Insight that enriches. Precision that empowers.

Corporate Presentation
October 2023
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These forward-looking statements reflect our current beliefs and expectations. Many factors may cause differences between current expectations and actual results, including the duration and impact of the COVID-19 pandemic on our business and market volatility, unexpected safety or efficacy data observed during preclinical or clinical studies, clinical site activation rates or clinical trial enrollment rates that are lower than expected, changes in expected or existing competition, changes in the regulatory environment, and unexpected litigation or other disputes. These and other risks are described more fully in our filings with the Securities and Exchange Commission (“SEC”), including the “Risk Factors” section of our Quarterly Report on Form 10-Q filed with the SEC on November 9, 2023, and other documents we subsequently filed with or furnished to the SEC. All forward-looking statements contained in this presentation speak only as of the date on which they were made. Except as required by law, we assume no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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Differentiated and expanding clinical-stage pipeline
- Lunresertib: First-in-class oral PKMYT1 inhibitor (Phase 1/2)
- Camonsertib: ATR inhibitor (Partnered with Roche)
- Additional near-term clinical programs
- Potential across multiple tumor types

Proprietary CRISPR-enabled SNIPRx platform
- Focused on genomic instability and DNA damage repair within cancer cells

Multiple clinical catalysts expected in 2023 and 2024

Cash runway into 2026
- Cash and investments of $250.1M as of September 30, 2023
Targeting the un-targetable through synthetic lethality

Genetic Alterations in Cancer

- **Targetable**
  - Gain-of-function ~29%
- **Un-targetable**
  - Loss-of-function ~54%
  - Gain-of-function ~17%

Specifically targeting and disrupting genes essential for cancer cell survival

- SNIPRx identifies and targets necessary genes to induce synthetic lethality
  - Highly targeted & tumor-type agnostic approach
  - Exploiting cancer cell genomic instability, including DNA damage repair

Platform validated with established and expanding clinical-stage pipeline
Enabling target identification & patient insights through SNIPRx®

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Select tumor lesion of interest</td>
</tr>
<tr>
<td>2</td>
<td>Execute SNIPRx® CRISPR-Cas9 enabled screen campaign in isogenic cell lines</td>
</tr>
<tr>
<td>3</td>
<td>Prioritize, select and validate druggable targets</td>
</tr>
<tr>
<td>4</td>
<td>Develop potent and selective inhibitors</td>
</tr>
<tr>
<td>5</td>
<td>Perform SNIPRx® Targeted Expansion of Patient Populations (STEP²) screens</td>
</tr>
<tr>
<td>6</td>
<td>Conduct clinical trials in an enriched patient population</td>
</tr>
</tbody>
</table>

**Diagram:**
- **CANCER-ASSOCIATED GENETIC LESION**
  - NORMAL CELL
  - Predicted non-responders
  - Viable
  - Lethal
  - POTENTIAL SL DRUG TARGETS
    - Small molecule inhibitor (clinical candidate)
  - DRUG TARGET
  - Prioritize, select and validate druggable targets
  - Develop potent and selective inhibitors
  - Perform SNIPRx® Targeted Expansion of Patient Populations (STEP²) screens
  - Conduct clinical trials in an enriched patient population

