND submission 2H23**
3rd Generation	DecoyTAC	DDR, Epigenetics, Transcription Factors	*Undisclosed*						IND enabling studies 2H24

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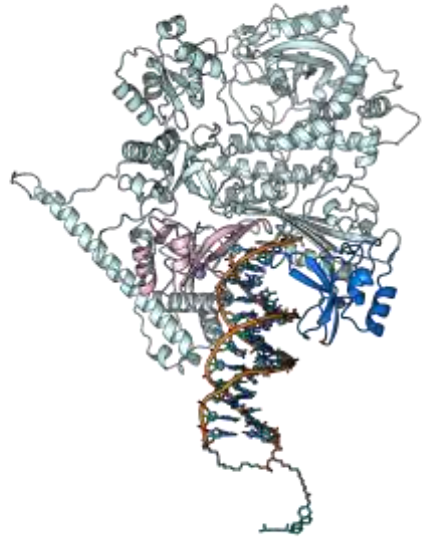
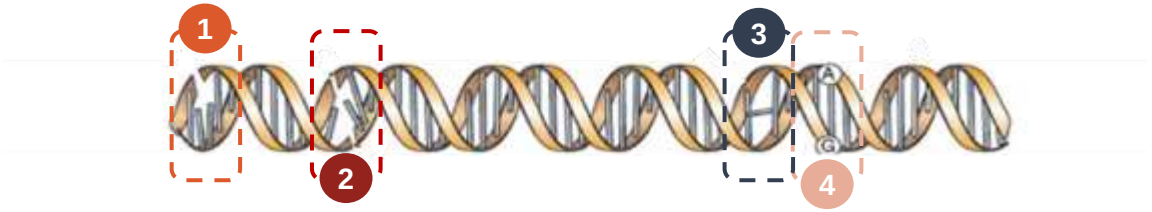
Therapeutic Targeting Of The DNA Damage Response (DDR) To Treat Cancer

- **The DNA repair process is a molecular mechanism activated to restore genomic integrity**
- Mutations in genes found in cancer cells can lead to the loss in function of one or more DNA repair pathways, causing cells become hyper-dependent on the remaining pathways
- **Inhibiting the remaining repair pathways (synthetic lethality)** causes the further damage to the DNA, turning single-strand breaks into double-strand breaks and **triggering cell death**
- **There are five PARP inhibitors (base excision repair mechanism) already on the market generating >$3.5B (2022):** olaparib (AZ), niraparib (GSK), rucaparib (Clovis Oncology), pamiparib (BeiGene) and talazoparib (Pfizer)





	1	2		3	4
DNA Damage Type	Single-Strand Break (SSB)	Double-Strand Break (DSB)		Bulky Adducts	Base Mismatches, Insertions, Deletions
Repair Pathway	Base Excision Repair (BER)	Homologous Recombination (HR)	Non-Homologous End Joining (NHEJ)	Nucleotide Excision Repair (NER)	Mismatch Repair (MMR)
Effector Proteins	PARP1 XRCC1	BRCA1 BRCA2 PALB2 ATM CHEK1 CHEK2 RAD52	KU70/KU80 DNA-PK	ERCC4 ERCC1	MSH2 MSH3 MSH6 MLH1 MLH2 MLH3

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Addressing The Severe Limitations With Current DDR Therapies

	Pathway Redundancy	Synthetic Lethality	Limited Tolerability	Intrinsic/Acquired Resistance	Indication Withdrawals
Current DDR Products (Lynparza olaparib, Zejula niraparib, Partruvix pamiparib, TALZENNA talazoparib, Rubraca rucaparib)	PARP inhibitors only abrogate PARP-related repair which leads to activation of compensatory DDR pathways	Current targeted DDR therapeutics (PARP, WEE1, ATR, DNA-PK inhibitors) rely on germline or somatic mutations	Severe myelosuppression + PARP inhibitors increase the risk of MDS/AML which can result in high mortality	~50% of patients with BRCA1/2 mutated cancers do not respond to PARP inhibitors and ~10-15% of tumors do not respond to initial platinum therapy Patients treated with PARP inhibitors develop reversion mutations in BRCA1/2 leading to tumor resistance	PARP inhibitors has failed to predict a survival benefit in the treatment setting leading to indication withdrawals by the FDA
VALERIO THERAPEUTICS	**Versatility In A Pan-DDR Approach**		**Better Safety Including Myelosuppression**	**No Limitations On Targeting**	
	Ability to trap multiple key DDR proteins leaving no salvage repair pathways	**Active regardless of sensitizing mutations (e.g. BRCA1/2)**	**Specific to cancer cells, translating in outstanding safety and possibility to use in combination**	**DNA decoy does not rely on enzymatic active sites thereby relieving evolutionary pressures and the development or resistance mutations**	

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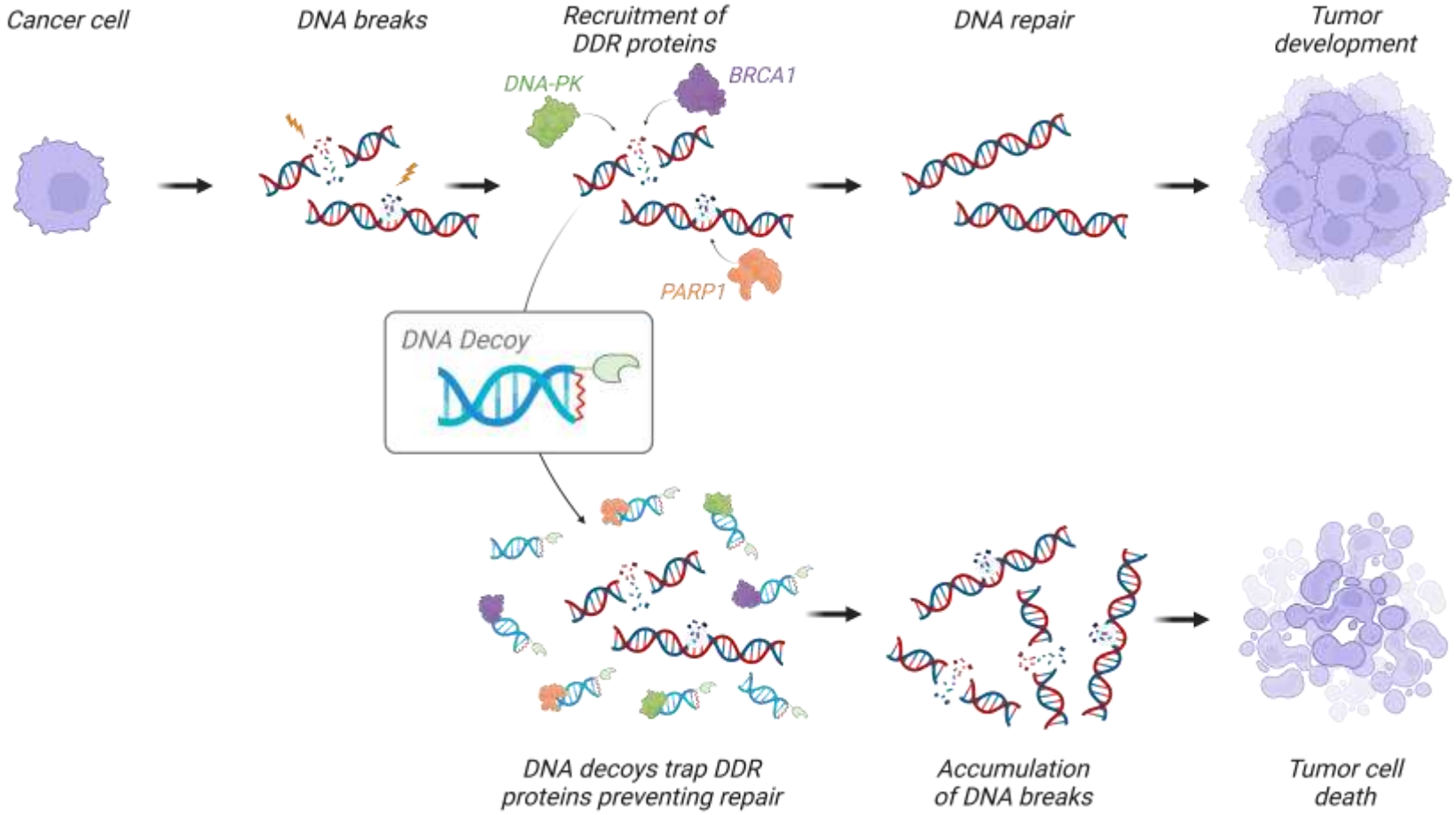
DNA Decoy: Sequestering Key DNA Repair Proteins With A Differentiated Mechanism Of Action



Trapping DNA Repair Proteins

*DNA decoys mimic DNA breaks in tumor cells, saturate them with false alarm signals (**decoy**), then traps key DDR proteins*

Hindering DNA Repair Functions

*This prolonged signaling, trapping and overactivation **depletes** the DDR and hinders DNA repair mechanisms*

Cell Death

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

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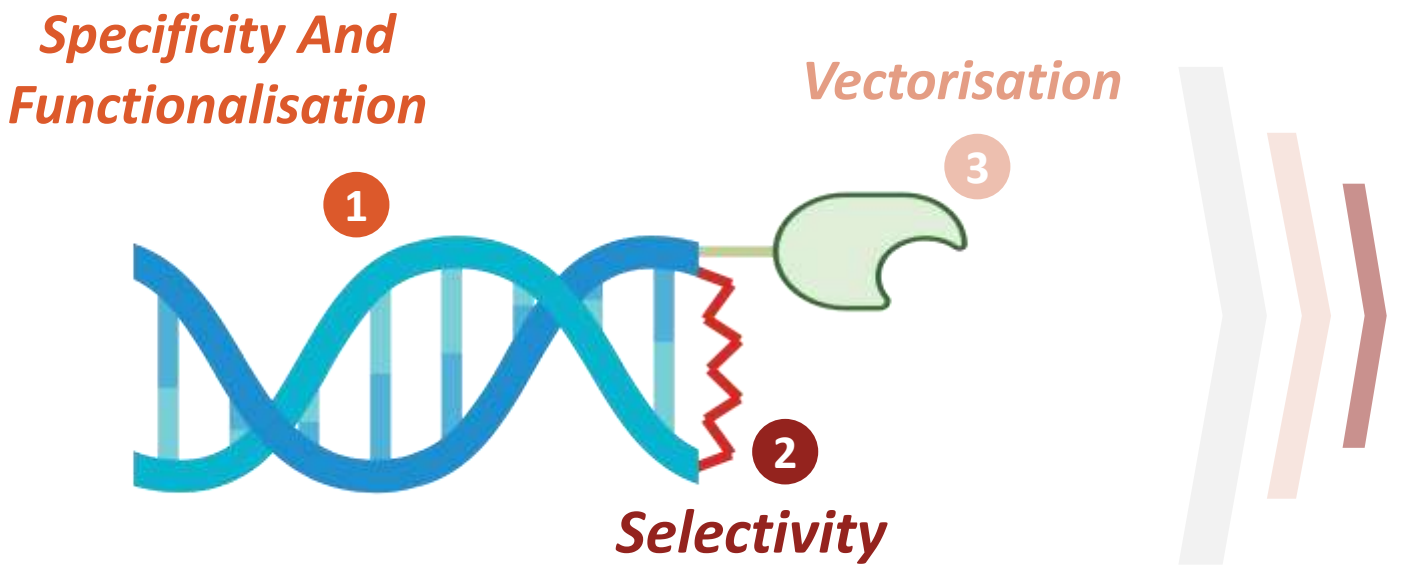
PlatON™, Proprietary DNA Decoy Platform Targeting Intracellular DNA-Binding Targets

The platON™ DNA Decoy platform uses three components:



1 DNA Decoy

- *Double-stranded DNA fragment (oligonucleotide) of variable sequence and length*
- *Ability to target DDR, epigenetic proteins and transcription factors*

2 Linker

- *Tethered with a loop to prevent dissociation*

3 Vectorisation

- *Facilitating tumoral and nuclear uptake*
- *Ongoing work to incorporate small molecules, nanobodies and aptamers*

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Imagining Beyond - Driven By The PlatON™ Platform

1st Generation

Cholesterol (cellular uptake)

DNA-PK decoy

AsiDNA™

2nd Generation

Cholesterol (cellular uptake)

Pan-DDR decoy

VIO-01

3rd Generation

Combining DNA decoy with PROTAC and tumor specific vectorization to develop cutting edge anti-cancer therapeutics

Active moiety (protein degradation)

Small molecule ligand

Transcription factor decoy

Aptamer

Single-domain antibody

DecoyTAC

Increase tumor specificity with aptamer, bispecific antibodies, etc.

