Precision Therapeutics
For Hard-To-Treat Cancers

2X Oncology
George O. Elston, CEO
Life Sciences Summit
November 2, 2017
About Us

- Precision therapeutics addressing significant unmet medical needs in hard-to-treat cancers

- Pipeline of Phase 2 compounds
  - PARP inhibitor positioned for Q4 2017 Phase 2 study initiation
    - Initial studies planned in metastatic breast and prostate cancer
  - Leveraging prior activity observed in ovarian, pancreatic & brain cancers

- Drug Response Predictor (DRP®) companion diagnostic leveraged to identify drug responders and non-responders for focused studies

- Phase 2 Data anticipated 2H 2018
  - Positive data triggers accelerated approval filing(s)

- Raising Institutional financing - $3.5M seed round complete
# Phase 2 Pipeline

<table>
<thead>
<tr>
<th>2X-121</th>
<th>PARP 1/2 and Tankyrase 1/2 Inhibitor</th>
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<tbody>
<tr>
<td></td>
<td>• Metastatic breast cancer</td>
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<tr>
<td></td>
<td>• Prostate cancer (mCRPC)</td>
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<td></td>
<td>• Recurrent ovarian cancer</td>
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<td>• Pancreatic cancer</td>
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<thead>
<tr>
<th>2X-111</th>
<th>Glutathione-enhanced PEGylated Liposomal Doxorubicin</th>
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<td>• Brain metastases from breast cancer</td>
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<td>• Recurrent glioblastoma multiforme</td>
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<tr>
<th>2X-131</th>
<th>Topoisomerase 1 Inhibitor</th>
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<td></td>
<td>• Recurrent ovarian cancer</td>
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<tr>
<th>Phase 2</th>
<th>DRP® Selected Phase 2</th>
<th>2018 Potential Milestones</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Phase 2 study results</td>
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<td></td>
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<td>Positioned for accelerated approval filings</td>
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</table>
Patterns in drug sensitivity from human cell lines (e.g. NCI60) reflect mechanism of action of a specific drug. This identifies a subset of genes responsible for sensitivity and resistance to that drug. This narrows the gene analysis from 20,000 into the “hundreds,” providing a raw DRP score a drug for additional filtering based on actual patient tumor data.

The raw DRP is filtered for clinical relevance against a proprietary database of over 3,250 human tumor samples from 27 different cancers. This metadata analysis eliminates clinically irrelevant gene expressions (“background noise”), creating the drug-specific DRP.

The drug-specific DRP produces a 0-100 score based on the specific genes represented in a patient’s tumor. A 100 score would identify a tumor as a highly likely responder, with all genes represented for sensitivity and none for resistance.

mRNA data from patient biopsies are compared to the drug-specific DRP, producing an individual score. A DRP cutoff (e.g. 70%) is selected based on clinical experience with a particular cancer type and drug.
DRP® Enables Dynamic Study Designs

Novel Precision Medicine Trial Designs

Umbrella trial
1 type of cancer
Different genetic mutations (●●●)

Test drug 1
Test drug 2
Test drug 3

Basket trial
Multiple types of cancer
1 common genetic mutation (●)

Test drug

*JAMA Oncology: doi:10.1001/jamaoncol.2106.5299*
2X-121: PARP 1/2 and TNKS 1/2 Inhibitor

- Orally bioavailable, brain penetrable, small molecule drug
- Potent inhibitor of
  - PARP1: A key molecule in sensing and repairing single-strand DNA breaks
  - PARP2: An additional repair mechanism
  - Tankyrase 1/2: Important regulators of canonical Wnt/β-catenin, a critical checkpoint in metastases, particularly in triple-negative breast cancer
- Dual inhibitory action of 2X-121 against PARP 1/2 and Tankyrase 1/2 provides broader activity than current PARP inhibitors
- Lack of transport by P-glycoprotein potentially overcomes resistance to current PARP inhibitors
- Established efficacy & safety profile; no myelotoxicity observed in Ph1 study

PARP: Poly(ADP)ribosylpolymerase


## 2X-121: PARP 1/2 and TNKS 1/2 Inhibitor

### Established Clinical History

<table>
<thead>
<tr>
<th>Single Agent</th>
<th>Patients</th>
<th>Indication</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Phase 1 (UK)</td>
<td>41</td>
<td>Solid Tumor “all comer” study</td>
<td>• Well tolerated</td>
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<tr>
<td></td>
<td>(28 at Rx dose)</td>
<td></td>
<td>• 46% disease control</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• 7.1% partial responses in all comers</td>
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<td>• 2 durable partial responses, 200+ days</td>
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Prior clinical study completed *without* use of 2X-121 DRP® CDx to select likely responders
2X-121: Patient Biopsies for DRP® Validation