**Legend:**
- Repare Therapeutics
Expanding pipeline of precision oncology therapeutics

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>TUMOR LESION</th>
<th>DRUG TARGET</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>RIGHTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camonsertib</td>
<td>ATM + 16 STEP2 lesions</td>
<td>ATR</td>
<td></td>
<td>Ph2 TAPISTRY</td>
<td>Ph1b/2 Morpheus-Lung</td>
<td>Ph1/2 TRESR: Mono + PARP (talazoparib) Combo</td>
<td>Roche</td>
</tr>
<tr>
<td>(RP-3500/ RG6526)</td>
<td></td>
<td></td>
<td></td>
<td>Ph1/2 TRESR: Mono + PARP (talazoparib) Combo</td>
<td>Ph1/2 ATTACC: PARP (olaparib/niraparib) Combo</td>
<td>Ph1/2 TRESR: Gemcitabine Combo</td>
<td></td>
</tr>
<tr>
<td>Lunresertib</td>
<td>CCNE1, FBXW7 + others</td>
<td>PKMYT1</td>
<td></td>
<td>Ph2 CCTG ISTs</td>
<td>Ph1 MYTHIC: Mono + Camonsertib Combo</td>
<td>Ph1 MAGNETIC: Gemcitabine Combo</td>
<td>REPAIRE</td>
</tr>
<tr>
<td>(RP-6306)</td>
<td></td>
<td></td>
<td></td>
<td>Ph1 MINOTAUR: FOLFIRI Combo</td>
<td>Ph1 MINOTAUR: FOLFIRI Combo</td>
<td>Ph1 Carboplatin/paclitaxel Combo IST</td>
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<tr>
<td>RP-1664</td>
<td>Undisclosed</td>
<td>Undisclosed</td>
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<td></td>
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<tr>
<td>RP-3467 Polθ Inhibitor</td>
<td>BRCA1/2 + others</td>
<td>Polθ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNIPRx® Platform</td>
<td>Additional SL targets in advanced stages of development</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Discovery and validation of new SL precision oncology targets</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Driving shareholder value through strategic collaborations

<table>
<thead>
<tr>
<th>Roche</th>
<th>Bristol Myers Squibb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global development and commercialization collaboration for Camonsertib</strong></td>
<td><strong>Multi-target discovery collaboration leveraging SNIPRx® discovery platform</strong></td>
</tr>
<tr>
<td>$135M upfront</td>
<td>$65M upfront</td>
</tr>
<tr>
<td>~$1.2B potential milestones</td>
<td>~$3B potential milestones</td>
</tr>
<tr>
<td>High single-digit to high-teens royalties</td>
<td>Royalties</td>
</tr>
<tr>
<td>50/50 U.S. co-development, profit/cost share and co-promotion option</td>
<td>Both SL targets and “undruggable” targets outside our focus</td>
</tr>
</tbody>
</table>
Proven experience in drug discovery and development

### Leadership Team

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lloyd M. Segal</td>
<td>President &amp; CEO</td>
</tr>
<tr>
<td>Steve Forte, CPA</td>
<td>Chief Financial Officer</td>
</tr>
<tr>
<td>Michael Zinda, PhD</td>
<td>Chief Scientific Officer</td>
</tr>
<tr>
<td>Maria Koehler MD, PhD</td>
<td>Chief Medical Officer</td>
</tr>
<tr>
<td>Cameron Black, PhD</td>
<td>Head of Discovery</td>
</tr>
<tr>
<td>Philip Herman</td>
<td>Chief Commercial, Portfolio Development Officer</td>
</tr>
<tr>
<td>Kim A. Seth, PhD</td>
<td>Chief Business Officer</td>
</tr>
<tr>
<td>Daniel Bélanger</td>
<td>Head of Human Resources</td>
</tr>
</tbody>
</table>

### Scientific Founders

<table>
<thead>
<tr>
<th>Name</th>
<th>Experience/Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daniel Durocher, PhD</td>
<td>Developed CRISPR SL platform, Deep DNA repair knowledge, Lunenfeld-Tanenbaum Research Institute (LTRI) &amp; professor at University of Toronto</td>
</tr>
<tr>
<td>Agnel Sfeir, PhD</td>
<td>DDR and cancer pathway investigator, Pioneer in Polθ, genome instability, Professor, MSKCC</td>
</tr>
<tr>
<td>Frank Sicheri, PhD</td>
<td>Globally recognized structural biologist, expert in eukaryotic cell signaling, drug mechanism of action, LTRI &amp; professor at University of Toronto</td>
</tr>
</tbody>
</table>
Lunresertib (RP-6306)
Lunresertib: First-in-class, oral, small molecule, PKMYT1 inhibitor

Combination therapy achieved strong anti-tumor activity across multiple tumor types and tested genotypes; 33% overall response at preliminary RP2D (N=18)