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Overview Of 1st Generation PlatON™ Product, AsiDNA™

1 Key DNA Targeting Decoy

Targeting and sequestering:

1) DNA Protein Kinase (DNA-PK),

a key kinase required for DSB repair by NHEJ, which is the primary DNA repair pathway for DSBs in human cells

DNA-PK is a key target for cancer therapies as genetic deficiencies sensitize cancer cells to radiotherapy and DNA damaging agents such as chemotherapy and PARP inhibitors

Trapping DNA-PK To Prevent Repair

AsiDNA™ traps DNA-PK and prevents a response to DNA damage

Potential Combination Therapy

AsiDNA™ can be combined with other DNA damage therapies without additive toxicity

Unique MoA

AsiDNA™ does not target the active site of DNA-PK, relieving the pressure to develop resistance mutations

Strong Patent Protection

A patent portfolio built on 9 different patent families, granted in major markets, covering compositions of matter, methods of use, and combinations

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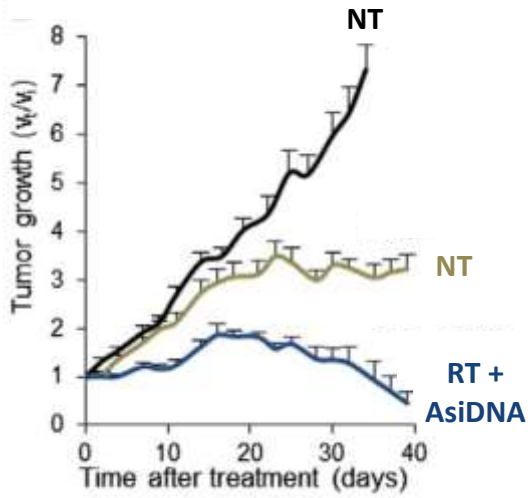
Preclinical Data Demonstrating Synergistic Effects Of AsiDNA™ With Standard Cancer Therapy

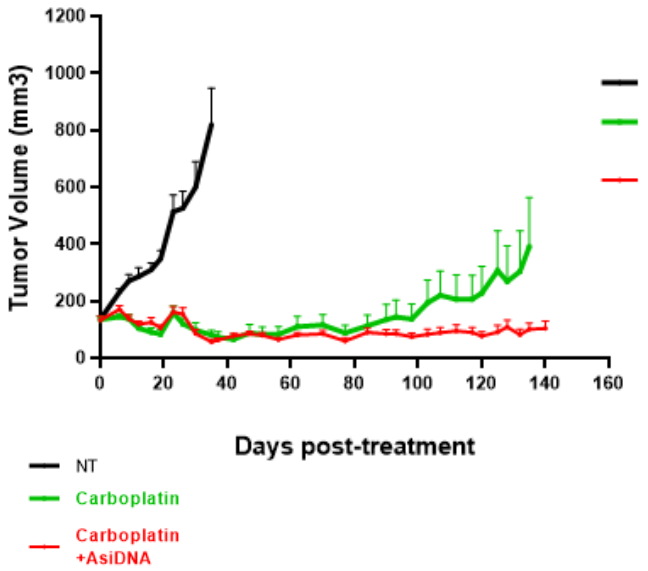
Radiotherapy

SK-28 (Human Melanoma) xenograft in mice



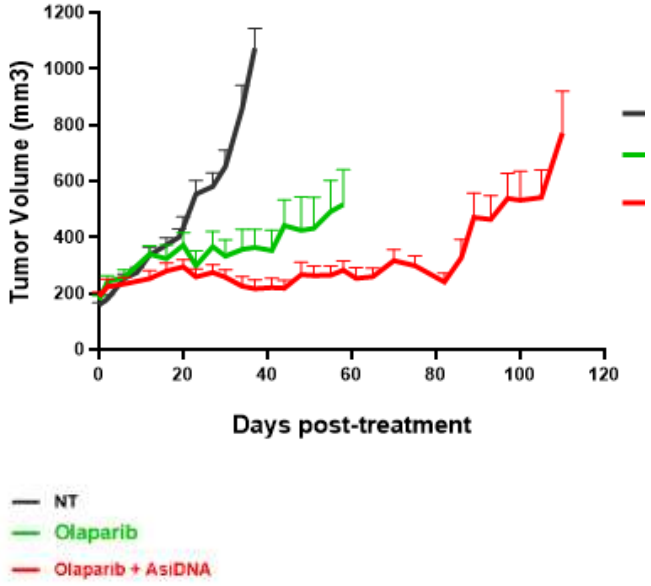
Chemotherapy

MDA-MB-436 (TNBC) xenograft in mice (HRD – BRCA1mutated)



PARP Inhibition

MDA-MB-436 (TNBC) xenograft in mice (HRD – BRCA1mutated)



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AsiDNA™ Clinical Proof Of Concept In Solid Tumors

- ***Approx. n=80 patients have already been treated with AsiDNA™ to date (completed and ongoing trials)***

Trial	Phase	No. Patients	Status	Key Results
DRIIM IT admin in combo with RT in Melanoma	1	n=23	Completed	✓ **ORR = 67%** (CR-5%; PR-62%) ✓ **Durable response** (up to 12-month follow-up period) ✓ Favorable safety profile
DRIIV Part 1 IV admin as monotherapy in advanced solid tumors	1	n=22	Completed	✓ **4 out of 17** evaluable patients **achieved SD** ✓ Proof of mechanism shown through hyper-activation of DNA-PK at the cell level ✓ Favorable safety profile: No drug-related SAEs < 900 mg; No DLTs < 900 mg
DRIIV Part 2 IV admin in combo w/wo Paclitaxel & Carboplatin	1	n=11	Completed	✓ Heavily pre-treated patients with advanced metastatic tumors, progressing at inclusion ✓ **1 PR and 4 SD** yielding a **DCR of 55.6%** ✓ Favorable tolerability in combination therapy
REVOCAN (IST) IV admin in combo with PARPi *(patients progressing on prior PARPi)*	1/2	n=15	Ongoing	✓ Interim analysis (10 patients): **1 CR, 6 SD** showing a **DCR of 70%** ✓ No new safety signals identified
High Grade GLIOMA (IST) IV admin in combo with RT *(children, adolescents & young adults)*	1/2	n=5	Ongoing	▪ Not reported yet

IT, intratumoral ; IN, intravenous ; ORR, objective response rate ; DCR, disease control rate ; CR, complete response ; PR, partial response ; SD, stable disease

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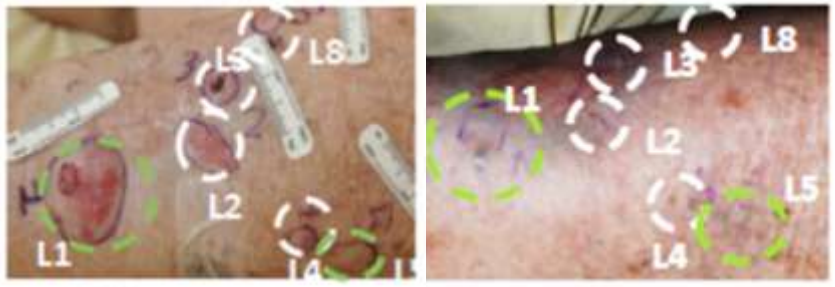
DRIIM: AsiDNA™ Clinical Proof Of Concept Demonstrated In Melanoma

DRIIM: AsiDNA™ Combination with Radiotherapy

- Intratumoral injection
- Combo with Radiotherapy in patients with skin metastases from Melanoma
- N = 23 patients (76 skin lesions)

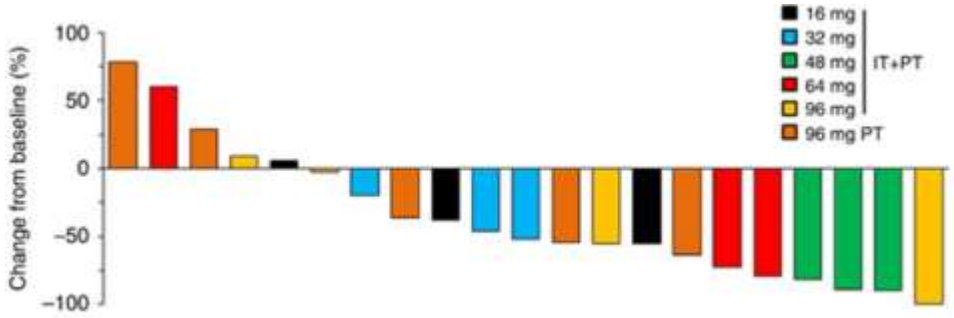
Melanoma skin lesion responses to treatment



Before Treatment 90 Days After Treatment

Established Proof of Concept

- **Favorable safety profile**
- **Overall response rate (ORR) of 67%** in 21 evaluable patients
  - 1 patient (5%) experienced a CR to treatment
  - 13 patients (62%) experienced a PR to treatment
- **Durable response** (up to 12-month follow-up period)



Source: Le tourneau C. et al, Br J Cancer. 2016, Vol.114, Issue 11

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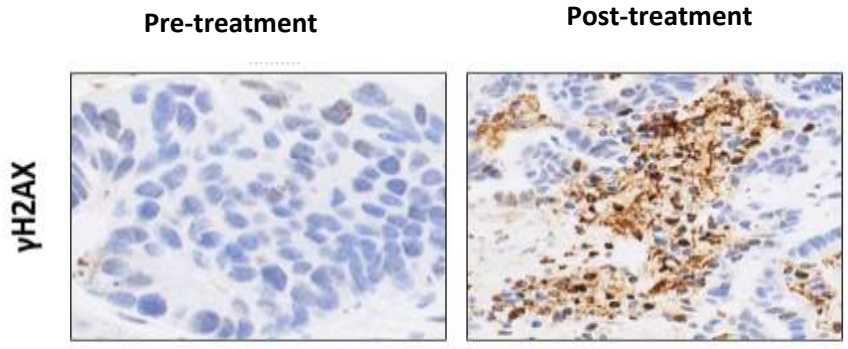
AsiDNA™/Chemotherapy Combination Achieves Disease Control In Solid Tumors

DRIIV-Part 1: Favorable Safety Outcome

- Open-label, 3+3 dose escalation n =22
- 5 doses (200mg - 1,300mg)
- Successful development of IV administration
- 600 mg dose selected for clinical development
- Mechanism of action demonstrated



γH2AX (DNA-PK biomarker) readout in tumor biopsies

DRIIV-Part 2: 56% Disease Control Rate

- Open label 3+3 cohorts: Patients eligible to carboplatin +/- paclitaxel
- Heavily pre-treated patients with advanced metastatic tumors, progressing at inclusion
- **No DLT and very good tolerance** of combo therapy in 8 evaluable patients
- **Efficacy signals** in 4 patients: **disease controlled for significantly longer** than with any of the prior lines

AsiDNA™ 600mg	Tumor	Treatment Line	Treatment Duration (Months)	Response
+ carboplatin	**TNBC**	6th line	5.5	Stable Disease
	NSCLC *(Epidermoid)*	3rd line	8.5	Stable Disease
+ carboplatin + paclitaxel	**NSCLC** *(Adenocarcinoma)*	4th line	3.0	**Partial Response - 40%**
	NSCLC *(Adenocarcinoma)*	2nd line	11	**Stable Disease**

Source: Kotecki N. Long Stabilization and Disease Control with AsiDNA™, a first-in-class DNA Repair Inhibitor in Combination with Carboplatin. Oncology & Cancer Case Reports 2021, Vol.07, Issue 2, 001-007 - 03/2021; Final results to be published

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REVOCAN Interim Analysis Shows Positive Efficacy Signals

REVOCAN: Phase Ib/II Study

- 26-patient, open label, multicentric, phase Ib/II to assess the safety and efficacy of AsiDNA™, administered IV in combination to PARPi
- Patients with relapsed platinum sensitive ovarian cancer already treated with PARPi
- 15 patients enrolled to date
- AsiDNA™ is combined with PARPi when patient have increased CA-125 level for two weeks

Interim Analysis On 10 Patients Shows 70% DCR

- One Complete Response (CR)*
- Six Stable diseases (SD)*
- Disease Control Rate: 70%
- Overall reduction in % of CA125 across responding patients: potential sign of disease stabilization

GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

*Note: * - as per RECIST 1.1*

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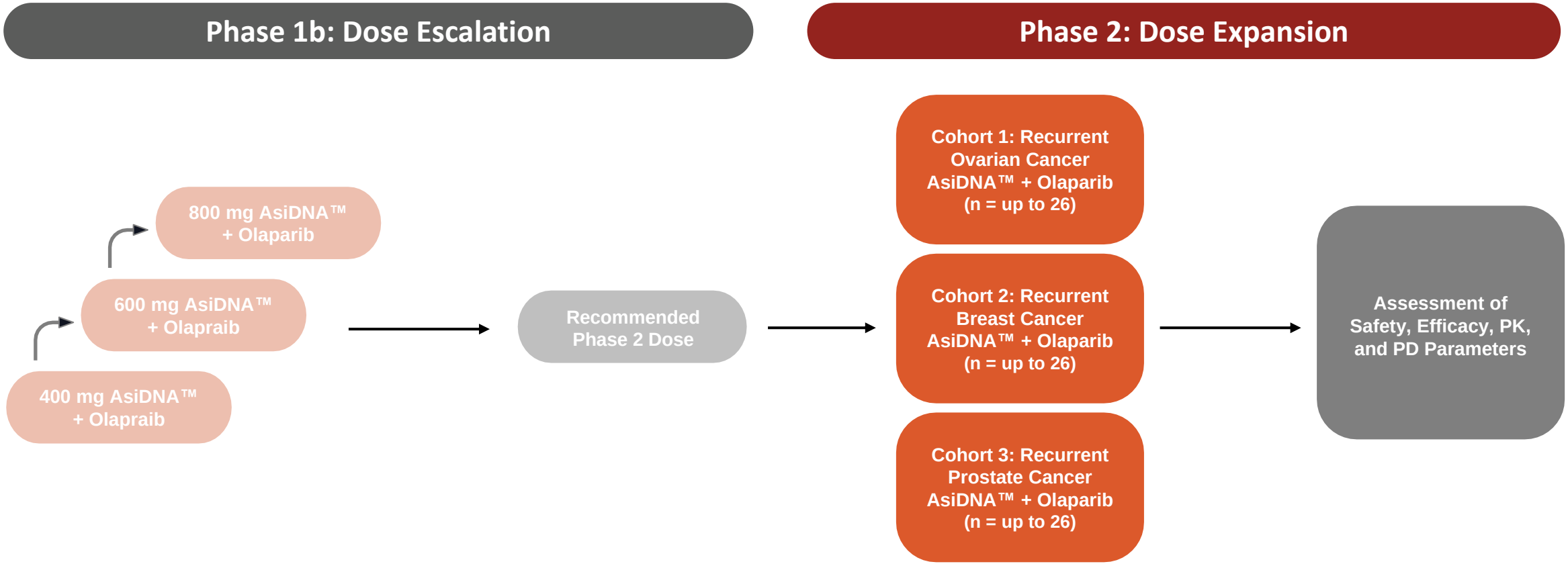
First US Clinical Trial Initiated: FPI Dosed On 21st March 2023

- *Evaluating AsiDNA™ in combination with olaparib to resensitize patients who have progressed on a prior PARP inhibitor*



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DecoyTAC - 3rd Generation

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Overview Of 2nd Generation PlatON™ Product, VIO-01

