Repare Therapeutics Inc.  
(Exact Name of Registrant as Specified in Its Charter)

Québec  
(State or Other Jurisdiction of Incorporation)

001-39335  
(Commission File Number)

Not applicable  
(I.R.S. Employer Identification No.)

7171 Frederick-Banting, Building 2  
St-Laurent, Québec, Canada  
(Address of Principal Executive Offices)  
H4S 1Z9  
(Zip Code)

Registrant’s Telephone Number, Including Area Code: (857) 412-7018  
(Not Applicable)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

<table>
<thead>
<tr>
<th>Title of each class</th>
<th>Trading Symbol</th>
<th>Name of each exchange on which registered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common shares, no par value</td>
<td>RPTX</td>
<td>The Nasdaq Stock Market LLC</td>
</tr>
</tbody>
</table>

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐
Item 7.01 Regulation FD Disclosure.

As previously announced, Repare Therapeutics Inc. (the “Company”) will host a conference call and live audio webcast today, October 13, 2023 at 5:30 p.m., Eastern Time, to discuss the presentation of positive initial data from Modules 1 and 2 of its ongoing Phase 1 MYTHIC clinical trial evaluating lunresertib alone and in combination with camonsertib, at the 2023 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, including a discussion of new, updated data of its product candidate lunresertib (RP-6306) in combination with camonsertib since the September 5, 2023 data cut-off date of the 2023 AACR-NCI-EORTC presentation.

The live audio webcast may be accessed through the “Events & Presentations” page in the “Investors and Media” section of the Company’s website at ir.reparerx.com. Alternatively, participants may dial (877) 870-4263 (U.S. and Canada) or (412) 317-0790 (international). A copy of the presentation to be used by the Company during the conference call is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Additionally, on October 13, 2023, the Company posted an updated corporate presentation to its website. The corporate presentation is available under the “Events & Presentations” tab in the “Investors & Media” section of the Company’s website, located at www.reparerx.com. The Company intends to use this presentation in meetings with analysts, investors and others from time to time. A copy of the presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any of the Company’s filings under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing.

The Company’s website and any information contained on the Company’s website are not incorporated into this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<table>
<thead>
<tr>
<th>Exhibit No.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.1</td>
<td>Conference Call Presentation dated October 13, 2023</td>
</tr>
<tr>
<td>99.2</td>
<td>Company Presentation dated October 2023</td>
</tr>
<tr>
<td>104</td>
<td>Cover Page Interactive Data File (embedded within the Inline XBRL document)</td>
</tr>
</tbody>
</table>
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REPARE THERAPEUTICS INC.

Date: October 13, 2023

By: /s/ Lloyd M. Segal
Lloyd M. Segal
President and Chief Executive Officer
Insight that enriches. Precision that empowers.

Lunresertib MYTHIC Clinical Trial Update
October 13, 2023
**Agenda**

**Welcome & Introduction**
Lloyd M. Segal, President & CEO

**Lunresertib Preliminary MYTHIC Monotherapy & Combination Therapy Clinical Trial Results**
Timothy Yap, MBBS, PhD, FRCP, Principal Investigator, MYTHIC Trial

**Conclusions & Lunresertib Development Plan**
Maria Koehler, MD, PhD, Chief Medical Officer

**Upcoming Catalysts**
Lloyd M. Segal, President & CEO

**Q&A**
Repare Therapeutics Leadership & Dr. Yap
Disclaimer

Statements contained in this presentation regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as “anticipates,” “believes,” “expects,” “intends,” “plans,” “potential,” “projects,” “would” and “future” or similar expressions are intended to identify forward-looking statements. Each of these forward-looking statements involves substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by such forward-looking statements. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including specifically our clinical trials of lunsartin (RP-6308) and carmonerbin; the expected timing of program updates and data disclosures; the timing of filing INDs and other regulatory documents; the timing and likelihood of seeking regulatory approval for our product candidates; the competitive landscape for our product candidates; our ability to identify and develop additional product candidates using our SNIPRx platform; and our estimates regarding expenses, future revenue, capital requirements, cash runway and needs for additional financing.