50% RECIST response observed in camonsertib combination in largest cohort (gynecological tumors) at preliminary RP2D (N=10)

Proof of concept established for monotherapy and camonsertib combination in MYTHIC Phase 1 trial

Large, genomically defined potential patient population ~90K addressable population including CCNE1, FBXW7 and PPP2R1A

Validated preclinical synergy hypothesis and patient selection approach from proprietary SNIPRx platform

Encouraging safety and tolerability profile observed for oral monotherapy and combination therapy
**Lunresertib: The only clinical-stage therapeutic targeting PKMYT1**

**Protein Kinase** within the Wee1 kinase family

**Regulates cell cycle** and is part of DNA damage repair-related signaling

**Inactivates CDK1** via phosphorylation of threonine14 (T14) holding the cell in S phase until ready to undergo mitosis

**CCNE1 amp or deleterious mutations in FBXW7 and PPP2R1A** result in an extended S phase and reliance on PKMYT1 activity

Inhibiting PKMYT1 in these genomic backgrounds **may result in cell death** via mitotic catastrophe

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Initially identified CCNE1 amplification sensitive to PKMYT1 inhibition

STEP² screen identified additional genes (FBXW7 and PPP2R1A)
Addressing unmet need in critical patient populations

~90K patients across tumor types; ~65K among top tumors

CCNE1 amplification or inactivating mutations in FBXW7 and PPP2R1A

Genetic alterations largely mutually exclusive

<table>
<thead>
<tr>
<th>Top Tumors (New Advanced Cases, US+UK/EU4)</th>
<th>Prevalence of Genes of Interest</th>
<th>Eligible Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Type</td>
<td>CCNE1</td>
<td>FBXW7</td>
</tr>
<tr>
<td>Uterine</td>
<td>3.8%</td>
<td>12.9%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>10.2%</td>
<td>19.0%</td>
</tr>
<tr>
<td>Stomach</td>
<td>13.1%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>11.8%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Bladder</td>
<td>9.1%</td>
<td>6.3%</td>
</tr>
<tr>
<td>Cervical</td>
<td>7.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Esophageal</td>
<td>7.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Sarcoma*</td>
<td>4.7%</td>
<td>7.6%</td>
</tr>
<tr>
<td>Lung Squamous*</td>
<td>7.1%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

* Based on estimated number of pts treated in 1st line, advanced setting for diagnosed and new recurrent patients (CancerMPact®, Treatment Architecture, United States, 2021; accessed 5/19/23) and lesion prevalence (TCGA). 1 Soft Tissue Sarcoma only; 2 Squamous subtype of Non-Small Cell Lung Cancer only
**Evolving broad trial program: sponsored and collaborative**

<table>
<thead>
<tr>
<th>Lunresertib Combination Therapy</th>
<th>Future Opportunities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAGNETIC</strong>: + Gemcitabine</td>
<td>Selected tumors with amplified CCNE1</td>
</tr>
<tr>
<td></td>
<td>Ovarian, Lung, Esophageal / Gastric</td>
</tr>
<tr>
<td><strong>MYTHIC</strong>: + Camonsertib</td>
<td>Selected tumors with FBXW7 loss</td>
</tr>
<tr>
<td><strong>MINOTAUR</strong>: + FOLFIRI</td>
<td>Tumors with high rate of sensitivity genes</td>
</tr>
<tr>
<td><strong>IST</strong>: + CCTG(^1)</td>
<td>Endometrial, Bladder</td>
</tr>
<tr>
<td><strong>IST</strong>: + Carbo/paclitaxel(^2)</td>
<td>Basket trial</td>
</tr>
<tr>
<td></td>
<td>Breast, Sarcoma, Bile Duct</td>
</tr>
</tbody>
</table>

\(^1\) Canadian Clinical Trial Group (CCTG) collaborations include NCT05605509 and NCT05601440.