- ***VIO-01 Traps Several DDR Proteins Inhibiting Different Repair Pathways***

1 Key DNA Targeting Decoy

Targeting and sequestering:

1) **KU70/KU80**, a part of the NHEJ machinery and is responsible for recruiting other proteins to assist in the NHEJ repair
2) **PARP-1**, a key DNA damage sensor protein that identifies and recruits DNA repair machinery to damage sites
3) **MRN**, a complex playing an important role in DDR recognition and signaling, and HR or NHEJ repair
4) **MSH2**, an important protein involved the recognition of single-base insertions

Multi-Trapping

VIO-01 traps several DNA repair proteins (PARP1, KU70/80, MRN, MSH2)

Pan-Inhibition

VIO-01 inhibits SSB and DSB repair leading to extensive DNA damage accumulation

Independence Of Repair Mechanisms

VIO-01 Displays Antitumor Activity Independently From Repair Status

Higher Antitumor Activity Vs Competitors

VIO-01 Displays Higher Antitumor Activity Compared To PARP And DNA-PK Inhibitors And An Enhanced Tumor Accumulation

Strong Patent Protection

A patent portfolio built on 3 different patent families, focused on compositions of matter

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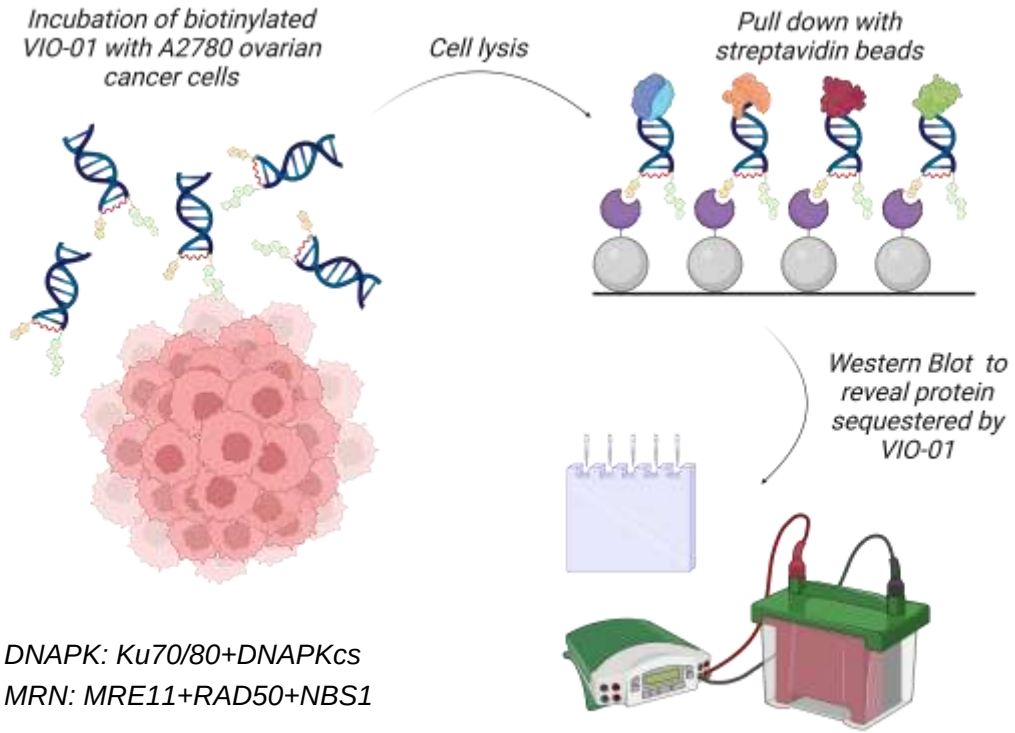
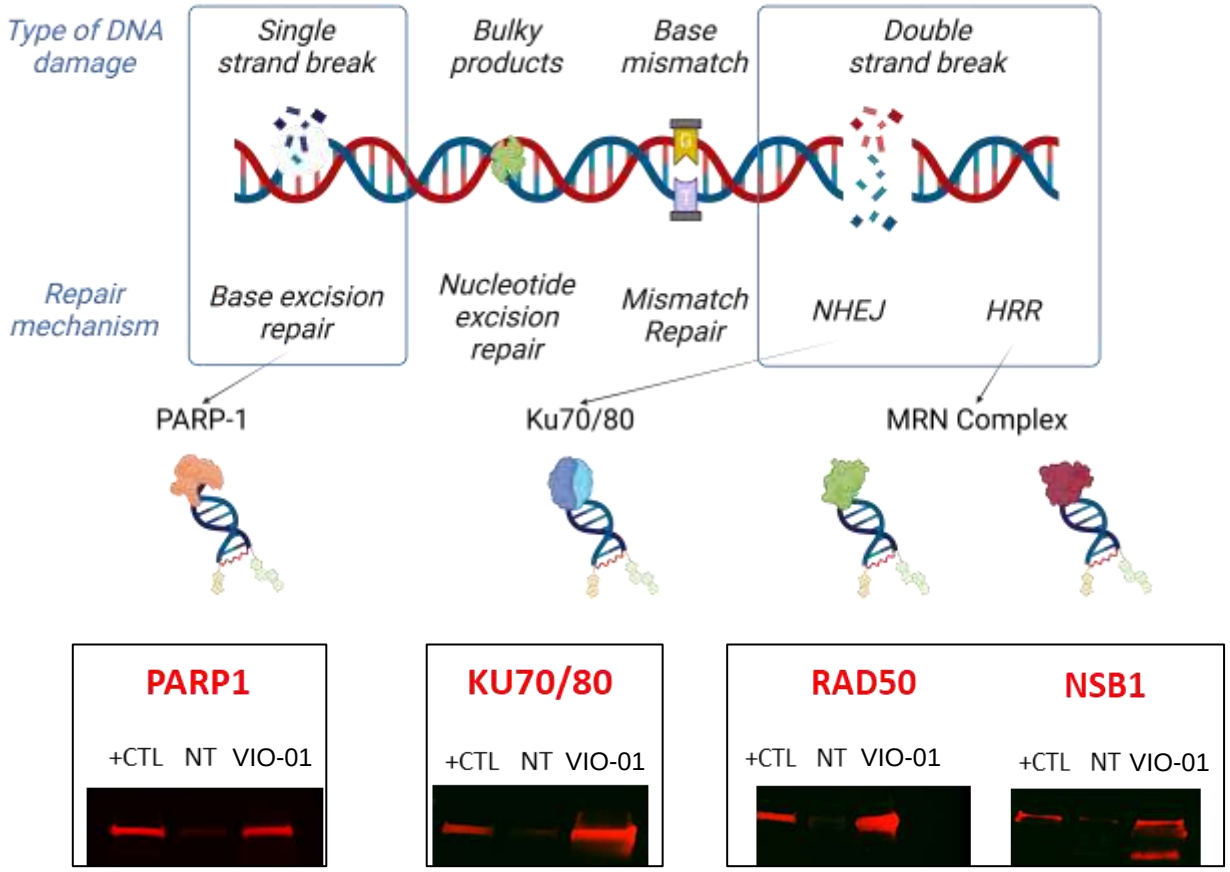
VIO-01 Is A Pan-DDR Decoy Trapping Multiple Repair Proteins In Tumor Cells



DNAPK: Ku70/80+DNAPKcs
MRN: MRE11+RAD50+NBS1



VIO-01 reaches the nucleus and acts as a decoy for several DNA repair enzymes

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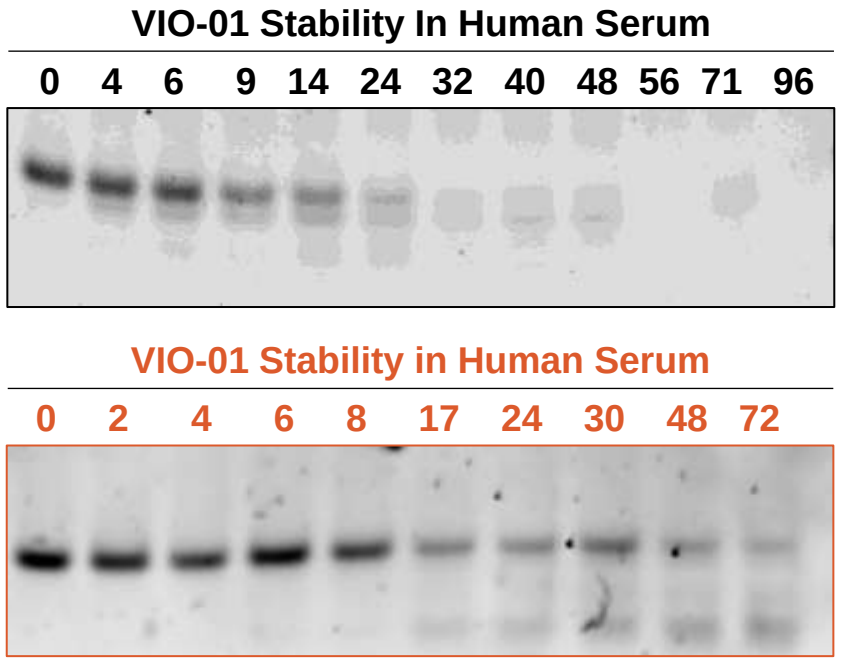
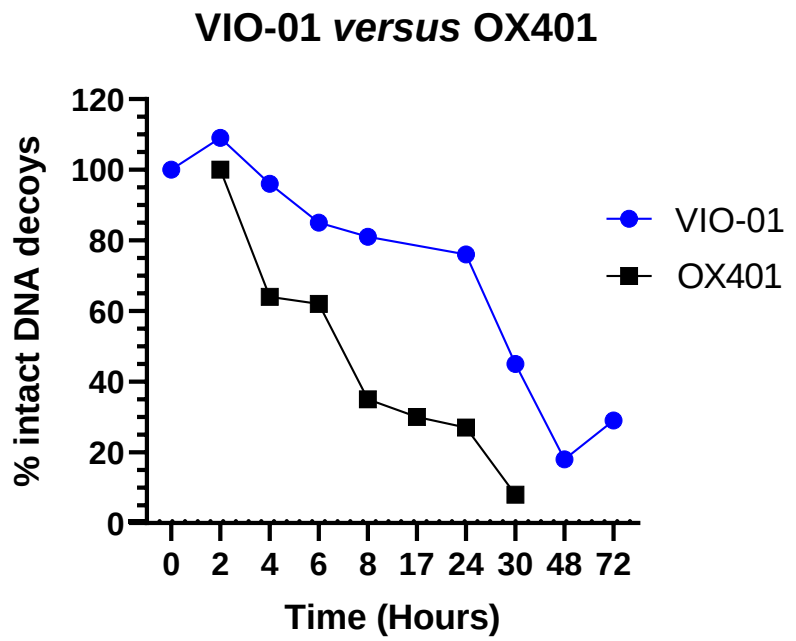
VIO-01 Resists Endonuclease Degradation In Human Serum



Electrophoresis of intact versus metabolized DNA decoys after incubation in human serum



VIO-01: 31% PS and 56% FANA modifications
OX401: just 18% PS

VIO-01 has an increased resistance to nucleases and plasmatic stability

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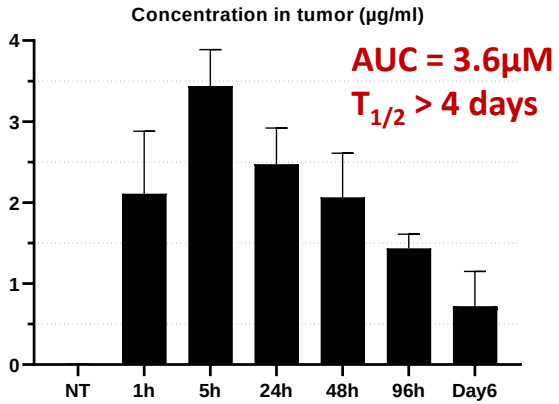
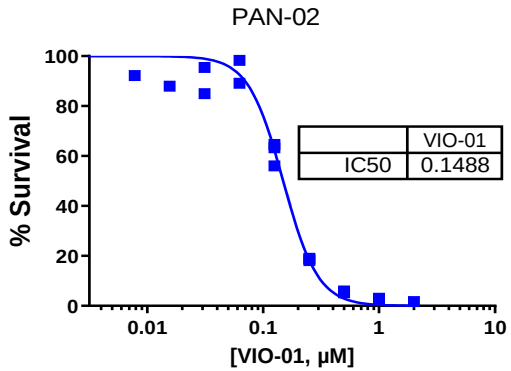
VIO-01 Accumulates In Tumors And Reaches The Nucleus

VIO-01 Tumor Accumulation

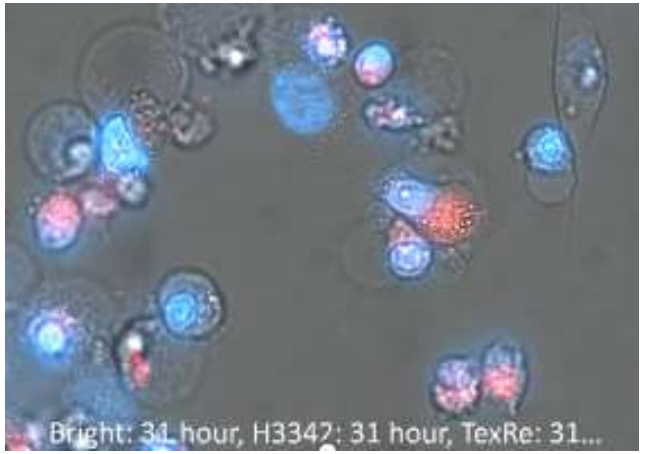




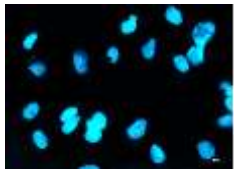
VIO-01 accumulates in tumors at 30x concentration needed to achieve anti-tumor activity for up to 1 week