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 August 9, 2023, and other documents we subsequently file with or furnish 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.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

So, for convenience, the trademarks and trade names in this presentation may be referred to without the © and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.
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
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, genometrically 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
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>Tumor Type</th>
<th>Prevalence of Genes of Interest</th>
<th>Eligible Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine</td>
<td></td>
<td>7,000</td>
</tr>
<tr>
<td>Ovarian</td>
<td></td>
<td>6,300</td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td>9,000</td>
</tr>
<tr>
<td>Colorectal</td>
<td></td>
<td>24,500</td>
</tr>
<tr>
<td>Bladder</td>
<td></td>
<td>6,200</td>
</tr>
<tr>
<td>Cervical</td>
<td></td>
<td>1,300</td>
</tr>
<tr>
<td>Esophageal</td>
<td></td>
<td>4,500</td>
</tr>
<tr>
<td>Sarcoma¹</td>
<td></td>
<td>1,200</td>
</tr>
<tr>
<td>Lung Squamous²</td>
<td></td>
<td>5,300</td>
</tr>
</tbody>
</table>

¹ Soft Tissue Sarcoma only; ² Squamous subtype of Non-Small Cell Lung Cancer only

*Based on estimated number of pts treated in Fis trials, advanced setting for diagnosed and new recurrent patients (CancerMAP), Treatment Architecture, United States, 2001; accessed 6/19/01 and lesion prevalence (TCGA); ¹ Soft Tissue Sarcoma only; ² Squamous subtype of Non-Small Cell Lung Cancer only
Lunresertib Preliminary Monotherapy & Combination Therapy Clinical Trial Results

Timothy Yap, MBBS, PhD, FRCP, Principal Investigator, MYTHIC Trial
Study principal investigator: Timothy Yap, MBBS, PhD, FRCP

Medical Oncologist and Physician-Scientist at the University of Texas, MD Anderson Cancer Center
- Professor, Department for Investigational Cancer Therapeutics (Phase 1 Program)
- Vice President, Head of Clinical Development in the Therapeutics Division
- Primary research focuses on the first-in-human and combinatorial development of molecularly targeted agents and immunotherapies, and their acceleration through clinical studies using novel predictive and pharmacodynamic biomarkers
- Main interests include the targeting of the DNA damage response with novel therapeutics, such as ATR and PARP inhibitors, as well as the development of novel immuno-therapeutics
- BSc degree in Immunology and Infectious Diseases and MD from Imperial College London, UK
Speaker disclosures: Timothy Yap, MBBS, PhD, FRCP

I have the following relevant financial relationships to disclose:

- **Employee of:** University of Texas MD Anderson Cancer Center, where I am Vice President, Head of Clinical Development in the Therapeutics Discovery Division, which has a commercial interest in DDR and other inhibitors (IACS30380/ART0380 was licensed to Artios)


- **Grant/Research support from:** Acrivon, Artios, AstraZeneca, Bayer, Belgene, BioNTech, Blueprint, BMS, Boundless Bio, Clovis, Constellation, Cytal, Eli Lilly, EMD Serono, Forbuis, F-Star, GlaxoSmithKline, Genentech, Hailie, Ideaya ImmuneSensor, Insilico Medicine, Ionis, Ipsen, Jounce, Karyopharm, KSO, Kyowa, Merck, Mirati, Novartis, Pfizer, Ribbon Therapeutics, Regeneron, Repare, Rubius, Sanofi, Scholar Rock, Seattle Genetics, Tango, Tesaro, Vivece and Zenith

- **Stockholder in:** Seagen
PKMYT1 was identified as a strong synthetic lethal partner to CCNE1 amplification

Cyclin E overexpression (O/E) drives premature S-phase entry, overloads the DNA replication machinery, resulting in genome instability.

Genome-wide CRISPR-Cas9 screen

**Chemogenomic screen identified novel sensitizers to PKMYT1i**

**Inactivating mutations in FBXW7, E3 ubiquitin ligase, increase cyclin E levels and replication stress.**

**Hotspot inactivating mutations in PP2A phosphatase increase replication stress.**

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SNP/INS/DEL: Indications that are essential for fitness in CCNE1-O/E cells but not their wild type counterparts. 

STEP (SNAP): Targeted Expansion of Patient Populations. 

LOF: Mutations that are essential for fitness in a cell in which the control. 

PKMYT1, protein kinase, mitogen associated tyrosine/threonine 1. 

Synthetic Lethal: Interactions for Precision Therapeutics platform. 