\(^2\) SOC for 1\(^{st}\) line ovarian cancer is carbo/paclitaxel (6 cycles) + PARPi maintenance therapy or carbo/paclitaxel with bevacizumab + bev maintenance therapy; this IST supports future potential 1\(^{st}\) line combination studies as triplet therapy in patients with CCNE1 amplified tumors.

---

**Key inclusion criteria:**
- Recurrent solid tumors
- **CCNE1** amplification or inactivating mutations
- **PPP2R1A**
- **FBXW7**

**Recurrent solid tumors**

**Lunresertib Combination Therapy**

- **MAGNETIC**: + Gemcitabine
- **MYTHIC**: + Camonsertib
- **MINOTAUR**: + FOLFIRI
- **IST**: + CCTG\(^1\)
- **IST**: + Carbo/paclitaxel\(^2\)

**4 collaboration trials in advanced discussion**

**Future Opportunities**

- Selected tumors with amplified CCNE1
- Ovarian, Lung, Esophageal / Gastric
- Selected tumors with FBXW7 loss
- CRC, Other GI, Pan Tumor
- Tumors with high rate of sensitivity genes
- Endometrial, Bladder
- Basket trial
- Breast, Sarcoma, Bile Duct

**Canadian Clinical Trial Group (CCTG) collaborations include NCT05605509 and NCT05601440.**

**SOC for 1\(^{st}\) line ovarian cancer is carbo/paclitaxel (6 cycles) + PARPi maintenance therapy or carbo/paclitaxel with bevacizumab + bev maintenance therapy; this IST supports future potential 1\(^{st}\) line combination studies as triplet therapy in patients with CCNE1 amplified tumors.**
Lunresertib:
MYTHIC Preliminary Phase 1 Trial Results
(M1: Monotherapy)
(M2: Camonsertib Combination Therapy)

**MONOTHERAPY**
Safe, well tolerated, and anti-tumor activity established (N=67)
Recommended Phase 2 dose: 80 to 100mg twice daily in intermittent schedule

**CAMONSERTIB COMBINATION THERAPY**
Safe, well tolerated, and promising anti-tumor activity across tumors and lunresertib-sensitizing genomic alterations (N=59)
23.6% OR; 41.8% CBR in efficacy-evaluable patients (N=55)
33.3% OR; 50.0% CBR at preliminary RP2D range, across all tumors (N=18)
38.5% OR; 57.7% CBR in patients with heavily pre-treated gynecologic cancers (N=26); 50% RECIST response at preliminary RP2D (N=10)

Preliminary recommended Phase 2 dose: Lunresertib 80mg twice daily and camonsertib 80mg once daily, dose/schedule optimization ongoing

OR, overall response; CBR, clinical benefit rate; RP2D, recommended phase 2 dose.
Anti-tumor activity with lunresertib monotherapy

One RECIST responder

Female
73 years old

Metastatic recurrent uterine carcinosarcoma

FBXW7 & PPP2R1A Mutations

3 prior lines of therapy

Lunresertib: 80mg BID-I

Baseline

TA #1 – Week 6

- Overall response: cPR (RECIST)
- RECIST target lesion decrease -41%
- Received therapy for 8.3 months

Further, 7 patients with <30% tumor shrinkage, and 2 patients with PFS > 6 and 14 months, respectively
PKMYT1 and ATR inhibitors synergize to enhance anti-tumor activity

Lunresertib-sensitizing alterations engage ATR through replication stress

Combination of ATR and PKMYT1 inhibition enhances CDK1 activation and premature mitosis

1ANE poster B057: Gallo et al. Preclinical development of PKMYT1 and ATR inhibitor combinations. ATR, ataxia telangiectasia and Rad-3 related; CDC25, cell division cycle-25; CDK, cyclin-dependent kinase; CHK1, checkpoint kinase 1; PKMYT1, protein kinase, membrane associated tyrosine/threonine 1.
Responses to combination observed across tumor types and lunresertib-sensitizing alterations