PAN-02 (Pancreatic cancer) xenograft in mice

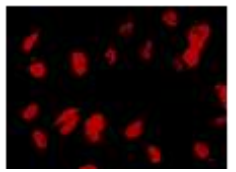
VIO-01 Nuclear Localization



Nucleus



VIO-01-Cy5



MDA-MB-231 TNBC cells

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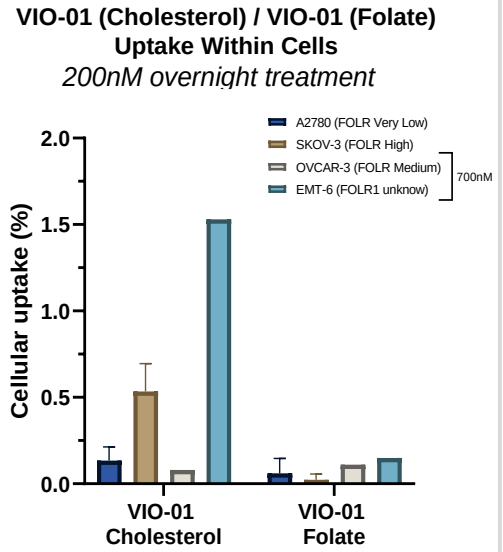
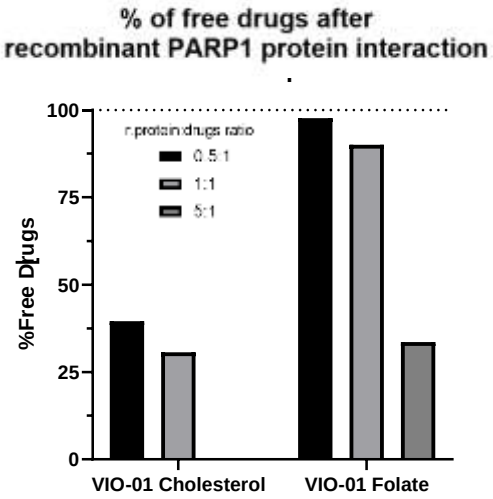
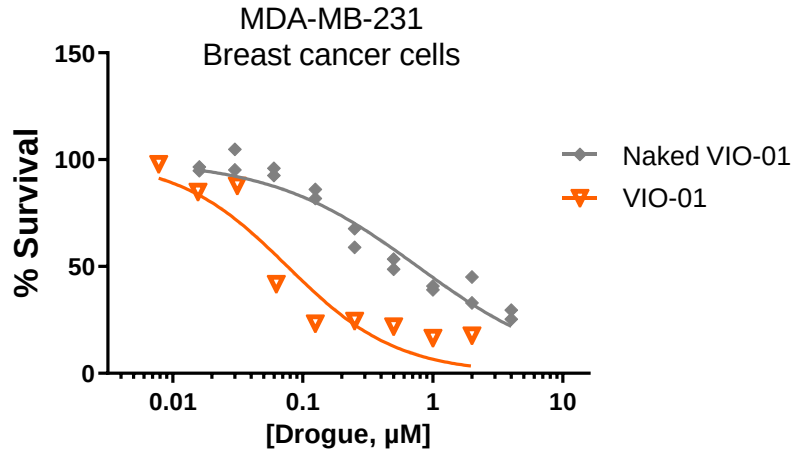
Cholesterol-Attached VIO-01 Shows Superior Cellular Uptake And Drug Efficacy

VIO-01 Cholesterol vs. VIO-01 Folate





VIO-01 With Cholesterol vs. Naked VIO-01



	VIO-01	Naked VIO-01
IC50	0.07623	0.7631

VIO-01 (with Cholesterol) shows higher cellular uptake and lower % of free drugs after PARP interaction, compared with VIO-01 Folate

VIO-01 (with Cholesterol) is more cytotoxic compared to naked VIO-01, as illustrated by lower cancer cell survival rates and IC50 values

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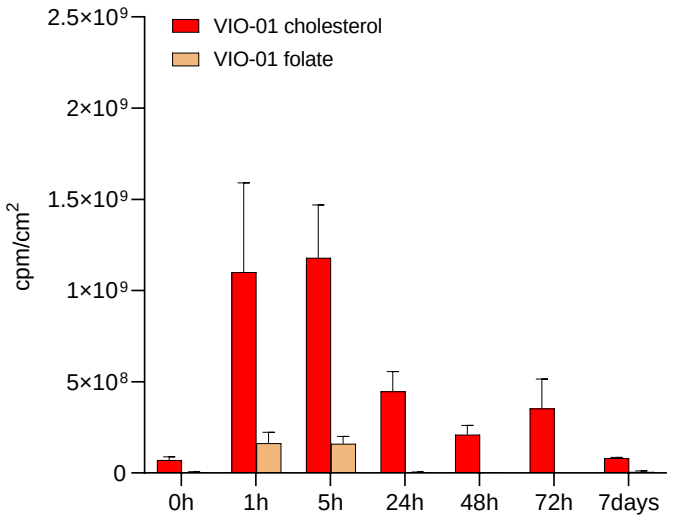
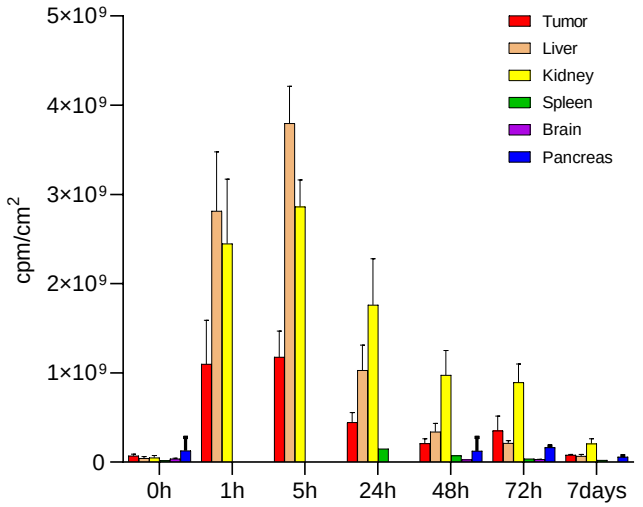
Delivery Vector: VIO-01 With Cholesterol Shows Increased Uptake In Tumor Vs VIO-01 With Folate

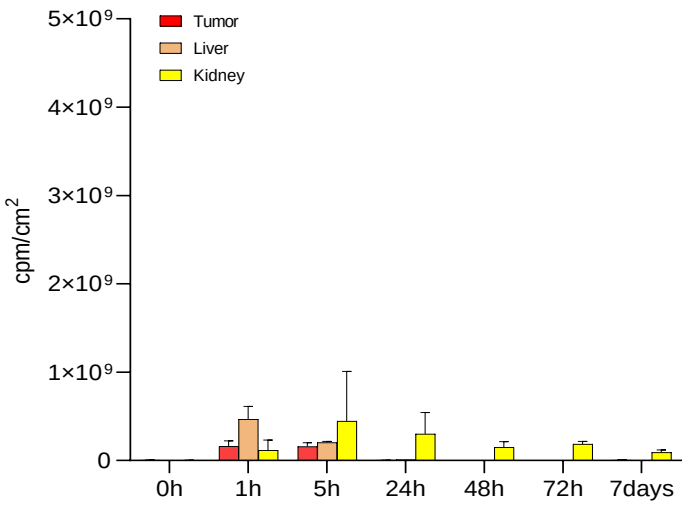
VIO-01 Ligands Biodistribution in Tumor



Biodistribution of VIO-01 Cholesterol



Biodistribution of VIO-01 Folate



VIO-01 Cholesterol shows superior ability to access and accumulate in the tumors

VIO-01 Cholesterol has a better biodistribution properties than VIO-01 Folate

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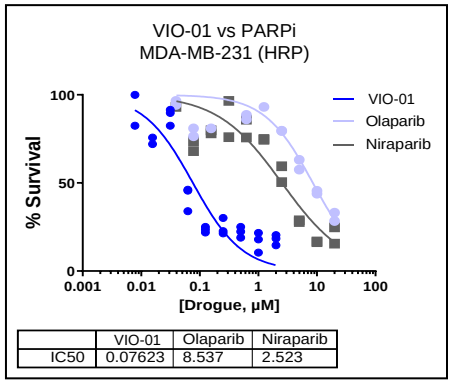
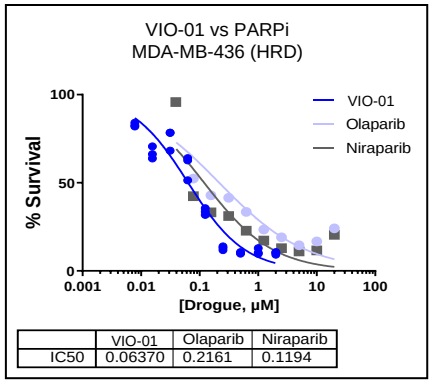
VIO-01 Displays Higher Anti-Tumor Activity Compared To PARP And DNA-PK Inhibitors

VIO-01 vs PARP Inhibitors

Breast Cancer Models

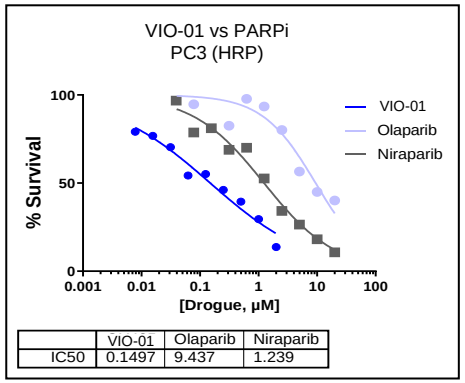


	VIO-01	Olaparib	Niraparib
IC50	0.07623	8.537	2.523

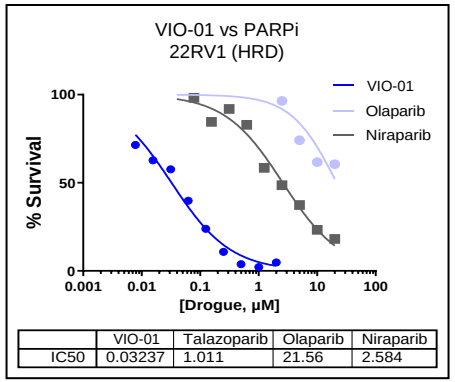


	VIO-01	Olaparib	Niraparib
IC50	0.06370	0.2161	0.1194

Prostate Cancer Models



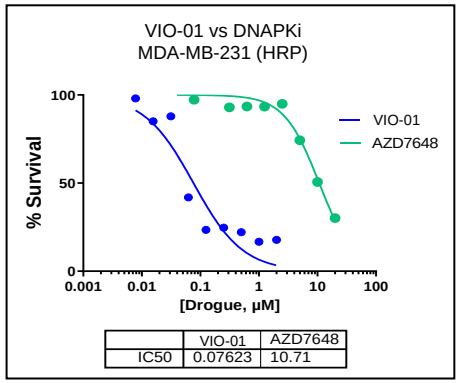
	VIO-01	Olaparib	Niraparib
IC50	0.1497	9.437	1.239



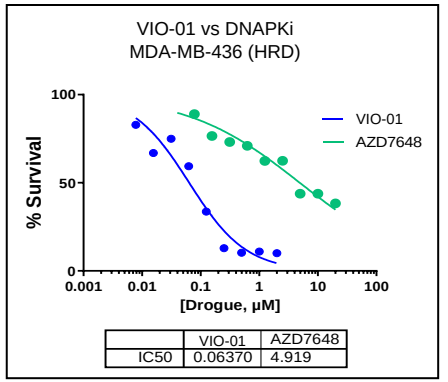
	VIO-01	Talazoparib	Olaparib	Niraparib
IC50	0.03237	1.011	21.56	2.584

VIO-01 vs DNA-PK Inhibitor

Breast Cancer Models

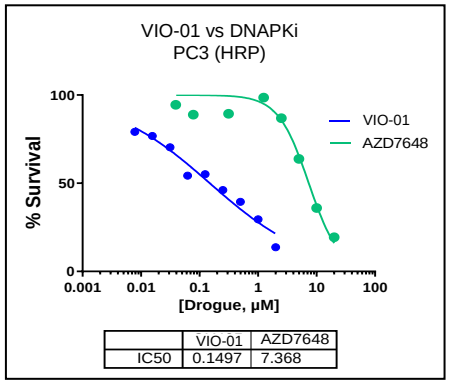


	VIO-01	AZD7648
IC50	0.07623	10.71

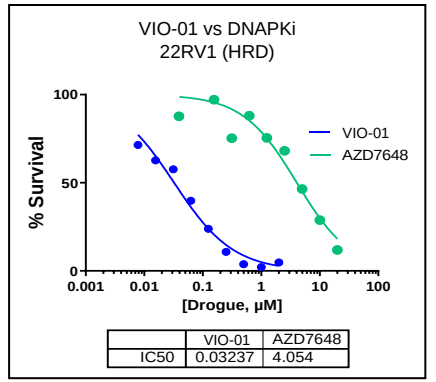


	VIO-01	AZD7648
IC50	0.06370	4.919

Prostate Cancer Models



	VIO-01	AZD7648
IC50	0.1497	7.368



	VIO-01	AZD7648
IC50	0.03237	4.054

Compared to PARP and DNA-PK inhibitors, VIO-01 is highly active independently of tumor type and genetic mutation