PP2A, protein phosphatase 2A.
## Lunresertib: Potent and selective first-in-class PKMYT1 inhibitor

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Lunresertib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme potency (IC₅₀, nM)</td>
<td>3</td>
</tr>
<tr>
<td>HCC1569 CDK1 T14 phosphorophorylation (IC₅₀, nM)</td>
<td>20</td>
</tr>
<tr>
<td>HCC1569 cell viability (EC₅₀, nM)</td>
<td>19</td>
</tr>
<tr>
<td>PKMYT1 selectivity over WEE1 (cell-based)</td>
<td>&gt;100-fold</td>
</tr>
<tr>
<td>CYP inhib (3A4, 2D6, 2C9, 1A2, 2C19)</td>
<td>all &gt;30 μM</td>
</tr>
<tr>
<td>Hepatocytes: rat, dog, human</td>
<td>28, &lt;5, &lt;6</td>
</tr>
<tr>
<td>CLₐu (μL/min/10⁶ cells)</td>
<td>79%</td>
</tr>
<tr>
<td>Human plasma protein binding</td>
<td></td>
</tr>
<tr>
<td>Rat PK (%F, t₁/₂)</td>
<td>44%, 2.6h</td>
</tr>
<tr>
<td>Dog PK (%F, t₁/₂)</td>
<td>74%, 5.5h</td>
</tr>
</tbody>
</table>

### Lunresertib profile:

- Highly potent and selective inhibitor
- PanLabs Lead Profiling screen on 68 assays showed no significant activity at 10 μM
- No activity (>100 μM) in patch clamp assays for hERG, hNaV1.5, and hCaV1.2 ion channels
- Favorable pre-clinical PK profile
- Low potential for clinical drug-drug interactions

ADME: absorption, distribution, metabolism, excretion; CDK, cyclin-dependent kinase; EC₅₀, effective concentration; F, bioavailability; tₐ/₂, half-arrival inhibition concentration; min, minute; PK, pharmacokinetics; PKMYT1, protein kinase, membrane associated tyrosine/threonine 1; Thr, threonine.
Lunresertib monotherapy inhibits xenograft growth across doses and schedules.
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

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1. AAN poster B67: Galt et al. Preclinical development of PKMYT1 and ATR inhibitor combinations. ATR, ataxia telangiectasia and Rad3-related; CDC25, cell division cycle 25; CDK, cyclin-dependent kinase; CHK1, checkpoint kinase 1; PKMYT1, protein kinase, membrane associated tyrosine/threonine 1.
Lunresertib and camonsertib combination treatment is active in **CCNE1** amplified or **FBXW7** altered tumor models

**Combination treatment drives tumor regressions at sub-efficacious single-agent doses**

**OVCAR3 Ovarian Cancer**
*CCNE1* amplified CDX model

- Vehicle
- Lunresertib 11.7 mg/kg BID 3-on/4-off
- Camonsertib 5 mg/kg QD 3-on/4-off
- Lunresertib 11.7 mg/kg + Camonsertib 5 mg/kg

**DLD1 Colorectal Cancer**
*FBXW7* Knockout CDX model

- Vehicle
- Lunresertib 5 mg/kg BID continuous
- Camonsertib 10 mg/kg QD 3-on/4-off
- Lunresertib 5 mg/kg + Camonsertib 10 mg/kg

Camonsertib alone has limited activity in **CCNE1** and **FBXW7** altered PDX models*

*Additional internal Repare data, not shown. Free drug exposure of 5-10 mg/kg dose in mice (AUC or Cmax) are comparable to that at the respective human PKPDs. 5-on/2-off, 5 days on / 2 days off; 3-on/off, 3 days on / 4 days off; AUC, area under the curve; BID, twice daily; Cam, camonsertib; Lun, lunresertib; QD, once daily. PKPD, recommended phase 1 dose.
Inclusion criteria:

- Patients ≥12 y with solid tumors resistant/intolerant to standard therapy
- Local NGS report (tissue or plasma)*
- Tumors with CCNE1 amplification**, deleterious Fbxw7 or PPP2R1A alterations***
- ECOG PS of 0-2
- Hgb ≥ 9 g/dL
- Platelets ≥ 100 K/uL
- ANC ≥ 1.5 K/uL

Study is ongoing NCT04855656

Primary endpoints:
- Safety and tolerability
- RP2D, schedule

Other endpoints:
- PK
- PD in paired tumor biopsies
- Preliminary antitumor activity
- Kinetics of ctDNA
### MYTHIC: Patient demographics