Waterfall plot of received biopsies
2X-121: Strong DRP® Prediction

Prospective/Retrospective DRP Validation

Overall survival

Predicted sensitive to 2X-121
Predicted resistant to 2X-121

16 patients with biopsies
mRNA extracted from 13

Days

P=0.07 HR=0.26
2X-121: PARP 1/2 and TNKS 1/2 Inhibitor

Clinical Opportunities with DRP® CDx

Metastatic breast cancer
Ovarian cancer
Pancreatic cancer
Brain metastases from breast cancer
Endometrial cancer
Prostate cancer

BRCA1+2 mutated
Other homologous Recombination deficient
Other DRP and Wnt pathways

High likelihood sensitive subgroups are identified by the 2X-121 DRP®

Likely non-responders to 2X-121
2X-121: Phase 2 Clinical Plans

Initial Focused Studies

<table>
<thead>
<tr>
<th>Phase 2 Study Plan</th>
<th>Potential Outcome Pathways</th>
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<tbody>
<tr>
<td><strong>Metastatic Breast Cancer</strong></td>
<td><strong>Prostate Cancer</strong></td>
</tr>
<tr>
<td>• Select top 20% DRP®</td>
<td>• Select top 20% DRP®</td>
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<tr>
<td>• &lt;30 heavily pre-treated patients</td>
<td>• &lt;30 heavily pre-treated patients</td>
</tr>
<tr>
<td>• Utilize 1,200+ patient registry in Denmark</td>
<td>• Initial EU study</td>
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<tr>
<td>• 2H 2018 data expected</td>
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</tr>
<tr>
<td>• 30%+ response rate anticipated</td>
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<tr>
<td>• Potential for accelerated approval</td>
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2X-121: Phase 2 Clinical Plans

U.S. Studies

**Relapsed Ovarian Cancer**
- Select top 20% DRP®
- Enroll <30 heavily pre-treated patients (incl. prior PARP refractory)
- 30%+ response rate anticipated
- Potential accelerated approval

**Pancreatic Cancer**
- Select top 20% DRP®
- Enroll <30 heavily pre-treated patients
- Opportunity for accelerated approval and orphan designation
2X-121: Current Status

• Product available for Phase 2 studies from Eisai
  - 13K capsules
  - 14kg of API
  - 78kg of intermediate product

• 2X-121 DRP® validated

• Phase 2 mBC study initiation expected Q4 2017
  - Registry of ~1,200 DRP-screened breast cancer patients in Denmark

• U.S. pre-IND meeting requested

• IND filing planned for Q1 2018
2X-111: Glutathione-enhanced PEGylated Liposomal Doxorubicin

Novel Trans-BBB Drug Candidate

- Glutathione (GSH) – enhancement of PEGylated liposome exploits the GSH transport pump in the BBB to allow transfer of 2X-111 into the brain
- IP includes GSH-PEGylated liposome delivery system in combination with anthracyclines
- Established clinical history in three prior studies
2X-131: Topoisomerase 1 Inhibitor

- Orally bioavailable small molecule camptothecin
- Binds to the topoisomerase 1-DNA complex
- Prevents re-ligation of single strand breaks that are induced by topoisomerase 1 to relieve torsional strain in DNA
- MOA: cytotoxicity from double strand DNA damage produced during DNA synthesis
- Completed Phase 1 & 2 studies in > 300 patients
  - Favorable safety profile
  - Clinically-demonstrated efficacy in wide range of cancers
- 16% response rate in PFI>6months in study without DRP®
**Near Term Catalysts**

<table>
<thead>
<tr>
<th>Q4 2017</th>
<th>Q1 2018</th>
<th>Q2 2018</th>
<th>Q3 2018</th>
<th>Q4 2018</th>
<th>2019</th>
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<tbody>
<tr>
<td><strong>2X-121</strong> Metastatic breast cancer - Phase 2</td>
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**Potential 2018 Company Profile**

- **2X-121** mBC in pivotal phase 2 study for accelerated approval
- **2X-111** Brain metastases from breast cancer confirmatory study for accelerated approval
- **2X-111** GBM positioned for accelerated approval
- **2X-131** Recurrent ovarian cancer accelerated approval study
- Endometrial cancer studies underway

**Positioned for Partnering, M&A and/or IPO**