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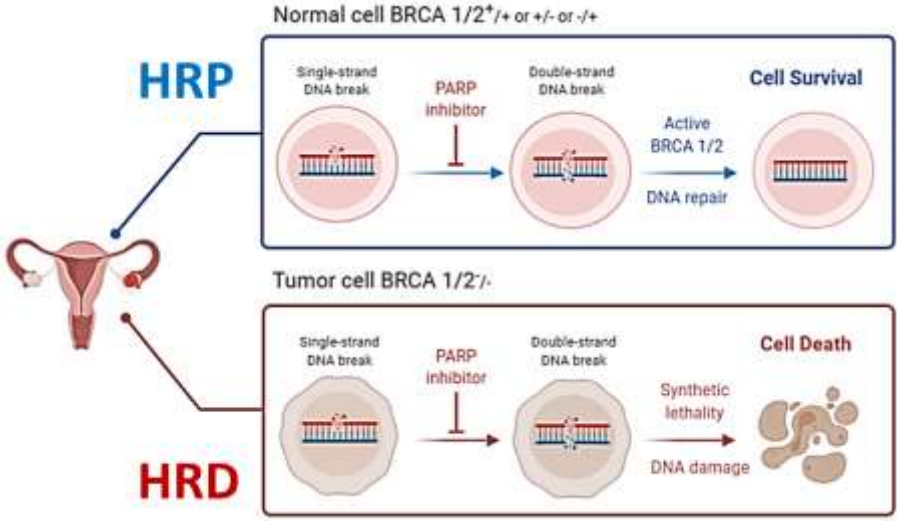
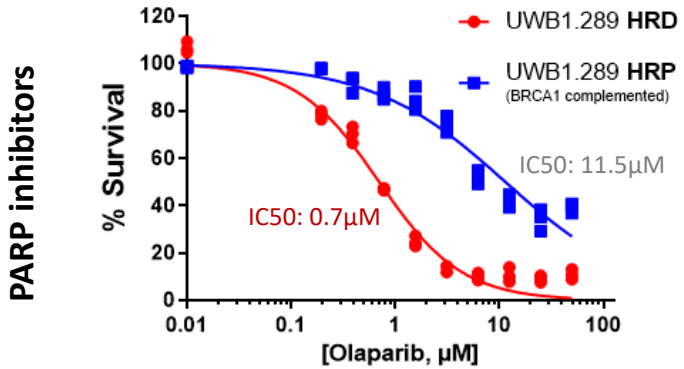
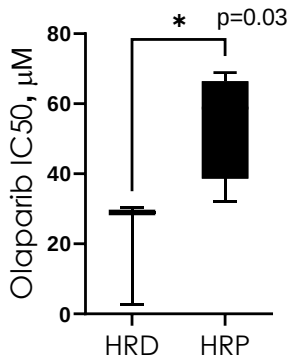
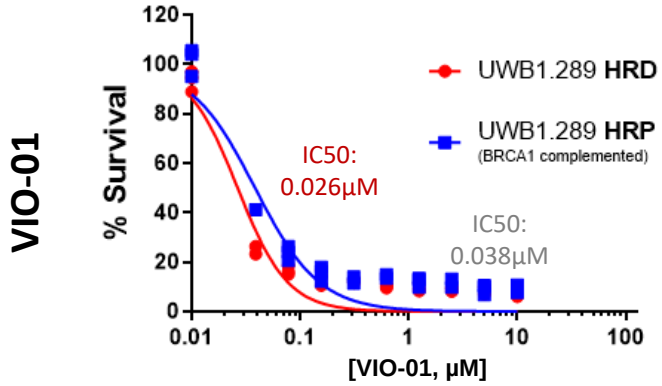
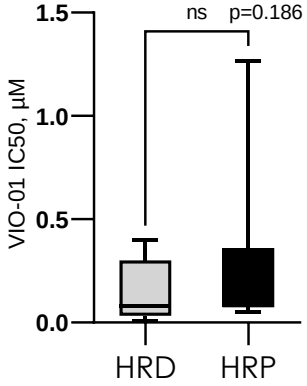
VIO-01 Anti-Tumor Activity In Ovarian Cancer Is Independent Of Genetic Mutations











- **PARP inhibitors require defects in HRR to be active (ie: BRCA1/2 mutation)**
- **Compared to PARP inhibitors, VIO-01 display the same activity in tumor cells with no defects in DNA repair**

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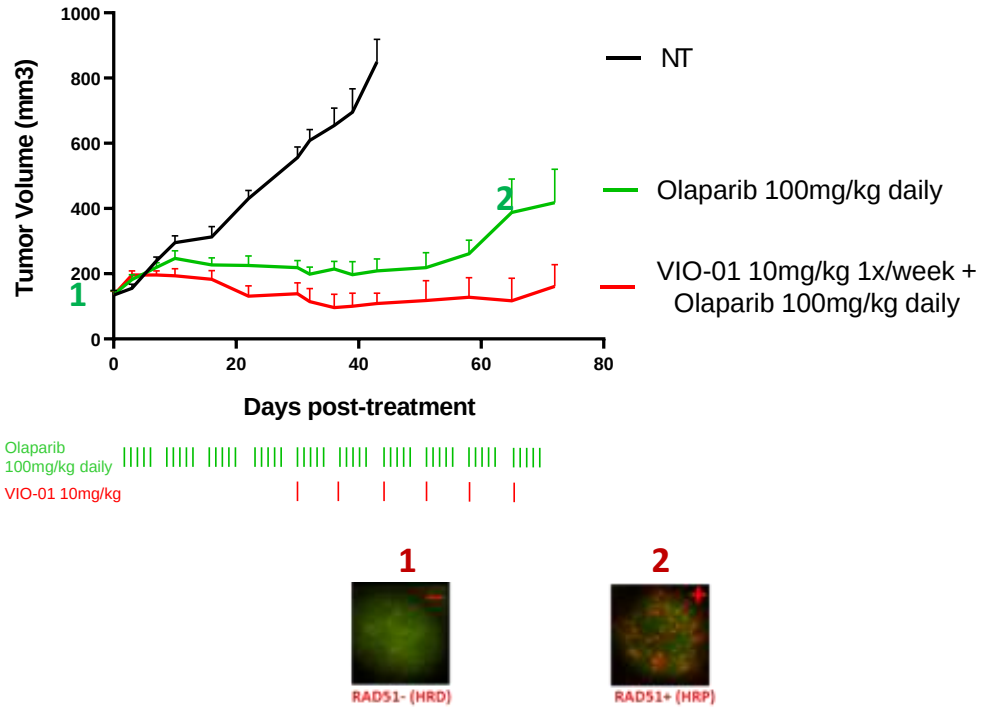
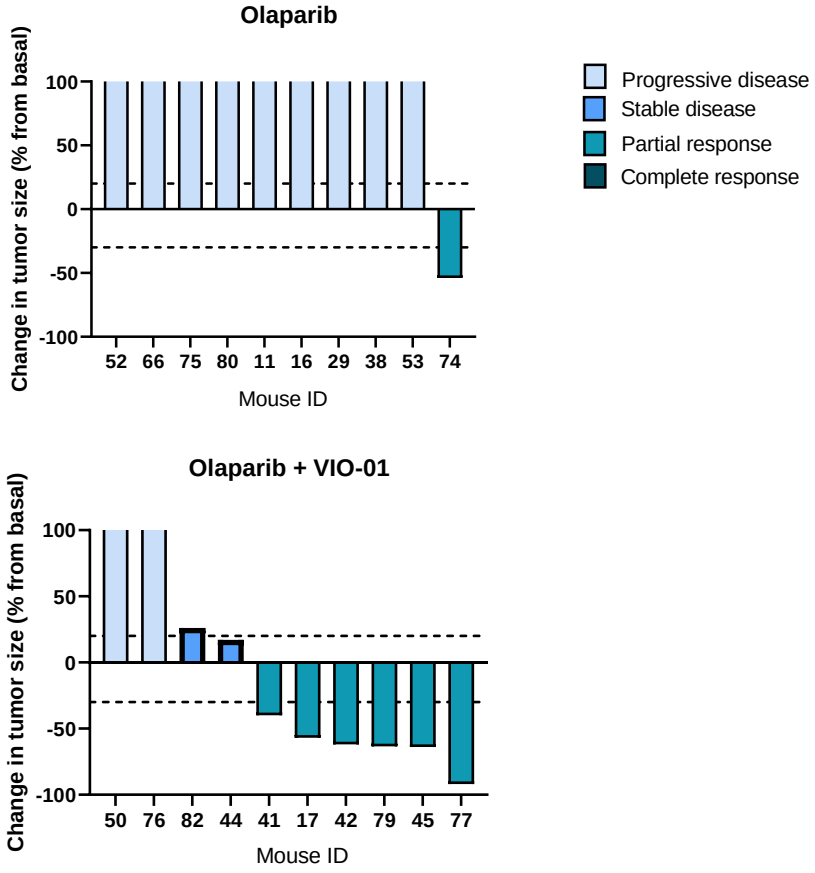
VIO-01 Resensitizes Tumors That Have Acquired Resistance To Olaparib





- **MDA-MB-436 CDXs developed a rapid acquired resistance to Olaparib (one to two months after treatment start)**
- **Addition of VIO-01 during early resistance delayed tumor progression**

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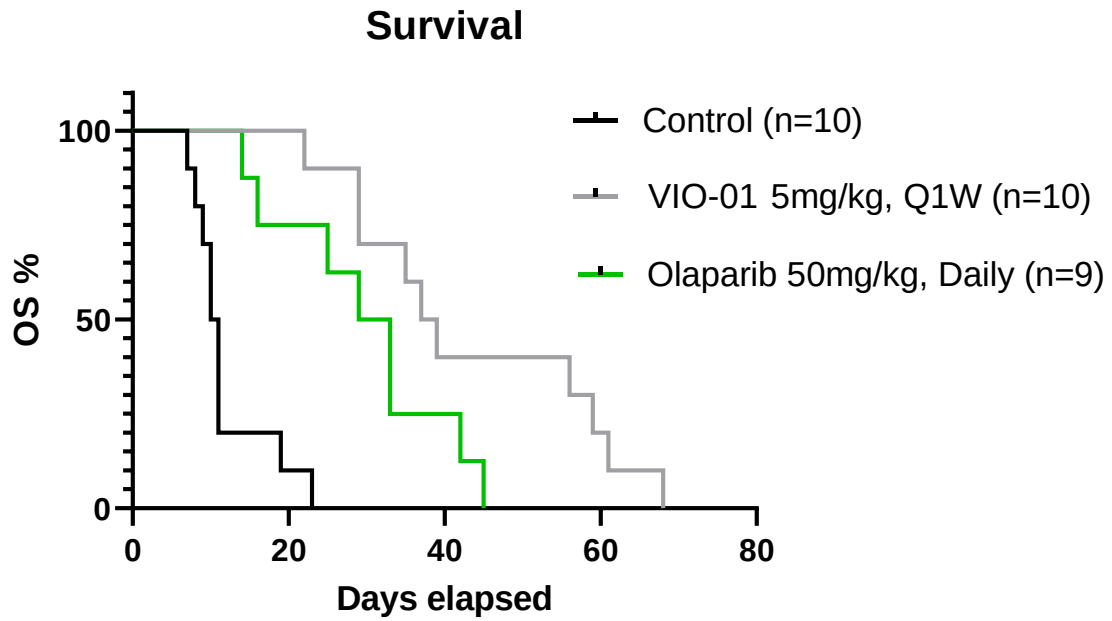
VIO-01 Displays Potent Antitumor Activity *In Vivo* Compared To Olaparib In HRD Models

M/D-driven Breast Cancer – Orthotopic Homologous Recombination Repair Deficient (HRD)



VIO-01 significantly improved OS compared to Olaparib even at a cumulative 50 times lower dose

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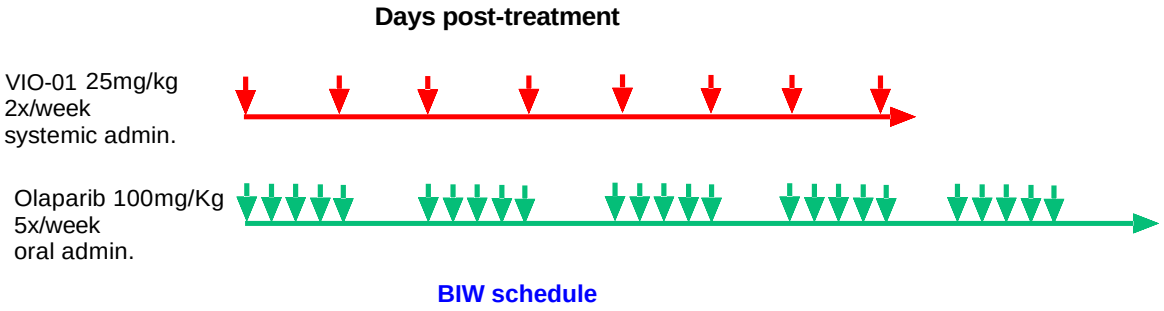
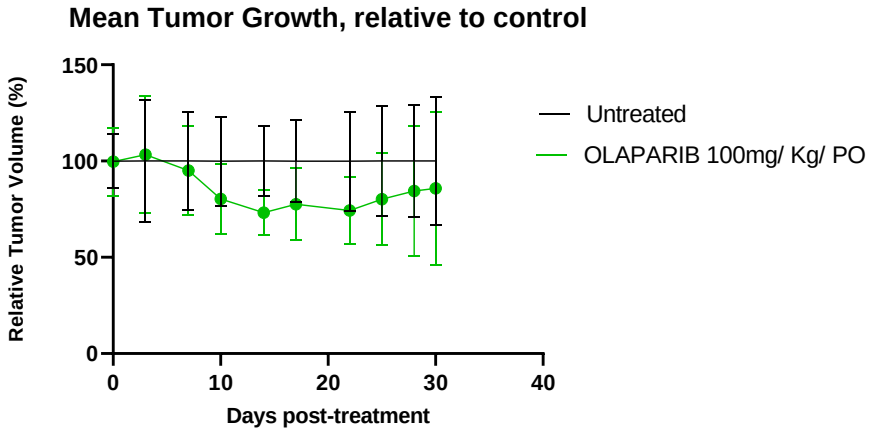
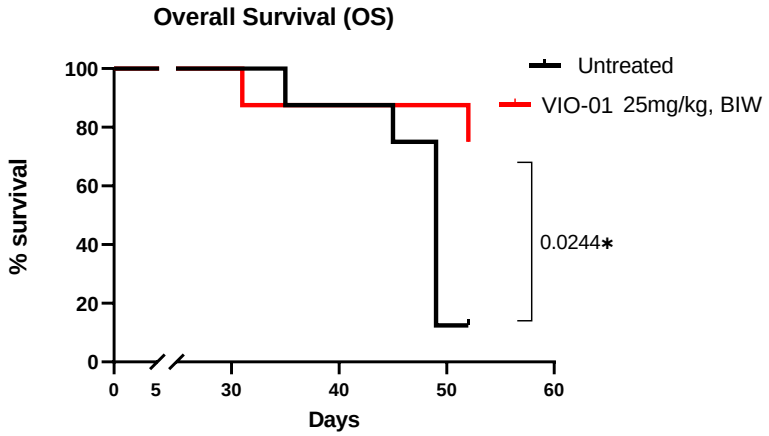
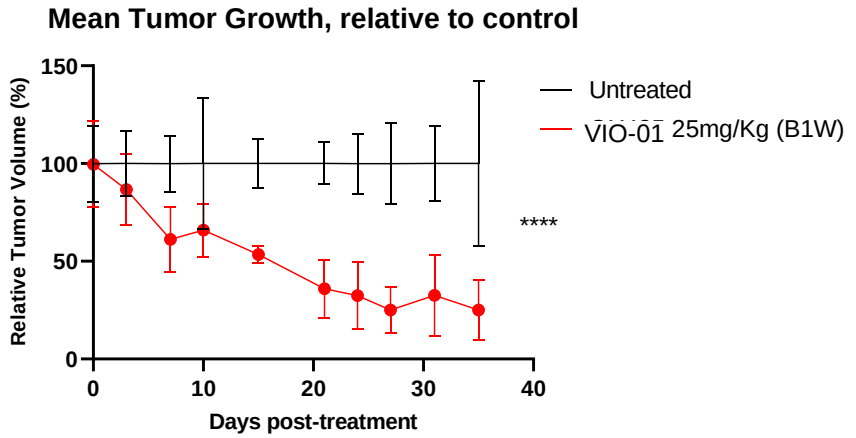
VIO-01 Displays Potent Tumor Shrinkage In Pancreatic Models Insensitive To Olaparib

