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
<table>
<thead>
<tr>
<th>Executive Team</th>
</tr>
</thead>
</table>
| **Peter Buhl Jensen, MD**  
Chairman  |
| • Founder and CEO of TopoTarget A/S  
• Secured EMA and FDA approval of Savene©/Totect©  
• Developed Belinostat, FDA-approved in 2014 |
| **George Elston**  
CEO  |
| • 20+ years veteran life science executive  
• Oncology, ophthalmology and women’s health  
• Board member Deutsche Bank DBX Trust and previously Celldex Therapeutics |
| **Marie Foegh, MD**  
CMO  |
| • 28 years in pharmaceutical and biotech  
• Executive at IPSEN and Bayer Pharma and Agile  
• 10+ drugs taken through development and FDA approval |
| **Jarne Elleholm**  
CFO  |
| • 20+ years in pharmaceutical and biotech  
• VC partner and Pharma executive experience  
• Chairman of Scandinavian Micro Biodevices, Meta-IQ |
Program Development Team

Oncology Venture team

- **Ulla H. Buhl**
  - Founder
  - Clinical Liaison

- **Steen Knudsen, Ph.D.**
  - DRP founder

- **Mogens Winkel Madsen, Ph.D.**
  - Manufacturing

- **Bruce Pratt, Ph.D.**
  - CMC

- **James G. Cullem**
  - J.D.
  - Founder
  - BD Liaison

Scientific Advisory Board

- **Dr. Joyce A. O’Shaughnessy**
  - Baylor University
  - US Oncology

- **Dr. Daniel D. Von Hoff**
  - U. of Arizona
  - Mayo Clinic
  - US Oncology

- **Dr. Mansoor Raza Mirza**
  - NSGO/DBCG Rigshospitalet
  - U. of Copenhagen

- **Dr. Mary Lake Polan**
  - Yale University
  - Dept. of OB/Gyn

- **Dr. Ursula A Matulonis**
  - Dana-Farber Cancer Institute
  - Smith Center for Women’s Cancers

- **Dr. Henry S. Friedman**
  - Duke University
  - Tisch Brain Tumor Center
## Phase 2 Pipeline

<table>
<thead>
<tr>
<th>2X-121</th>
<th>Phase 2</th>
<th>DRP® Selected Phase 2</th>
<th>2018 Potential Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARP 1/2 and Tankyrase 1/2 Inhibitor</td>
<td>• Metastatic breast cancer</td>
<td>• Prostate cancer (mCRPC)</td>
<td>• Recurrent ovarian cancer</td>
</tr>
<tr>
<td>2X-111</td>
<td>Glutathione-enhanced PEGylated Liposomal Doxorubicin</td>
<td>• Brain metastases from breast cancer</td>
<td>• Recurrent glioblastoma multiforme</td>
</tr>
<tr>
<td>2X-131</td>
<td>Topoisomerase 1 Inhibitor</td>
<td>• Recurrent ovarian cancer</td>
<td></td>
</tr>
</tbody>
</table>
A Patient-unique “Fingerprint” of Genes Predicts Responsiveness to a Drug

1. **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.

2. 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.

3. The drug-specific DRP produces a score from 0-100 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.

4. 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® Validated in 40+ Clinical Trials

- **Epirubicin** in metastatic breast cancer [http://abstracts.asco.org/199/AbstView_199_192238.html](http://abstracts.asco.org/199/AbstView_199_192238.html)


- **Cisplatin, Epirubicin** and **Capecitabine** in gastroesophageal cancer [http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0148070](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0148070)

- **Adjuvant 5FU** in colon cancer [http://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0155123](http://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0155123)


- **Fulvestrant** in breast cancer [http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0087415](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0087415)

- **CHOP** and **CHOEP** in lymphomas [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4333339/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4333339/)
DRP® Enables Dynamic Study Designs

Novel Precision Medicine Trial Designs

2X-121: PARP 1/2 and Tankyrase 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 Overview

> "For the translational scientist, the identification of reliable biomarkers will be critical for the success of this targeted agent"a

<table>
<thead>
<tr>
<th></th>
<th>Response biomarker</th>
<th>PgP mediated resistance</th>
<th>Myelotox</th>
<th>Tankyrase</th>
<th>WNT</th>
<th>PARP trapping</th>
<th>BBB penetration</th>
<th>Strong maintenance opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>olaparib</td>
<td>BRCA</td>
<td>Yes (1,2)</td>
<td>Yes</td>
<td>No (8)</td>
<td>No</td>
<td>Yes</td>
<td>No (1)</td>
<td>Yes</td>
</tr>
<tr>
<td>niraparib</td>
<td>BRCA/Myriad (3) HRD</td>
<td>Yes SPC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>veliparib</td>
<td>BRCA</td>
<td>Yes (4,5)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No (4,5)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>rucaparib</td>
<td>BRCA</td>
<td>Yes (6)</td>
<td>Yes</td>
<td>Yes (8)</td>
<td>Yes (7)</td>
<td>Yes</td>
<td>No (6)</td>
<td>Yes</td>
</tr>
<tr>
<td>talazoparib</td>
<td>BRCA</td>
<td>Yes</td>
<td>Yes</td>
<td>No (10)</td>
<td>No</td>
<td>Yes</td>
<td>No (11)</td>
<td>Yes</td>
</tr>
<tr>
<td>BGB-290 (12)</td>
<td>BRCA HRD</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2X-121</td>
<td>DRP (9)</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

a) in: Profile of veliparib and its potential in the treatment of solid tumors [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4524591](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4524591)

