Developing Novel DNA Decoy Therapeutics For Precision DDR Oncology Therapeutics

Corporate Presentation
4Q 2023

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Robin Sutherland  
Head of HR
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.
Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

Summary
## Innovative Pipeline Of DNA Decoy Therapeutics

<table>
<thead>
<tr>
<th>PlatON™</th>
<th>Program (Route Of Admin)</th>
<th>Target</th>
<th>Target Indication</th>
<th>Discovery</th>
<th>IND-Enabling</th>
<th>Phase 1/2</th>
<th>Phase 3</th>
<th>Partner(s)</th>
<th>Next Milestone</th>
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<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Generation</td>
<td>AsiDNA™ 1.0 (IV)</td>
<td>DNA-PK</td>
<td>Recurrent ovarian, breast, prostate cancer (combination with PARPi)</td>
<td>US Clinical Trial</td>
<td>REVOCAN</td>
<td></td>
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<td>FPI U.S. trial Mar-23</td>
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<td>Maintenance for ovarian cancer with rising CA-125 (combination with PARPi)</td>
<td>[GUSTAVE ROUSSY]</td>
<td>[INSTITUT CURIE]</td>
<td>Readout in 1Q24</td>
<td></td>
<td></td>
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<tr>
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<td></td>
<td>Pediatric and adolescent glioma (combination with radiotherapy)</td>
<td>GLIOMA</td>
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<td>Readout in 1Q24</td>
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<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; Generation</td>
<td>VIO-01 (IV)</td>
<td>PARP1, MRN, KU70/80</td>
<td>mHRR or HRD+ solid tumors (monotherapy)</td>
<td>IND submission 2H23</td>
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<td>3&lt;sup&gt;rd&lt;/sup&gt; Generation</td>
<td>DecoyTAC</td>
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<td>IND enabling studies 2H24</td>
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</table>
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 to 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)
Addressing The Severe Limitations With Current DDR Therapies

### Current DDR Products

- **Pathway Redundancy**: PARP inhibitors only abrogate PARP-related repair which leads to activation of compensatory DDR pathways.
- **Synthetic Lethality**: Current targeted DDR therapeutics (PARP, WEE1, ATR, DNA-PK inhibitors) rely on germline or somatic mutations.
- **Limited Tolerability**: PARP inhibitors increase the risk of MDS/AML which can result in high mortality.
- **Intrinsic/Acquired Resistance**: Approximately 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.

### Indication Withdrawals

- PARP inhibitors has failed to predict a survival benefit in the treatment setting leading to indication withdrawals by the FDA.

### Versatility In A Pan-DDR Approach

- Ability to trap multiple key DDR proteins leaving no salvage repair pathways.

### Better Safety Including Myelosuppression

- Active regardless of sensitizing mutations (e.g. BRCA1/2) specific to cancer cells, translating in outstanding safety and possibility to use in combination.

### No Limitations On Targeting

- 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
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

Specificity And Functionalisation

Selectivity

Vectorisation
**1st Generation**

- **DNA-PK decoy**
- Cholesterol (cellular uptake)

**2nd Generation**

- **Pan-DDR decoy**
- Cholesterol (cellular uptake)

**3rd Generation**

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

- **Active moiety (protein degradation)**

- **Transcription factor decoy**

- **Small molecule ligand**

- **Aptamer**

- **Single-domain antibody**

- **Increase tumor specificity with aptamer, bispecific antibodies, etc.**

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*AsiDNA™ VIO-01 DecoyTAC*
Agenda

Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

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

**Radiotherapy**
- SK-28 (Human Melanoma) xenograft in mice
- NT
- RT + AsiDNA

**Chemotherapy**
- MDA-MB-436 (TNBC) xenograft in mice (HRD – BRCA1mutated)
- NT
- Carboplatin
- Carboplatin + AsiDNA

**PARP Inhibition**
- MDA-MB-436 (TNBC) xenograft in mice (HRD – BRCA1mutated)
- NT
- Olaparib
- Olaparib + AsiDNA
AsiDNA™ Clinical Proof Of Concept In Solid Tumors

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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Phase</th>
<th>No. Patients</th>
<th>Status</th>
<th>Key Results</th>
</tr>
</thead>
</table>
| 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
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

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)

Before Treatment 90 Days After Treatment

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

**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

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

*yH2AX (DNA-PK biomarker) readout in tumor biopsies*

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
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