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Genotype</th>
<th>Response</th>
<th>Best % change in TL from BL</th>
<th>Therapy (weeks)</th>
<th>Lines of prior Tx/prior platinum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial</td>
<td>PPP2R1A/FBXW7</td>
<td>cPR</td>
<td>-55.9</td>
<td>30.4</td>
<td>3/Y</td>
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<tr>
<td></td>
<td>PPP2R1A/CCNE1</td>
<td>cPR</td>
<td>-53.0</td>
<td>18.1</td>
<td>2/Y</td>
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<tr>
<td></td>
<td>FBXW7</td>
<td>cPR*</td>
<td>-100.0</td>
<td>11.1+</td>
<td>3/Y</td>
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<tr>
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<td>FBXW7</td>
<td>uPR</td>
<td>-39.6</td>
<td>16.0</td>
<td>3/Y</td>
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<tr>
<td></td>
<td>FBXW7</td>
<td>uPR*</td>
<td>-44.7</td>
<td>11.4+</td>
<td>3/Y</td>
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<tr>
<td>Ovarian</td>
<td>CCNE1</td>
<td>cPR*</td>
<td>-70.2</td>
<td>21.4+</td>
<td>2/Y</td>
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<tr>
<td></td>
<td>CCNE1†</td>
<td>cPR*</td>
<td>-30.8</td>
<td>12.6+</td>
<td>3/Y</td>
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<tr>
<td></td>
<td>CCNE1</td>
<td>CA-125</td>
<td>-16.9</td>
<td>29.0+</td>
<td>9/Y</td>
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<tr>
<td></td>
<td>CCNE1</td>
<td>CA-125</td>
<td>-23.1</td>
<td>37.0+</td>
<td>2/Y</td>
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<tr>
<td></td>
<td>CCNE1</td>
<td>CA-125</td>
<td>13.6</td>
<td>12.9+</td>
<td>5/Y</td>
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<tr>
<td>Cervical</td>
<td>PPP2R1A</td>
<td>cPR*</td>
<td>-44.4</td>
<td>11.0+</td>
<td>1/Y</td>
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<td>Colorectal</td>
<td>FBXW7</td>
<td>cPR</td>
<td>-43.3</td>
<td>27.6</td>
<td>3/Y</td>
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<tr>
<td>Bile duct</td>
<td>CCNE1</td>
<td>cPR</td>
<td>-35.0</td>
<td>28.1</td>
<td>2/Y</td>
</tr>
<tr>
<td>Breast</td>
<td>FBXW7†</td>
<td>uPR</td>
<td>-43.8</td>
<td>18.1</td>
<td>2/N</td>
</tr>
</tbody>
</table>

RECIST and tumor marker responses occurred early despite heavily pre-treated, relapsed/refractory patient population

* One response evaluable patient became uPR and four patients had responses confirmed after the Sept. 5, 2023 cutoff, data as of Oct. 6, 2023. Relevant patient tumor co-mutations †BRCA1 rearrangement and ‡BRCA2 biallelic loss. +Treatment ongoing. BL, baseline; cPR, confirmed partial response; RECIST, Response Evaluation Criteria in Solid Tumors; TL, target lesion; Tx, treatment; uPR, unconfirmed partial response.
Frequent and deep tumor reductions with lunre + cam combination across multiple tumor types

- In evaluable patients*, across all tumors/doses:
  - OR: 23.6% (n=55)
  - CBR: 41.8% (n=55)
  - MRR: 50.0% (n=24)

- At preliminary RP2D, across all tumors:
  - OR: 33.3% (n=18)
  - CBR: 50.0% (n=18)

*Efficacy evaluable patients only (≥1 post-baseline tumor assessment). Other tumor types include cervical (n=1), esophageal (n=1), GI (n=1), liver (n=1), lung (n=3), melanoma (n=1), osteosarcoma (n=1), pancreatic (n=2), and upper GI (n=1). CBR: overall response or time on treatment ≥16 wk w/o progression; CRC, colorectal cancer; RECIST, Response Evaluation Criteria in Solid Tumors (RECIST) Gynecologic Cancer InterGroup (GCIG); MRR, molecular response rate; OR, overall response based on RECIST or GCIG CA-125 response; RP2D, recommended phase 2 dose.
Most patients with gynecologic cancers had tumor reductions with combination treatment