#### Similar patient characteristics in monotherapy and combination therapy cohorts

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(Lun alone) N=67</th>
<th>(Lun + Cam) N= 59</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (25.4)</td>
<td>15 (25.4)</td>
</tr>
<tr>
<td>Female</td>
<td>50 (74.6)</td>
<td>44 (74.6)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>60 (15, 81)</td>
<td>65 (16, 81)</td>
</tr>
<tr>
<td>≥65 years, n (%)</td>
<td>25 (37.3)</td>
<td>30 (50.8)</td>
</tr>
<tr>
<td><strong>ECOG PSa, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>21 (31.3)</td>
<td>23 (39.0)</td>
</tr>
<tr>
<td>1/2</td>
<td>44 (65.7) / 1 (1.5)</td>
<td>36 (59.3) / 0</td>
</tr>
<tr>
<td><strong>Prior lines of therapy, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (1.5)</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>21 (31.3)</td>
<td>24 (40.7)</td>
</tr>
<tr>
<td>3-4</td>
<td>25 (37.3)</td>
<td>24 (40.7)</td>
</tr>
<tr>
<td>≥5</td>
<td>20 (29.9)</td>
<td>11 (18.6)</td>
</tr>
<tr>
<td><strong>Prior platinum, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=67</td>
<td>58 (88.6)</td>
<td>51 (86.4)</td>
</tr>
</tbody>
</table>

#### Tumor types, n (%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(Lun alone) N=67</th>
<th>(Lun + Cam) N= 59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrialb</td>
<td>23 (34.3)</td>
<td>17 (28.8)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>11 (16.4)</td>
<td>13 (22.0)</td>
</tr>
<tr>
<td>Ovarian</td>
<td>11 (16.4)</td>
<td>11 (18.6)</td>
</tr>
<tr>
<td>Breast</td>
<td>3 (4.5)</td>
<td>3 (5.1)</td>
</tr>
<tr>
<td>Lung</td>
<td>0</td>
<td>3 (5.1)</td>
</tr>
<tr>
<td>Otherc</td>
<td>19 (28.4)</td>
<td>12 (20.3)</td>
</tr>
</tbody>
</table>

#### Most common genotypesd, n (%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(Lun alone) N=67</th>
<th>(Lun + Cam) N= 59</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCNE1</td>
<td>31 (46.3)</td>
<td>20 (33.9)</td>
</tr>
<tr>
<td>FBXW7</td>
<td>21 (31.3)</td>
<td>23 (39.0)</td>
</tr>
<tr>
<td>PPP2R1A</td>
<td>12 (17.9)</td>
<td>13 (22.0)</td>
</tr>
<tr>
<td>PPP2R1A and CCNE1</td>
<td>0</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>PPP2R1A and FBXW7</td>
<td>1 (1.5)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>FBXW7 and CCNE1</td>
<td>0</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Unselected endometriale</td>
<td>2 (3)</td>
<td>0</td>
</tr>
</tbody>
</table>

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*a* Each pediatric patient is included in monotherapy and combination with ECOG Performance Status score 0 and 10, respectively. **b** Includes uterine cervix, endometrium, and breast. **c** Other tumor types in monotherapy: esophageal (n=1), head and neck (n=2), osteosarcoma (n=3), osteosarcoma (n=3) and one each (bladder, brain, cervical, gallbladder, and melanoma). **d** Includes esophageal: adenocarcinoma, gallbladder: adenocarcinoma, and melanoma: malignant. **e** Includes endometrial: CCNE1, FBXW7, or PPP2R1A. **f** ECOG PS, Eastern Cooperative Oncology Group Performance Status; GI, gastrointestinal; Lun, lunercisertib; Cam, camisertib; ECOG PS, Eastern Cooperative Oncology Group Performance Status.
Multiple doses/schedules of lunresertib tested

- Adaptive BOIN design, sufficient cohort sizes to establish MTD/RP2D
- QD dose tested first, once half-life known, BID dose was then tested
- Continuous and intermittent schedules showed similar activity in preclinical efficacy models
- DLT: reversible rash
- Intermittent weekly schedule minimized rash**
- Exposure with and without food was similar at preliminary RP2D

- 5 days on/2 days off and 3 days on/4 days off were evaluated.
- ** Investigation of the mechanism of rash ongoing.