PAN-02 (Pancreatic Cancer) Xenograft In Mice
Homologous Recombination Repair Proficient (HRP)









VIO-01 is more active in HRP tumors despite a x4 lower dose compared to Olaparib

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Preliminary Results From The IND-Enabling GLP Toxicology Study In NHP Demonstrates VIO-01's Favorable Safety Profile

4-week treatment / 4-week recovery IND enabling study

- No evidence of myelosuppression
- Transient increases in complement factors and cytokines
- No body weight loss
- Minimal neuro-toxicity at high doses
- No liver or kidney toxicities

Wide therapeutic window: minimal active dose 1.25mg/kg (equivalent to 5mg/kg in mice)

Clinical chemistry (Day 25, n=5)

	Vehicle	VIO-01 20mg/kg
$AST_{U/L}$	52	43_{ns}
$ALT_{U/L}$	55	50_{ns}
$ALB_{g/L}$	46	44_{ns}
$UREA_{mmol/L}$	7	6.25_{ns}

ns: Not significant compared to vehicle

Compared to Olaparib, VIO-01 did not induce neutropenia, thrombocytopenia or anemia

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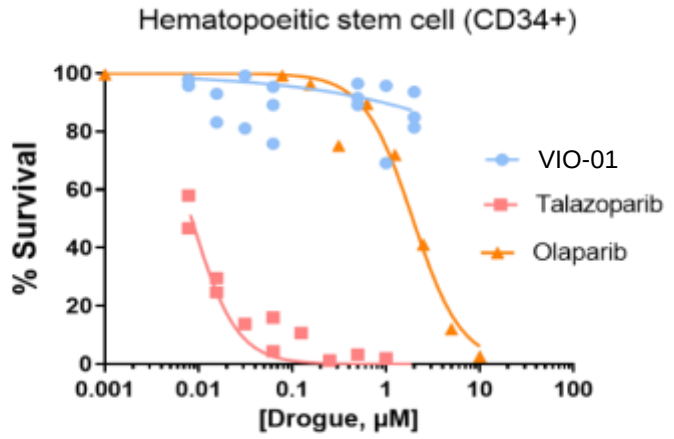
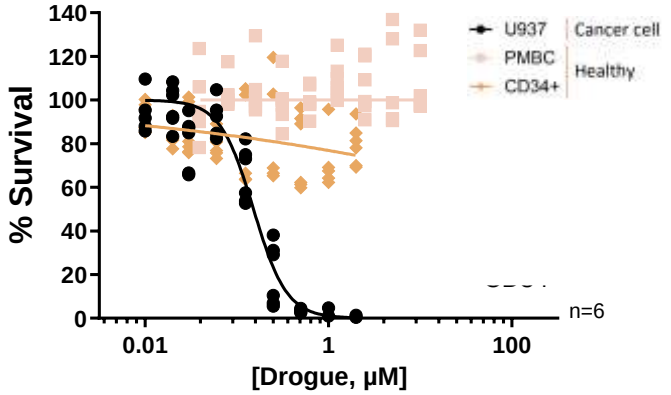
VIO-01 Does Not Induce Myelosuppression And Is Highly Selective In Its Cytotoxic Effects

PARP Inhibitors vs VIO-01



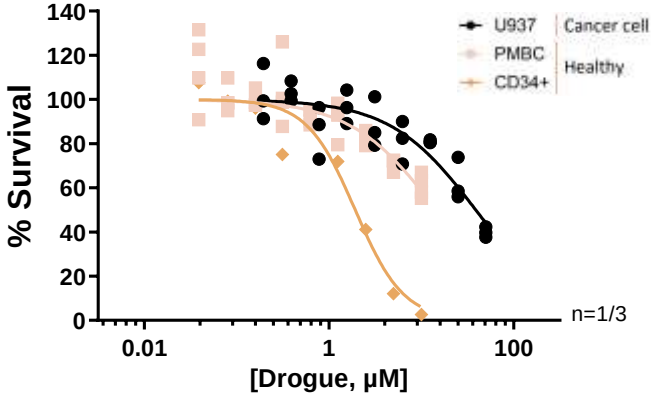
	VIO-01	Talazoparib	Olaparib
IC50	298.9	0.008425	1.924

VIO-01



	U937	PMBC	CD34+
IC50	0.1523	~ +infinity	874.0

Olaparib (Lynparza)



	U937	PMBC	CD34+
IC50	38.81	14.49	1.924

- **VIO-01 shows negligible cytotoxic effects on healthy PMBC and CD34+ cells**
- **Whilst demonstrating a stronger cancer-cell killing effect than Olaparib**

Note: Figures compare cytotoxic effect on cancer and healthy cells 3 days of treatment with Olaparib vs. VIO-01 cholesterol

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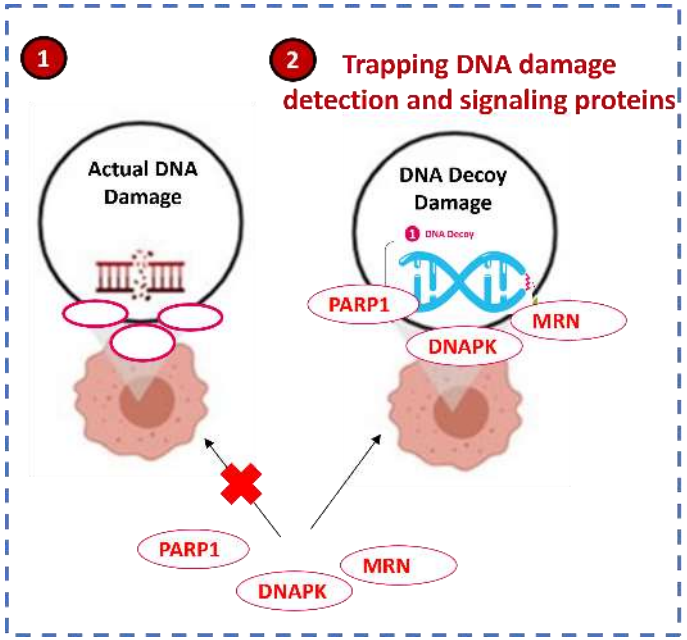
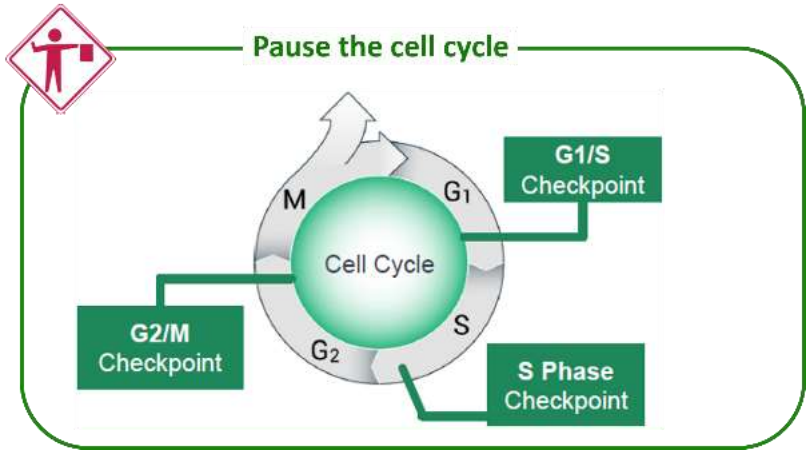
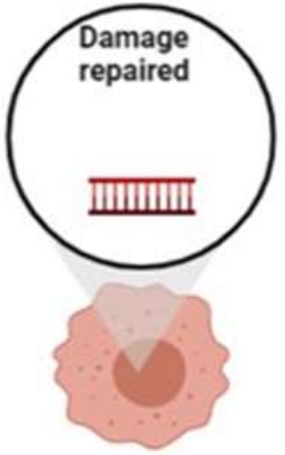
VIO-01 Transiently Delays Healthy Cell Proliferation (1/2)

Healthy Cell

1 Damage Sensing → **2** Cell Cycle Arrest Until Drug Withdrawal * → **3** Efficient DNA Repair







*** In tumor cells, cell cycle checkpoints are usually inefficient → no cell cycle arrest → no efficient DNA repair → tumor cell death**

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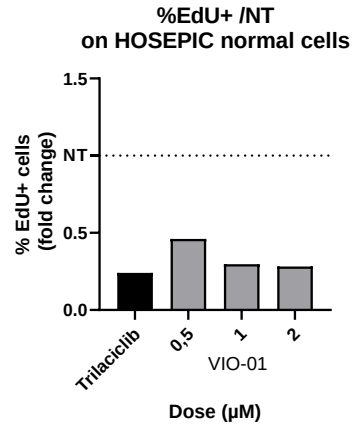
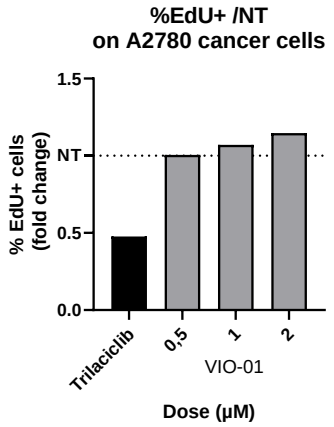
VIO-01 Transiently Delays Healthy Cell Proliferation (2/2)

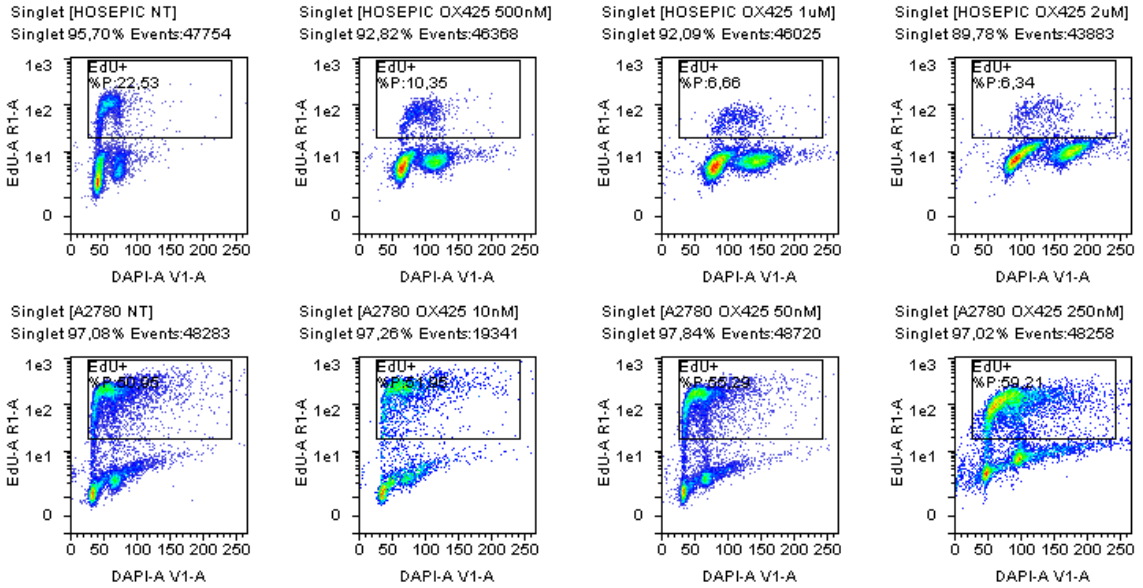
Ovarian Epithelial cells
48 hours of treatment



Cancer cells
48 hours of treatment

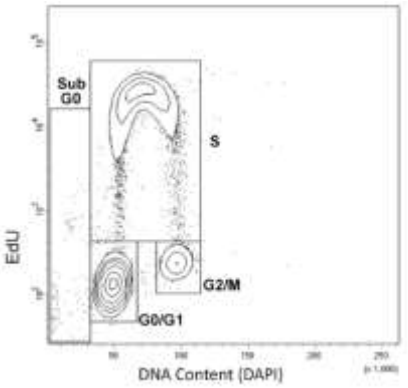


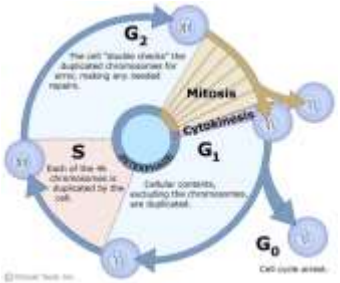
Cell Cycle Analysis



VIO-01 induces a delay in cell cycle on normal cells and not in cancer cells

EdU assay :
- Incorporation of nucleoside analog to thymidine into DNA during active DNA synthesis, which allow to determined cells cycle step