Meaningful tumor reductions and durable clinical benefit observed in heavily pre-treated patients

Across all doses (n=26):
- Overall response: 38.5%; RECIST Response: 26.9%
- CBR: 57.7%; MRR: 8/10 (80%)

- Patients had 1-9 prior therapies (median=3); treatment ongoing in 11 patients; enrollment in expansion cohorts at RP2D continues

At preliminary RP2D (n=10):
- Overall response: 60%; RECIST Response: 50%
- CBR: 70%

* Gynecologic cancers: ovarian, endometrial, and cervical cancers. Data represent the efficacy evaluable population (≥1 post-baseline tumor assessment). CBR, clinical benefit rate; OR, overall response based on RECIST or GCIG CA-125 response; MRR, molecular response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; Gynecological Cancer InterGroup (GCIG); RP2D, recommended phase 2 dose.
Early response in recurrent FBXW7 mutated colorectal adenocarcinoma

- Male
- 63 years old
- Recurrent colorectal adenocarcinoma
- Mutation: FBXW7
- TP53 mutant
- 3 prior lines of therapy
- Lunre 240mg QD 3/4
- Cam 80mg QD 3/4

**Overall response:**
- cPR (RECIST)

**RECIST target lesion decrease:**
- -43.3%

**Received therapy for:**
- 27.6 weeks

**Gene alterations:**
- ALK p.L1118F
- APC p.A1485fs
- APC p.E984*
- FANCA p.L1167F
- FBXW7 p.R505C
- H3F3A p.HA114HG
- TP53 p.R213*

**Allele frequency**

3/4, 3 days on/4 days off; cPR, confirmed partial response; ctDNA, circulating tumor DNA; RECIST, Response Evaluation Criteria in Solid Tumors; QD, once daily; RP2D, recommended phase 2 dose; TA, tumor assessment; Thr, threonine.
Gradual response heralded by CA-125 decrease; recurrent \textit{CCNE1} amplified ovarian cancer

Overall response: cPR (RECIST)

RECIST target lesion decrease -70.2%

Therapy ongoing for >21 weeks

Female 56 years old

High grade serous ovarian carcinoma

\textbf{CCNE1}

Amplification

TP53 mut

2 prior lines of therapy

\textbf{RP2D:}

Lunre 80mg BID 3/4 Cam 80mg QD 3/4

<table>
<thead>
<tr>
<th>Tumor assessment</th>
<th>Baseline</th>
<th>6 wks</th>
<th>12 wks</th>
<th>18 wks</th>
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</thead>
<tbody>
<tr>
<td>T01 Peritoneum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>LA: 1.8 cm</td>
<td>LA: 0.7 cm</td>
<td>LA: 0.5 cm</td>
<td>LA: 0.7 cm</td>
</tr>
<tr>
<td>T02 Peritoneum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>LA: 2.0 cm</td>
<td>LA: 1.3 cm</td>
<td>LA: 1.0 cm</td>
<td>LA: 1.0 cm</td>
</tr>
<tr>
<td>Pelvis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>LA: 2.1 cm</td>
<td>LA: 1.2 cm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Images not available in RECIST report

No visible lesion reported

CA-125 dynamics

ctDNA dynamics

Gene alteration:

\begin{align*}
\text{ARID1B} & \ p.Q122\_Q128dup \\
\text{CIC} & \ p.N1133fs \\
\text{RET} & \ p.EV62D \\
\text{LTP53} & \ p.R280* \\
\end{align*}

3/4, 3 days on/4 days off; cPR, confirmed partial response; ctDNA, circulating tumor DNA; RECIST, Response Evaluation Criteria in Solid Tumors; QD, once daily; RP2D, recommended phase 2 dose.
Prompt response in recurrent cervical carcinosarcoma with a PPP2R1A mutation