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

**Phase 1b: Dose Escalation**
- 800 mg AsiDNA™ + Olaparib
- 600 mg AsiDNA™ + Olaparib
- 400 mg AsiDNA™ + Olaparib

**Recommended Phase 2 Dose**

**Phase 2: Dose Expansion**
- **Cohort 1:** Recurrent Ovarian Cancer AsiDNA™ + Olaparib (n = up to 26)
- **Cohort 2:** Recurrent Breast Cancer AsiDNA™ + Olaparib (n = up to 26)
- **Cohort 3:** Recurrent Prostate Cancer AsiDNA™ + Olaparib (n = up to 26)

Assessment of Safety, Efficacy, PK, and PD Parameters

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Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

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

Incubation of biotinylated VIO-01 with A2780 ovarian cancer cells

Cell lysis

Pull down with streptavidin beads

Type of DNA damage

Single strand break

Bulky products

Base mismatch

Double strand break

Repair mechanism

Western Blot to reveal protein sequestered by VIO-01

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

**VIO-01 Stability In Human Serum**

<table>
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<th>Time (Hours)</th>
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<th>4</th>
<th>6</th>
<th>9</th>
<th>14</th>
<th>24</th>
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<th>40</th>
<th>48</th>
<th>56</th>
<th>71</th>
<th>96</th>
</tr>
</thead>
</table>

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

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

**VIO-01 versus OX401**

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

VIO-01 Resists Endonuclease Degradation In Human Serum

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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
- AUC = 3.6µM
- $T_{1/2} > 4$ days

VIO-01 Nuclear Localization

- VIO-01 accumulates in tumors and reaches the nucleus
- 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) shows higher cellular uptake and lower % of free drugs after PARP interaction, compared with VIO-01 Folate

VIO-01 With Cholesterol vs. Naked VIO-01

VIO-01 (with Cholesterol) is more cytotoxic compared to naked VIO-01, as illustrated by lower cancer cell survival rates and IC50 values
Delivery Vector: VIO-01 With Cholesterol Shows Increased Uptake In Tumor Vs VIO-01 With 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
VIO-01 Displays Higher Anti-Tumor Activity Compared To PARP And DNA-PK Inhibitors

**VIO-01 vs PARP Inhibitors**

**Breast Cancer Models**

<table>
<thead>
<tr>
<th>Drogue, µM</th>
<th>IC50</th>
<th>% Survival</th>
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<tbody>
<tr>
<td>VIO-01 Olaparib Ninaparib</td>
<td>0.001 0.01 0.1 1 10 100</td>
<td>0 50 100</td>
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**Prostate Cancer Models**

<table>
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<tr>
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**VIO-01 vs DNA-PK Inhibitor**

**Breast Cancer Models**

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<th>% Survival</th>
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<tr>
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<td>0 50 100</td>
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**Prostate Cancer Models**

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<th>% Survival</th>
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<tr>
<td>VIO-01 AZD7448</td>
<td>0.001 0.01 0.1 1 10 100</td>
<td>0 50 100</td>
</tr>
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</table>

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

VIO-01 significantly improved OS compared to Olaparib even at a cumulative 50 times lower dose.
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 25mg/kg 2x/week systemic admin.
Olaparib 100mg/Kg 5x/week oral admin.

Overall Survival (OS)

% survival

0 5 10 15 20 25 30 35
0 20 40 60 80 100

Days post-treatment

0.0244

Mean Tumor Growth, relative to control

Relative Tumor Volume (%)

0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150

Days post-treatment

Untreated

VIO-01 25mg/kg, BIW

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

<table>
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<tr>
<th>Clinical chemistry (Day 25, n=5)</th>
<th>Vehicle</th>
<th>VIO-01 20mg/kg</th>
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<tr>
<td>AST_{U/L}</td>
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<td>43_{ns}</td>
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<tr>
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<td>55</td>
<td>50_{ns}</td>
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<tr>
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<td>44_{ns}</td>
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<tr>
<td>UREA_{mmol/L}</td>
<td>7</td>
<td>6.25_{ns}</td>
</tr>
</tbody>
</table>

_ns: Not significant compared to vehicle_

Compared to Olaparib, VIO-01 did not induce neutropenia, thrombocytopenia or anemia
VIO-01 Does Not Induce Myelosuppression And Is Highly Selective In Its Cytotoxic Effects

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

**1. Damage Sensing**
- Actual DNA Damage
- DNA Decoy Damage
- PARP1 
- DNA-PK 
- MRN 

**2. Cell Cycle Arrest Until Drug Withdrawal**
- Pause the cell cycle
  - G1/S Checkpoint
  - S Phase Checkpoint

**3. Efficient DNA Repair**
- Damage repaired

*In tumor cells, cell cycle checkpoints are usually inefficient → no cell cycle arrest → no efficient DNA repair → tumor cell death*
VIO-01 Transiently Delays Healthy Cell Proliferation (2/2)