**BOIN: Bayesian optimal interval; DLT, dose-limiting toxicity; MTD, maximum tolerated dose; QD, once daily; RP2D, recommended phase 2 dose.
Lunresertib monotherapy: Treatment related adverse events (TRAEs)

Limited and reversible low-grade toxicity in monotherapy is encouraging for combination therapies

<table>
<thead>
<tr>
<th>TRAEs in ≥15% of patients, n (%)</th>
<th>All Patients N=67</th>
<th></th>
<th>Preliminary RP2D 80-100mg BID-I N=8</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades</td>
<td>G3</td>
<td>G4</td>
<td>All Grades</td>
</tr>
<tr>
<td>Rash*</td>
<td>23 (34.3)</td>
<td>5 (7.5)</td>
<td>0</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>21 (31.3)</td>
<td>1 (1.5)</td>
<td>0</td>
<td>2 (25.0)</td>
</tr>
<tr>
<td>Anemia</td>
<td>15 (22.4)</td>
<td>4 (6.0)</td>
<td>0</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15 (22.4)</td>
<td>1 (1.5)</td>
<td>0</td>
<td>3 (37.5)</td>
</tr>
</tbody>
</table>

- **Safety profile encouraging**
  - Infrequent Grade 3 and no reported Grade 4 TRAEs across all doses evaluated
  - Preliminary RP2D range (80-100mg BID, intermittent) demonstrates encouraging tolerability profile

- **Favorable tolerability, with manageable AEs**
  - Dose reductions limited to 14.9% of patients
  - Rash* improves, as early as 48 hours, with supportive care or lunresertib interruption

* Rash terms included: dermatitis confluent, acne; erythema, flushing, pruritis, rash; rash erythematous; rash maculopapule; rash pruritic; skin exfoliation. BID-I: twice daily; RP2D: recommended phase II dose.
Human lunresertib PK is linear up to daily doses of 160-240 mg with a half-life of ~9 hours.

PK exposures similar between QD and BID schedules and exceeded the target exposure for inhibition of pCDK1.
Lunresertib monotherapy mechanism of action confirmed in paired biopsies

**pCDK1-Thr14** (Direct Target Inhibition IHC, pCDK1 target -50%*)

![Graph showing relative change from baseline (%) for pretreatment vs. on-treatment (n=17; p=0.003).]

Enrollment gene
- CCNE1
- FBXW7
- Unselected

-50%

- Pretreatment vs. On-treatment (n=17; p=0.003)

**YH2AX** (Induction of DNA Damage IHC, YH2AX target 2-fold)

![Graph showing relative change from baseline (%) for pretreatment vs. on-treatment (n=25; p=0.022).]

Enrollment gene
- FBXW7
- PPP2R1A
- CCNE1
- Unselected

Due to assay differences, IHC -50% target inhibition corresponds to ~60% inhibition by ELISA when maximal tumor growth inhibition in preclinical models was measured. Protein expression using paired samples with Wilcoxon sign rank test comparing ~20 pCDK1 and YH2AX positive cells pre-treatment vs. on-treatment. CCNE1, cyclin-dependent kinase 1; ELISA, enzyme-linked immunosorbent assay; IHC, immunohistochemistry; Lunre, lunresertib; pCDK1, phosphorylated cyclin-dependent kinase 1; PKMYT1, protein kinase, membrane-associated tyrosine/threonine 1; Thr, threonine.
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

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

MOI, twice daily; intermittent; cPR, complete partial response; LN, lymph node; RECIST, Response Evaluation Criteria in Solid Tumors; PFS, progression-free survival; RP2D, recommended phase 2 dose; TA, tumor assessment.
MYTHIC: PKMYT1 inhibition for the treatment of Cancers (N=126)

Inclusion criteria:
- Patients ≥12 y with solid tumors resistant/intolerant to standard therapy
- Local NGS report (tissue or plasma)*
- Tumors with CCNE1 amplification**, deleterious FBXW7 or PPP2R1A alterations
- ECOG PS of 0-1
- Hgb ≥ 10 g/dL
- Platelets ≥ 100 K/uL
- ANC ≥ 1.5 K/uL

Study ongoing NCT04855656

Module 1:
- Single agent lunresertib
  - 67 patients

Module 2:
- Lunresertib with camonsertib
  - 59 patients

Primary endpoints:
- Safety and tolerability
- RP2D, schedule

Other endpoints:
- PK
- PD in paired tumor biopsies
- Preliminary antitumor activity
- Kinetics of ctDNA