Female
66 years old

Recurrent cervical carcinosarcoma

PPP2R1A
Mutation

MYC amp
TP53 mut

1 prior line of therapy

RP2D:
Lunre 80mg BID 3/4
Cam 80mg QD 3/4

Tumor assessment

Baseline 6 weeks 12 weeks

T01 Lymph node external iliac left

CA-125 dynamics

- Overall response: cPR (RECIST)
- RECIST target lesion decrease -44.4%
- Therapy ongoing at 11 weeks

3/4, 3 days on/4 days off; BID, twice daily; CN, copy number; cPR, confirmed partial response; RECIST, Response Evaluation Criteria in Solid Tumors; QD, once daily; RP2D, recommended phase 2 dose; TA, tumor assessment.
Camonsertib
(RP-3500 / RG6526)
**Camonsertib:**
Potential best-in-class ATR inhibitor

| Expanded potential with combination therapy |
| Proof of concept established in Phase 1/2 monotherapy trial |
| **Durable antitumor activity** in combination with PARP inhibitors and gemcitabine; meaningful clinical benefit in ovarian cancer |
| **Demonstrated synthetic lethal interaction of ATR** and a network of genes identified by SNIPRx and STEP² process |
| **Global development and commercialization collaboration with Roche:** Initially advancing TAPISTRY Phase 2 and Morpheus Lung Phase 1b/2 trials |
Potential across additional patient populations

**Top 10 Tumor Types* with Highest Prevalence of ATM Deficiency**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>% ATM Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder Urothelial Carcinoma</td>
<td>3.6%</td>
</tr>
<tr>
<td>Pancreatic Adenocarcinoma</td>
<td>3.4%</td>
</tr>
<tr>
<td>Lung Adenocarcinoma</td>
<td>2.8%</td>
</tr>
<tr>
<td>Adrenocortical Carcinoma</td>
<td>2.5%</td>
</tr>
<tr>
<td>Rectum Adenocarcinoma</td>
<td>2.4%</td>
</tr>
<tr>
<td>Stomach Adenocarcinoma</td>
<td>2.4%</td>
</tr>
<tr>
<td>Breast Invasive Carcinoma: LumB</td>
<td>2.4%</td>
</tr>
<tr>
<td>Breast Invasive Carcinoma: LumA</td>
<td>1.6%</td>
</tr>
<tr>
<td>Breast Invasive Carcinoma</td>
<td>1.4%</td>
</tr>
<tr>
<td>Skin Cutaneous Melanoma</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

**Top 10 Tumor Types* with Highest Prevalence of ATM Deficiency or STEP² Genomic Alterations**

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>% STEP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Serous Cystadenocarcinoma</td>
<td>18.7%</td>
</tr>
<tr>
<td>Uterine Corpus Endometrial Carcinoma</td>
<td>17.6%</td>
</tr>
<tr>
<td>Breast Invasive Carcinoma: Basal</td>
<td>13.8%</td>
</tr>
<tr>
<td>Stomach Adenocarcinoma</td>
<td>10.9%</td>
</tr>
<tr>
<td>Bladder Urothelial Carcinoma</td>
<td>10.9%</td>
</tr>
<tr>
<td>Breast Invasive Carcinoma: LumB</td>
<td>9.1%</td>
</tr>
<tr>
<td>Breast Invasive Carcinoma</td>
<td>9.0%</td>
</tr>
<tr>
<td>Lung Adenocarcinoma</td>
<td>8.6%</td>
</tr>
<tr>
<td>Colon Adenocarcinoma</td>
<td>8.6%</td>
</tr>
<tr>
<td>Cervical Squamous Cell Carcinoma</td>
<td>8.5%</td>
</tr>
</tbody>
</table>

*Source: *TCGA; Not weighted for tumor prevalence
Expanding clinical development through Roche collaboration

Repare Trials

- TRESR Phase 1/2
  - Monotherapy (M1)
  - + Talazoparib (M3)
  - + Gemcitabine (M4)

- ATTACC Phase 1/2
  - + Olaparib / Niraparib

Roche Collaboration

- TAPISTRY
  - Phase 2 (Initiation expected 2H 2023)