1) [http://www.nature.com/nm/journal/v19/n11/full/nm.3369.html?message=global=remove](http://www.nature.com/nm/journal/v19/n11/full/nm.3369.html?message=global=remove)


3) [http://dmd.aspetjournals.org/content/39/7/1161](http://dmd.aspetjournals.org/content/39/7/1161)


6) [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4882768/pdf/bjc201641a.pdf](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4882768/pdf/bjc201641a.pdf)


8) [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4027629/pdf/ml400292s.pdf](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4027629/pdf/ml400292s.pdf)

9) Novel strategies in biomarker discovery are determination of the genomic or expressional signatures of PARP inhibitor sensitive tumors. The rationale behind this approach is that one can define a specific profile of, for example, HR-deficient tumors. RNA profiling or gene expression arrays have been used for this purpose and show potential in identifying PARP inhibitor sensitive tumors [http://www.medscape.com/viewarticle/842072](http://www.medscape.com/viewarticle/842072);

10) [http://files.shareholder.com/downloads/MDV/2370126714x0x898732/BB3A5044-7FBC-4CDA-96CB-810A55269B7D/Talazoparib_IR_Presentation_2016-07-06_FINAL.pdf](http://files.shareholder.com/downloads/MDV/2370126714x0x898732/BB3A5044-7FBC-4CDA-96CB-810A55269B7D/Talazoparib_IR_Presentation_2016-07-06_FINAL.pdf)


12) Source: Beigene filing with SEC on 19 Jan 2016
2X-121: PARP 1/2 and Tankyrase 1/2 Inhibitor

Established Clinical History

<table>
<thead>
<tr>
<th>Single Agent</th>
<th>Patients</th>
<th>Indication</th>
<th>Results</th>
</tr>
</thead>
</table>
| Phase 1 (UK) | 41       | Solid Tumors (including breast, pancreatic and ovarian) | • Well tolerated  
• 46% disease control  
• 7.1% partial responses in all comers  
• 2 durable partial responses, 200+ days |

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

• Blinded study, 13 patients
• 2X-121 DRP predicted patients likely to respond and not respond to treatment
• 2X-121 DRP correctly predicted response to treatment and Overall Survival (p=0.07)
  - Hazard ratio on Overall Survival = 0.26

<table>
<thead>
<tr>
<th></th>
<th>Total Patients in Group</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted responders</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Predicted non-responders</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>

- Clear separation between responders & non-responders
- Identified responders irrespective of BRCA mutation status
Phase 1 Trial: E7449/2X-121

Unblinding: Clinical Response

2X-121 DRP correctly identified
• The 2 patients with partial response
• Non-responders
2X-121: Strong DRP® Prediction

Prospective/Retrospective DRP Validation

P = 0.07 HR = 0.26

16 patients with biopsies mRNA extracted from 13
**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

**DRP®**

**Other**

**Wnt pathways**

**Homologous Recombination**

**BRCA1+2**

**Metastatic breast cancer**

**Ovarian cancer**

**Pancreatic cancer**

**Brain metastases from breast cancer**

**Endometrial cancer**

**Prostate cancer**
2X-121: Phase 2 Clinical Plans - Initial Focused Studies

### Metastatic Breast Cancer
- Select top 20% DRP®
- <30 heavily pre-treated patients
- Utilize 1,200+ patient registry in Denmark

- 2H 2018 data expected
- 30%+ response rate anticipated
- Potential for accelerated approval

### Prostate Cancer
- Select top 20% DRP®
- <30 heavily pre-treated patients
- Initial EU study

- 2H 2018 data expected
- 30%+ response rate anticipated
- Potential for accelerated approval
## 2X-121: Phase 2 Clinical Plans – U.S. Studies

<table>
<thead>
<tr>
<th>Phase 2 Study Plan</th>
<th>Potential Outcome Pathways</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Relapsed Ovarian Cancer</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>- Select top 20% DRP®</td>
<td>- 30%+ response rate anticipated</td>
</tr>
<tr>
<td>- Enroll &lt;30 heavily pre-treated patients (incl. prior PARP refractory)</td>
<td>- Potential accelerated approval</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2X-121: Phase 2 Clinical Plans - Basket

**NCI Collaboration – Pediatric Cancer**
- Cancer type selection based on known PARPi activity
  - e.g. Neuroblastoma
- DRP® cutoff TBD