* NGS report centrally reviewed and annotated by Precision Oncology Decision Support (PODS) Group at MDACC. ** CCNE1 amplification (Copy number ≥6), ANC: absolute neutrophil count; ctDNA, circulating tumor DNA; ECOG, Eastern Cooperative Oncology Group; Hgb, hemoglobin; NGS, next generation sequencing; PD, pharmacodynamics; PK, pharmacokinetics; RP2D, recommended phase 2 dose.
Lunresertib with camonsertib dose escalation

**Thorough dose/schedule evaluation**

- **Camonsertib**
  - 80mg* QD
  - 3d on / 4d off

- **Lunresertib**
  - 40mg BID, Continuous
    - N=5
  - 80mg BID
    - 3d on / 4d off
    - N=21**
  - 60mg BID
    - 3d on / 4d off
    - N=15
  - 120mg QD
    - Continuous
    - N=6
  - 240mg QD
    - 3d on / 4d off
    - N=12

**RP2D/schedule optimization**

- **Camonsertib**
  - 80mg QD
    - 3d on / 4d off

- **Lunresertib**
  - 80mg BID
    - 3d on / 4d off

**Preliminary RP2D:** N=20

---

* Tested doses derived from single agent exposure values. ** Of the 59 patients, 57 were given 80mg and 2 patients received 120mg of camonsertib. ** One patient started at the daily dose of lunresertib 80mg QD 3d on / 4d off and was then escalated to 80mg BID. BID, twice daily; QD, once daily; RP2D, recommended phase 2 dose.
Lunresertib + camonsertib: Treatment related adverse events (TRAES)

<table>
<thead>
<tr>
<th>TRAEs in ≥15% of patients, n (%)</th>
<th>All Grades</th>
<th>G3</th>
<th>G4</th>
<th>All Grades</th>
<th>G3</th>
<th>G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>40 (67.8)</td>
<td>25 (42.4)</td>
<td>0</td>
<td>13 (65.0)</td>
<td>9 (45.0)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>38 (64.4)</td>
<td>0</td>
<td>0</td>
<td>9 (45.0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>24 (40.7)</td>
<td>0</td>
<td>0</td>
<td>5 (25.0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Rash*</td>
<td>23 (39.0)</td>
<td>1 (1.7)</td>
<td>0</td>
<td>7 (35.0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>12 (20.3)</td>
<td>2 (3.4)</td>
<td>0</td>
<td>3 (15.0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>11 (18.6)</td>
<td>7 (11.9)</td>
<td>2 (3.6)</td>
<td>3 (15.0)</td>
<td>2 (10.0)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>9 (15.3)</td>
<td>0</td>
<td>0</td>
<td>3 (15.0)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- Combination therapy DLT: anemia, rash/mucositis, and neutropenia
- Preliminary RP2D: lunresertib 80 mg BID + camonsertib 80 mg QD; both 3d on/4d off
  - Weekly or 2 weeks on/1 week off — schedule optimization ongoing
  - Dose of camonsertib is ~50% lower than the monotherapy RP2D

\[\text{TRAEs in ≥15% of patients, n (%)}\]

\[\text{Anemia}\] was the most common TRAE
- Likely due to synergy and ATRi effect\(^1\)
- Grade 3 anemia detected early (<6w) in patients with high-risk features\(^1\); others had later onset (>6w)
- Did not lead to discontinuations
- Usually improved with 1w drug hold

\[\text{Nausea/vomiting, alleviated with food}\]

---


\(^*\) Rash terms included: dermatisis confluent, exzema, erythema, flaking, pruritus, rash, rash-erythematous, rash maculopapular, rash pruritic, skin exfoliation.

\(^\dagger\) Median values at entry: Pts = 70, F = 77, F; previous therapy = 4; median age = 59 y.