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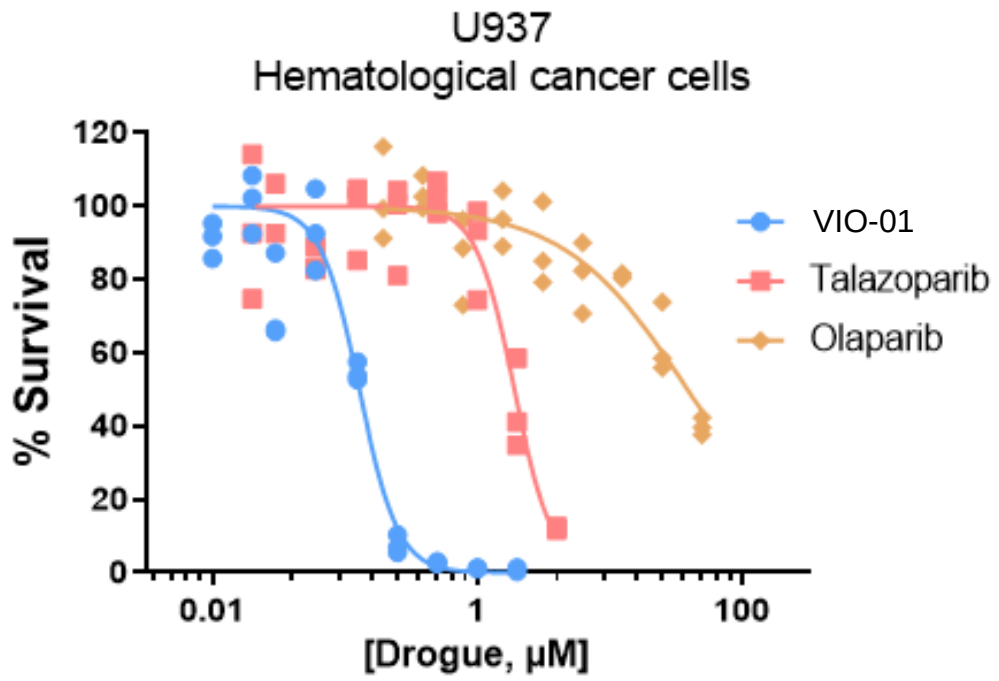
VIO-01's Broad Potential Therapeutic Applications Beyond DNA Repair

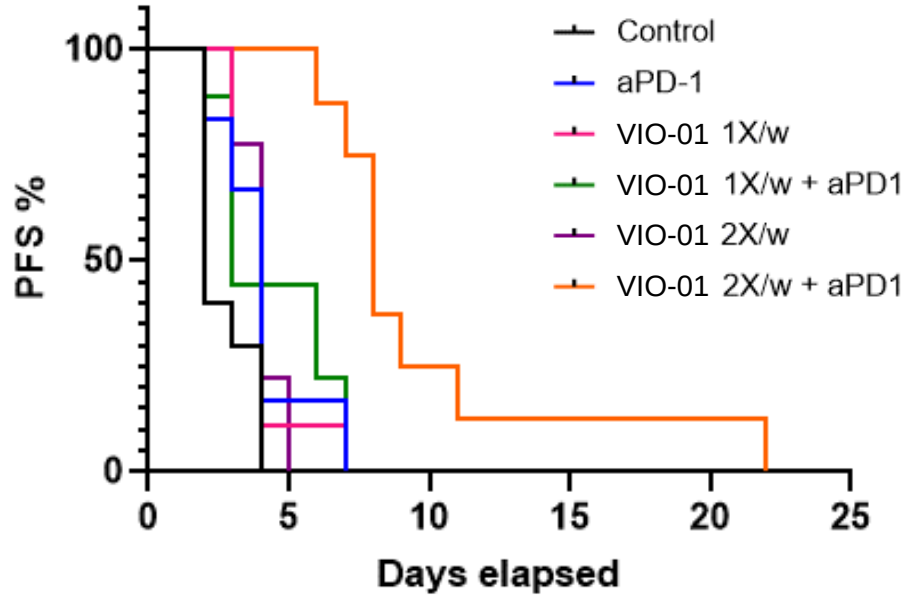
High Anti-Tumor Activity In Hematological Cancer Models



	VIO-01	Talazoparib	Olaparib
IC50	0.1290	1.910	38.81

Synergy With Immune Checkpoint Inhibitors

M/D-Driven Breast cancer – orthotopic



Through STING Pathway Activation And Increase Of Tumor Infiltrating Leucocytes

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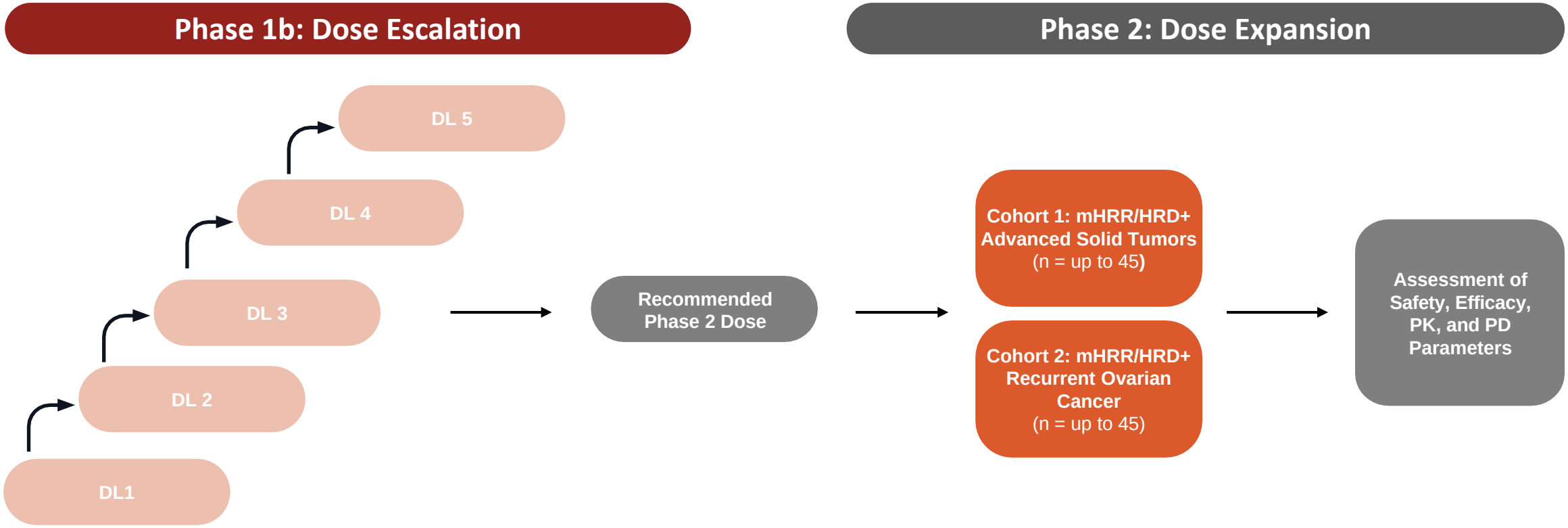
VIO-01 Proposed IND Opening Study: FPI Expected 2H23

- Pursuing tumors with HRR genomic alterations or HRD+ score
- (BRCA1, BRCA2, ATM, ATR, CHK1, CHK2, DSS1, RPA1, NBSI, FANCD2, FANCA, CDK12, PALB2, BRIP1, RAD51B, RAD51C, RAD51D, RAD54)



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Agenda

Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

Summary

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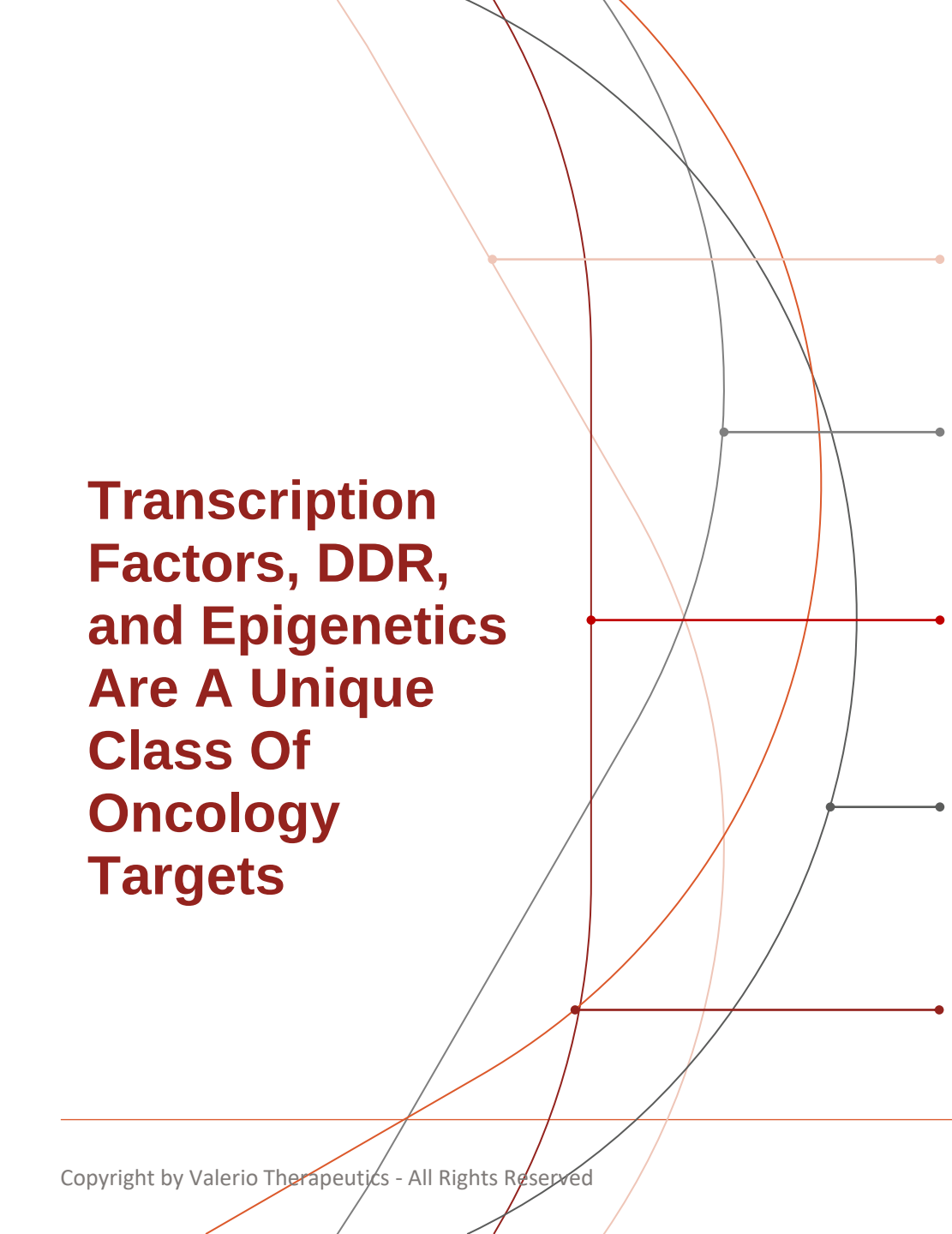
Transcription Factors, DDR, and Epigenetics Are A Unique Class Of Oncology Targets



Transcription Factors are proteins that **bind to DNA and mediate gene expression** programs involved in fundamental cellular processes such as differentiation, cell death, and proliferation.

Mutated or dysregulated **transcription factors** are frequently **expressed in numerous cancers** leading to aberrant downstream genes expression

Mutated transcriptions factors are key drivers of tumor formation and oncogenesis

Undruggable - traditional small molecule inhibitors and antibodies are limited in the ability to drug transcription factors due to their interaction with DNA

DNA decoys can bind and trap transcriptions factors overcoming the key limitations of other therapies

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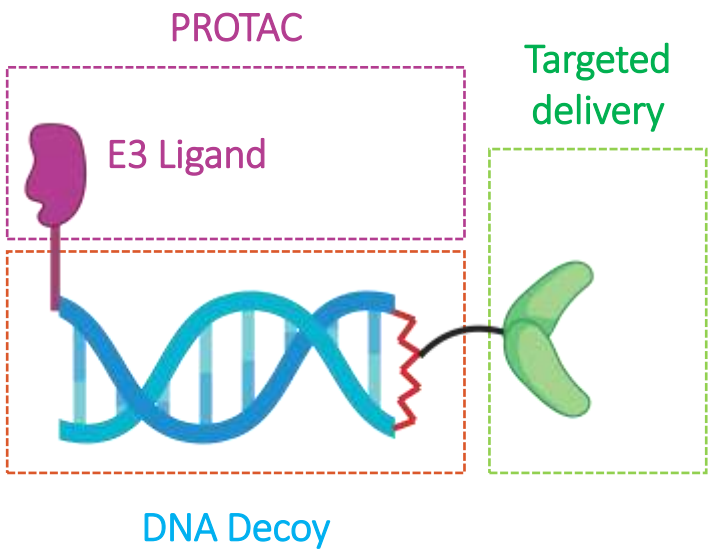
DecoyTAC - Targeting Oncogenic DNA interacting proteins (such as Transcription Factors)

DecoyTAC: Degradation Of TF Through UPS



DecoyTAC can drug the "undruggable"

- Does not rely on an enzymatic binding pocket for activity
- Can enter the nucleus
- Can mitigate off-target effects through use of selective delivery technologies
  - Bispecific Small Molecule ligands – PSMA, FOLRa, EphA2
  - Nanobodies
  - Aptamers

DecoyTAC combines DNA decoy with protac and tumor specific vectorization for targeted suppression of oncogene expression