- Morpheus Lung
  - Phase 1b/2

Robust clinical program potential

Note: Camonsertib monotherapy TRESR Module 2 expansion phase to be integrated into partnered clinical development plans under Roche IND
Camonsertib:
TRESR & ATTACC
Phase 1/2
Trial Results

MONOTHERAPY

Favorable safety profile (N=120)

Proof-of-concept established in ovarian cancer

25% OR; 75% CBR; 8+ months PFS

Clinical benefit in patients with BRCA1/2 mutations

COMBINATION THERAPY

Clinically meaningful anti-tumor activity in combination with all leading PARP inhibitors

Confirmed efficacy in platinum- and PARPi-resistant cancers

48% overall CBR (N=90)

32% OR; 58% CBR; ~7 months PFS in advanced ovarian cancer (N=19)

OR, overall response; CBR, clinical benefit rate; PFS, progression free survival
Anti-tumor activity in ovarian cancer with monotherapy

- **25%** Overall response (5/20*)
- **35w** Median PFS
- **75%** Clinical benefit rate (CBR)
- **90%** (18/20) patients had prior PARPi
- **85%** (17/20) patients platinum refractory/resistant*

*Platinum refractory/resistant: progression on platinum or a platinum-free interval of <6 mo. CBR: OR or ≥16w on therapy without progression

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**Time on Treatment (wk) – Ovarian**

**Time to Disease Progression or Death – Ovarian**

* Y = Yes, N = No

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*CR, PR, confirmed, PR, unconfirmed, Tumor marker response*

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28
Clinically relevant benefit in patients with BRCA1/2 mutations with monotherapy

14%
Overall response in BRCA1/2 (RECIST, 5/37)

43%
CBR for BRCA1/2 tumors

48%
CBR for post-PARPi BRCA1/2 tumors

CBR (OR or ≥16w on therapy without progression) was 48% for BRCA1 population, and 36% for BRCA2
Durable clinical benefit observed with combination therapy

48% overall CBR (N=90)

Benefit observed across multiple tumors, regardless of previous PARPi treatment

Similar benefit observed in patients with platinum-resistant tumors (ORR 12%, CBR 49%) and non-platinum-resistant tumors (ORR 13%, CBR 46%)

Included patients from efficacy analysis set.

ORR is based on overall response as best response of confirmed or unconfirmed CR or PR per RECIST v1.1 criteria or confirmed CA-125 response per Gynecological Cancer Intergroup; CBR is based on overall response or ≥16 weeks on treatment without progression; MRR is based on ctDNA molecular response as >50% decline in mVAF assessed by GuardantINFINITY or Tempus xF gene panel for patients with detectable somatic alterations.

CBR, clinical benefit rate; CR, complete response; PR, partial response; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumors.
Upcoming milestones

2H 2023
- Camonsertib Phase 2
  TAPISTRY trial initiation
- Lunresertib +
  carboplatin/paclitaxel
  combination Phase 1
  IST initiation
- RP-1664 and RP-3467 (Polθi)
  focused investor event

1H 2024
- RP-1664
  clinical trial initiation
  Initial lunresertib + FOLFIRI
  combination Phase 1 data

2H 2024
- RP-3467 (Polθi)
  clinical trial initiation
- Lunresertib + gemcitabine
  combination Phase 1 data
- Lunresertib + camonsertib
  combination Phase 1 data
  (expansion cohorts)
Differentiated and expanding clinical-stage pipeline
- Lunresertib: First-in-class oral PKMYT1 inhibitor (Phase 1/2)
- Camonsertib: ATR inhibitor (Partnered with Roche)
- Additional near-term clinical programs
- Potential across multiple tumor types

Proprietary CRISPR-enabled SNIPRx platform
- Focused on genomic instability and DNA damage repair within cancer cells

Multiple clinical catalysts expected in 2023 and 2024

Cash runway into 2026
- Cash and investments of $250.1M as of September 30, 2023
Insight that enriches. Precision that empowers.

Corporate Presentation
October 2023