**PARPi Tumor Studies**
- Selection based on known PARPi activity in specific tumor types
- DRP® cutoff TBD

- Minimum of doubling existing response rate vs. other PARPi
- Opportunity for accelerated approval
2X-121: Current Status

- Product available from Eisai
  - 13K capsules for initial studies
  - 14kg of API
  - 78kg of intermediate product
- 2X-121 DRP® established & 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 expected Q1 2018
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
DRP® for Anthracycline Predicts Response in mBC

In 135 patients with mBC treated with epirubicin the DRP predicted PFS with a Hazard Ratio of 0.5 (p=0.02)

13 months PFS with DRP® at 75%

7 months PFS with DRP® at 25%

## Established Clinical History

<table>
<thead>
<tr>
<th>Single Agent</th>
<th>Patients</th>
<th>Indication</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>37</td>
<td>Safety</td>
<td>Well tolerated</td>
</tr>
</tbody>
</table>
| Phase 2a     | 17       | Brain metastases from breast cancer | PR: 2 (12%)  
SD: 9 (52%) |
| Phase 2a     | 20       | GBM        | PR: 1 (5%)  
SD: 7 (35%) |

Prior clinical studies completed *without* use of 2X-111 DRP® CDx to select likely responders
2X-111: Clinical Development Plans

### Glioblastoma Multiforme

- Select top 20% DRP®
- Enroll <20 patients

#### Potential Outcome Pathways

- **a)** 4+ patients PR/SD at 6+ months → accelerated approval discussion with FDA
- **b)** 2-3 patients PR/SD → enroll 10 additional patients

### Brain Metastases from Breast Cancer

- Select top 40% DRP®
- Enroll <20 patients

#### Potential Outcome Pathways

- **a)** 6+ patients PR → repeat study; accelerated approval discussion with FDA
- **b)** 4-5 patients PR → pivotal Phase 2 with evaluation of other metastases
2X-111: Glutathione-enhanced PEGylated Liposomal Doxorubicin

Current Status

• U.S. IND obtained June 2017
• Drug product manufacturing underway (Taiwan)
• 2X-111 DRP® established & validated
• Danish registry of ~1,200 DRP-screened breast cancer patients available for mBC Phase 2 study – umbrella study
• Glioblastoma patients to be screened with 2X-111 DRP® CDx at Copenhagen and Duke University Hospitals
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
- Favourable safety profile
- Clinically-demonstrated efficacy in wide range of cancers
## 2X-131: Established Clinical History

Completed Phase 1 & Phase 2 Studies in > 300 Patients
Conducted in EU, US, Japan and China

<table>
<thead>
<tr>
<th>Phase</th>
<th>Treated Patients</th>
<th>Tumor types</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>108</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>1</td>
<td>35</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>1</td>
<td>43</td>
<td>Glioma</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>ADME</td>
</tr>
<tr>
<td>1</td>
<td>157</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>1</td>
<td>26</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>Breast</td>
</tr>
<tr>
<td></td>
<td>69</td>
<td>Ovarian</td>
</tr>
</tbody>
</table>

ADME-Absorption Distribution Metabolism Excretion
## 2X-131: Topoisomerase 1 Inhibitor

### Established Clinical History

<table>
<thead>
<tr>
<th>Single Agent</th>
<th>Patients</th>
<th>Indication</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 2</td>
<td>69</td>
<td>Ovarian cancer</td>
<td>• Well tolerated with improved efficacy &amp; safety profile vs. topotecan &amp; irinotecan</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 47% response rate in 19 patients with Platinum Free Interval (PFI) ≥6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 16% PR in patients with PFI&lt;6 months</td>
</tr>
</tbody>
</table>

Prior clinical study completed *without* use of 2X-131 DRP® CDx to select likely responders
# 2X-131: Phase 2 Clinical Development Plan

## Ovarian Cancer
- Select top 30% DRP®
- Enroll <20 heavily pre-treated patients with PFI <6 months

  **Potential Outcome Pathways**
  
  a) 3+ patients → repeat study; discuss accelerated approval with FDA
  
  b) <3 patients → revisit DRP® cutoff

## Endometrial Cancer
- Select top 20% DRP®
- Enroll <20 late-stage pre-treated patients

  **Opportunity for accelerated approval and orphan designation**
2X-131: Current Status

• Drug product available from partner for Phase 2 studies
• Planning DRP®-selected Phase 2 study in recurrent ovarian cancer
• Expanded collaboration discussions with China partner
• U.S. IND filing/reopening planned for Q1 2018
### Development Timeline

<table>
<thead>
<tr>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2019</th>
<th>2019</th>
<th>2019</th>
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<tbody>
<tr>
<td>Q4 2017</td>
<td>Q1 2018</td>
<td>Q2 2018</td>
<td>Q3 2018</td>
<td>Q4 2018</td>
<td>2019</td>
</tr>
</tbody>
</table>

#### 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
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