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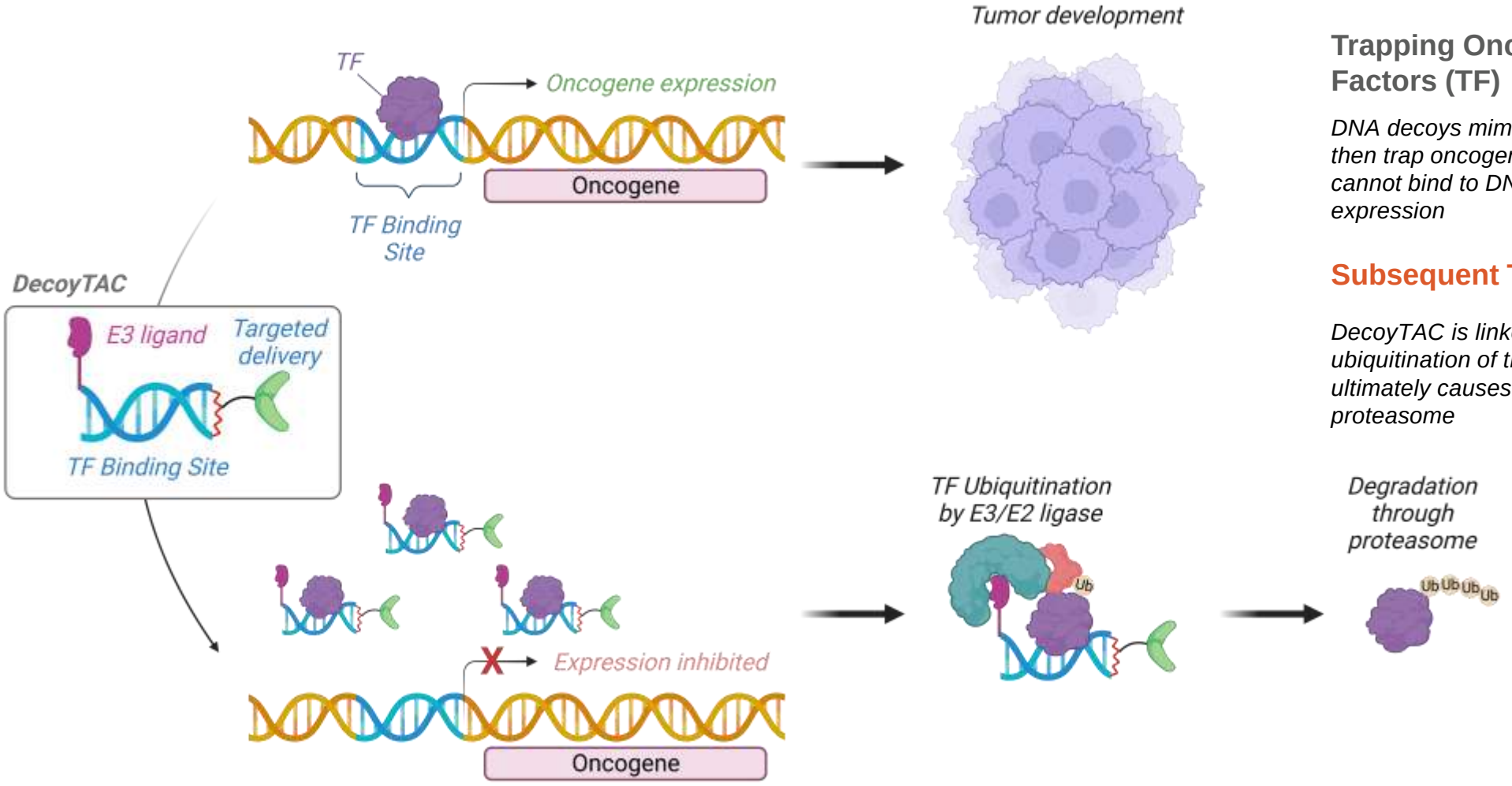
Mechanism of Action of DecoyTAC



Trapping Oncogene Transcription Factors (TF)

*DNA decoys mimic TF binding site (**decoy**), then trap oncogene transcription factor. TF cannot bind to DNA and induce oncogene expression*

Subsequent TF Degradation

DecoyTAC is linked to E3 ligand leading to ubiquitination of the Oncogene TF, which ultimately causes TF degradation through the proteasome

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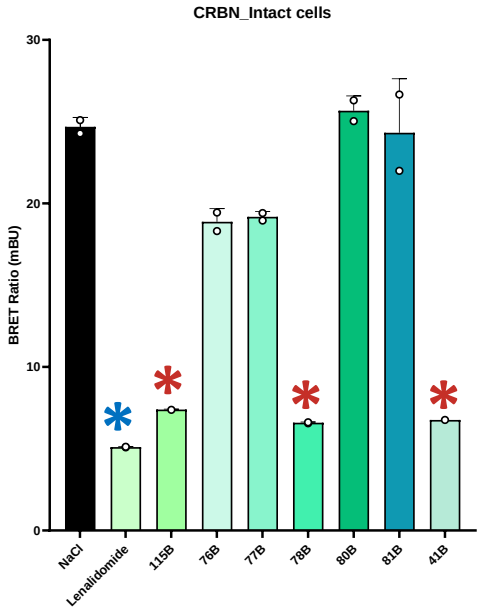
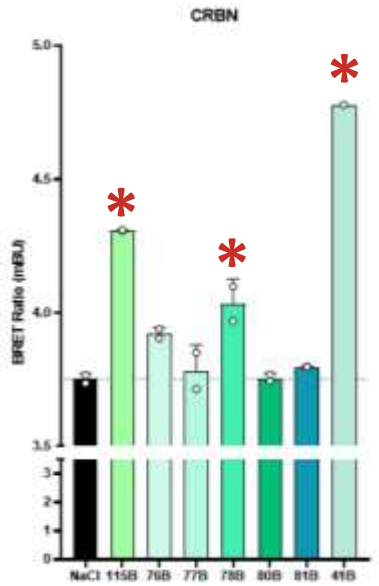
DecoyTAC Proof Of Concept Validated In Discovery Stage Assays

Cell Membrane Permeability Analysis



DecoyTAC screening compounds almost as permeable as the **small molecule PROTAC positive control**

Formation Of Ternary Complex Analysis



DecoyTAC traps the target TF and recruits E3 ligase

DecoyTACs are efficiently delivered to tumor cells and form ternary complexes with the target TF and E3 ligase

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Agenda

Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

Summary

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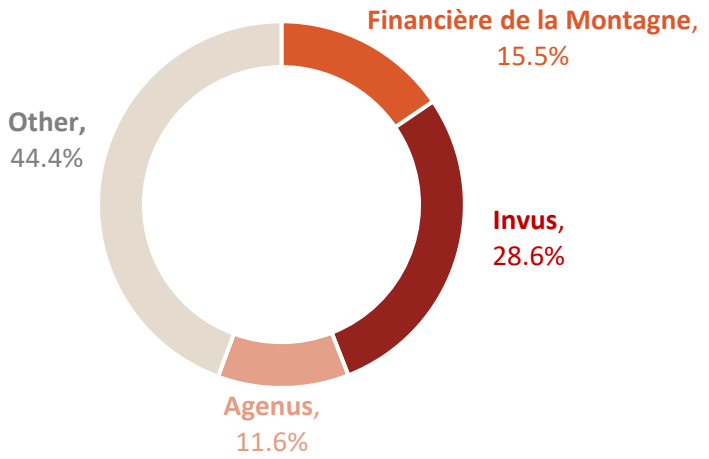
Financial Resources To Execute Key Development Milestones Objectives

- **Net cash position of €14.6 million as of December 31, 2022***
- **Financial visibility until the 2nd quarter of 2024**

Listing Details

EURONEXT GROWTH | Paris - EPA: **ALVIO**
ISIN: FR00100955

Strong Support From Two Core Shareholders



** - including EUR 14.3 million commitment from Invus, Financière de la Montagne and a new investor*

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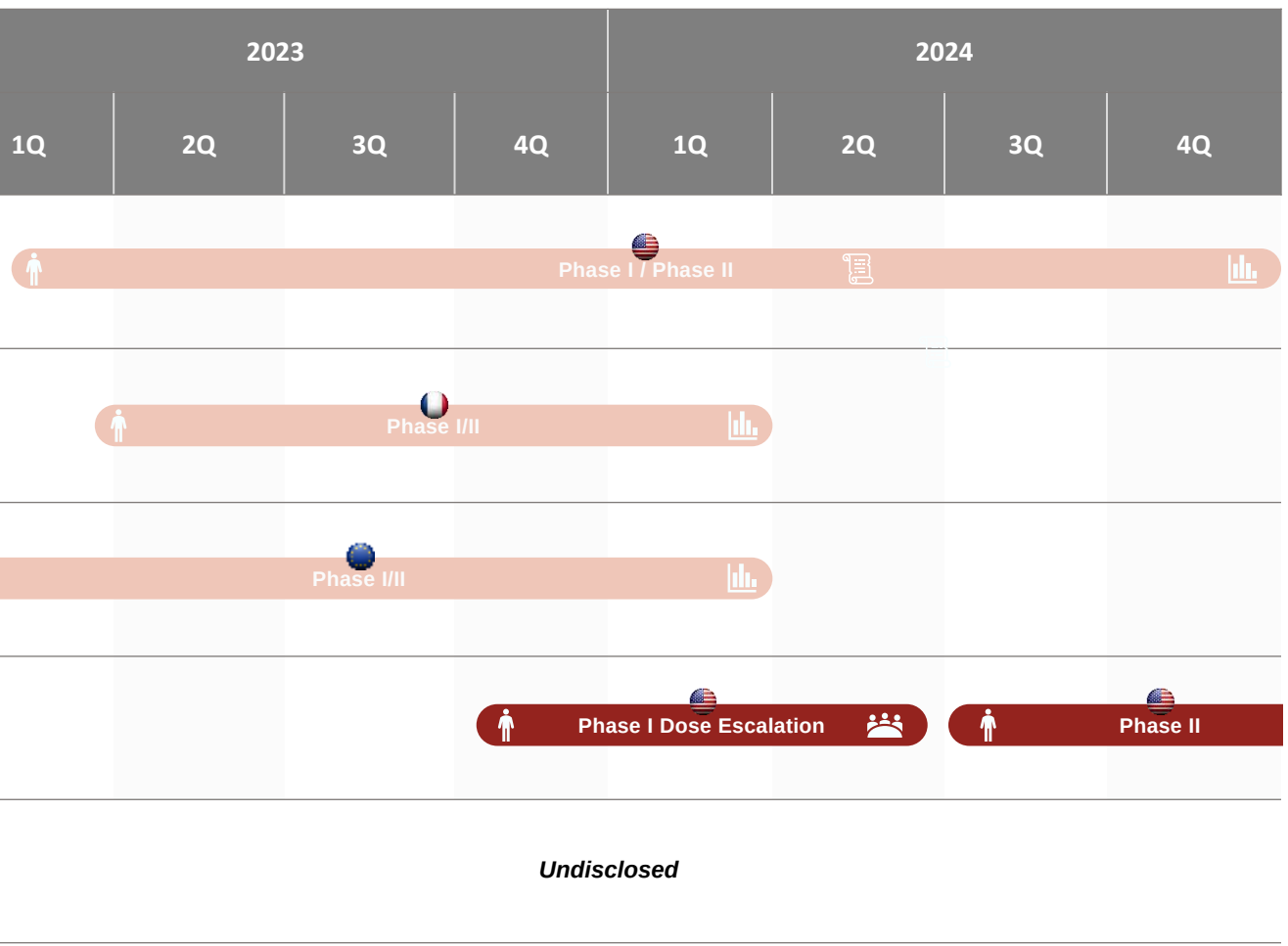
Near Term Catalysts Driving Value Over The Next 18 Months

PlatON™	Program (Route Of Admin)	Target Indication	Current Stage
1st Generation	AsiDNA™ 1.0 (IV)	*Recurrent **ovarian, breast, prostate** cancer (combination with PARPi)*	*Phase I*
		*Maintenance for **ovarian** cancer with rising CA-125 (combination with PARPi)*	*Phase I/II*
		*Pediatric and adolescent **glioma** (combination with radiotherapy)*	*Phase I/II*
2nd Generation	VIO-01 (IV)	***mHRR or HRD+ solid tumors** (monotherapy)*	*IND*
3rd Generation	DecoyTAC	*Undisclosed*	*Discovery*



- *First in human trial start*
- *Full readout*
- *Publication / Abstract Presentation*
- *End of clinical trial meeting*

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Valerio Therapeutics Investment Highlights

Unique MoA Sequestering DDR Proteins	▪ **DNA fragments** called **DNA decoys mimic DNA damage and trap multiple proteins** in charge of repairing DNA, leading to an **accumulation of unrepaired DNA and tumor death**
1st-In-Class DNA Decoy Therapeutics Pipeline	▪ **AsiDNA™ (DNA-PK) - Phase I/II -** x3 oncology trials ongoing in combination with PARP or radiotherapy ▪ **VIO-01 (MRN, KU70/80, PARP-1) - IND -** Highly promising pre-clinical monotherapy data and superior data in head-to-head studies with competitive landscape
PlatON™: A Versatile Toolbox And Library Of DNA Sequences	▪ DNA decoy capabilities beyond DDR proteins including transcription factors, and incorporating additional targeting moieties such E2/E3 ligases, aptamers and bispecific antibodies ▪ Early-stage PoC data using PROTAC-like approach to permanently degrade target proteins
Deep Industry Experience	▪ **Management / Advisors:** Strong management and R&D team located across France and US, supported by a world-class DDR-focused SAB ▪ **Investors:** Invus, Agenus, Financiere de la Montagne ▪ **Cash Runway:** Financial visibility until 2Q24
Near Term Catalysts	▪ AsiDNA™ (Phase I): Ovarian, breast, prostate cancer (with PARP) interim clinical trial readout in 2Q24 ▪ AsiDNA™ (Phase I/II): Ovarian (with PARP) clinical trial readout at the end of 1Q24 ▪ AsiDNA™ (Phase I/II): Glioma (with radiotherapy) clinical trial readout at the end of 1Q24 ▪ VIO-01 (Phase I): Entering Phase I in 4Q23

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