Cell Cycle Analysis

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

VIO-01 induces a delay in cell cycle on normal cells and not in cancer cells
VIO-01’s Broad Potential Therapeutic Applications Beyond DNA Repair

High Anti-Tumor Activity In Hematological Cancer Models

U937 Hematological cancer cells

<table>
<thead>
<tr>
<th></th>
<th>VIO-01</th>
<th>Talazoparib</th>
<th>Olaparib</th>
</tr>
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<tbody>
<tr>
<td>IC50</td>
<td>0.1290</td>
<td>1.910</td>
<td>38.81</td>
</tr>
</tbody>
</table>

Through STING Pathway Activation And Increase Of Tumor Infiltrating Leucocytes

Synergy With Immune Checkpoint Inhibitors

M/D-Driven Breast cancer – orthotopic

Control
aPD-1
VIO-01 1X/w
VIO-01 1X/w + aPD1
VIO-01 2X/w
VIO-01 2X/w + aPD1
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, NBS1, FANCD2, FANCA, CDK12, PALB2, BRIP1, RAD51B, RAD51C, RAD51D, RAD54)

Phase 1b: Dose Escalation

- DL 1
- DL 2
- DL 3
- DL 4
- DL 5

Recommended Phase 2 Dose

Phase 2: Dose Expansion

- Cohort 1: mHRR/HRD+ Advanced Solid Tumors (n = up to 45)
- Cohort 2: mHRR/HRD+ Recurrent Ovarian Cancer (n = up to 45)

Assessment of Safety, Efficacy, PK, and PD Parameters

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Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

Summary
Transcription Factors are a unique class of oncology targets. DNA decoys can bind and trap transcription factors overcoming the key limitations of other therapies.

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

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

DecoyTAC: Degradation Of TF Through UPS

- PROTAC
- Targeted delivery
- DNA Decoy

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
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.
DecoyTAC Proof Of Concept Validated In Discovery Stage Assays

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

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

DecoyTAC traps the target TF and recruits E3 ligase
Agenda

Overview Of Valerio Therapeutics

AsiDNA™ - Targeted Sequestering Of DNA-PK

VIO-01 - Multi-Modal DDR Decoy

DecoyTAC - 3rd Generation

Summary
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: FR001009555

Strong Support From Two Core Shareholders

- Financière de la Montagne, 15.5%
- Invus, 28.6%
- Agenus, 11.6%
- Other, 44.4%

* Including EUR 14.3 million commitment from Invus, Financière de la Montagne and a new investor
Near Term Catalysts Driving Value Over The Next 18 Months

<table>
<thead>
<tr>
<th>PlatON™</th>
<th>Program (Route Of Admin)</th>
<th>Target Indication</th>
<th>Current Stage</th>
<th>2023</th>
<th>2024</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Generation</td>
<td>AsiDNA™ 1.0 (IV)</td>
<td>Recurrent ovarian, breast, prostate cancer (combination with PARPi)</td>
<td>Phase I</td>
<td></td>
<td>1Q 2Q 3Q 4Q</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintenance for ovarian cancer with rising CA-125 (combination with PARPi)</td>
<td>Phase I/I</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pediatric and adolescent glioma (combination with radiotherapy)</td>
<td>Phase I/I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd Generation</td>
<td>VIO-01 (IV)</td>
<td>mHRR or HRD+ solid tumors (monotherapy)</td>
<td>IND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3rd Generation</td>
<td>DecoyTAC</td>
<td>Undisclosed</td>
<td>Discovery</td>
<td></td>
<td></td>
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### Valerio Therapeutics Investment Highlights

<table>
<thead>
<tr>
<th>Unique MoA Sequestering DDR Proteins</th>
<th>- 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</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st-In-Class DNA Decoy Therapeutics Pipeline</td>
<td>- 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</td>
</tr>
<tr>
<td>PlatON™: A Versatile Toolbox And Library Of DNA Sequences</td>
<td>- 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</td>
</tr>
<tr>
<td>Deep Industry Experience</td>
<td>- <strong>Management / Advisors:</strong> Strong management and R&amp;D team located across France and US, supported by a world-class DDR-focused SAB - <strong>Investors:</strong> Invus, Agenus, Financiere de la Montagne - <strong>Cash Runway:</strong> Financial visibility until 2Q24</td>
</tr>
<tr>
<td>Near Term Catalysts</td>
<td>- 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</td>
</tr>
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