\(^\ddagger\) ATRi, axitinib and lenalidomide and fludarabine-related TRAE; BID, twice daily; G, grade; Hbg, hemoglobin; QD, once daily; RP2D, recommended phase 2 dose; TRAE, treatment-related adverse events; n, week.
Direct target inhibition (pCDK1-Thr14) is enhanced with combination treatment

- More tumors had a 50% pCDK1 reduction with combination (69%, 11/16) compared to monotherapy (47%, 8/17)

*Due to assay differences, IHC ≥50% target inhibition corresponds to ≥80% inhibition by ELISA when maximal tumor growth inhibition in preclinical models was recorded. ATR, ataxia telangiectasia and Rad3-related; Cam, camosertib; CDK1, cyclin-dependent kinase 1; Lurra, lunresertib; pCDK1, phosphorylated cyclin-dependent kinase 1; PKMYT1, protein kinase, membrane associated tyrosine/threonine 1; Thr, threonine.
## 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><strong>PPP2R1A/FBXW7</strong></td>
<td>cPR</td>
<td>-55.9</td>
<td>30.4</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td><strong>PPP2R1A/CCNE1</strong></td>
<td>cPR</td>
<td>-53.0</td>
<td>18.1</td>
<td>2/Y</td>
</tr>
<tr>
<td></td>
<td><strong>FBXW7</strong></td>
<td>cPR</td>
<td>-100.0</td>
<td>11.1+</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td><strong>FBXW7</strong></td>
<td>uPR</td>
<td>-39.6</td>
<td>16.0</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td><strong>FBXW7</strong></td>
<td>uPR</td>
<td>-44.7</td>
<td>11.4+</td>
<td>3/Y</td>
</tr>
<tr>
<td>Ovarian</td>
<td><strong>CCNE1</strong></td>
<td>cPR</td>
<td>-70.2</td>
<td>21.4+</td>
<td>2/Y</td>
</tr>
<tr>
<td></td>
<td><strong>CCNE1</strong></td>
<td>cPR</td>
<td>-30.8</td>
<td>12.6+</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td><strong>CCNE1</strong></td>
<td>CA-125</td>
<td>-16.9</td>
<td>29.0+</td>
<td>9/Y</td>
</tr>
<tr>
<td></td>
<td><strong>CCNE1</strong></td>
<td>CA-125</td>
<td>-23.1</td>
<td>37.0+</td>
<td>2/Y</td>
</tr>
<tr>
<td></td>
<td><strong>CCNE1</strong></td>
<td>CA-125</td>
<td>13.6</td>
<td>12.9+</td>
<td>5/Y</td>
</tr>
<tr>
<td>Cervical</td>
<td><strong>PPP2R1A</strong></td>
<td>cPR</td>
<td>-44.4</td>
<td>11.0+</td>
<td>1/Y</td>
</tr>
<tr>
<td>Colorectal</td>
<td><strong>FBXW7</strong></td>
<td>cPR</td>
<td>-43.3</td>
<td>27.6</td>
<td>3/Y</td>
</tr>
<tr>
<td>Bile duct</td>
<td><strong>CCNE1</strong></td>
<td>cPR</td>
<td>-35.0</td>
<td>28.1</td>
<td>2/Y</td>
</tr>
<tr>
<td>Breast</td>
<td><strong>FBXW7</strong></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 date as of Oct. 6, 2023. Relevant patient tumor characteristics: "BRCA1 rearrangement and "BRCA2 deleterious mutation. *Treatment ongoing. BL, baseline; cPR, confirmed partial response; 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), esophagus (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: 9/10 (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 (n=1 post-baseline tumor assessment). CBR, clinical benefit rate; OR, overall response based on RECIST v1.1; CA-125 response; MRR, molecular response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; Gynecologic Cancer InterGroup (GCIG) RP2D, recommended phase 2 dose.
Meaningful tumor reductions across lunresertib-sensitizing alterations

- **OR across all genotypes:**
  - 33.3% in **CCNE1** (n=18)
  - 17.4% in **FBXW7** (n=23)
  - 21.4% in **PPP2R1A** (n=14)

- **CBR is promising across genotypes:**
  - 44% in **CCNE1** (n=18)
  - 35% in **FBXW7** (n=23)
  - 50% in **PPP2R1A** (n=14)

- **MRR:**
  - 40% in **CCNE1** (n=10)
  - 44% in **FBXW7** (n=9)
  - 80% in **PPP2R1A** (n=5)

*Treatment ongoing

Tumor genomic alteration: CCNE1, FBXW7, PPP2R1A

*Patients with lunresertib-sensitizing co-alterations: 1 each (FBXW7/CCNE1, PPP2R1A/CCNE1, and PPP2R1A/FBXW7). Data represent the efficacy evaluable patient population with ≥ 1 post-baseline tumor assessment. CBR, clinical benefit rate; MRR, molecular response rate; OR, overall response based on RECIST or CR, CC-45 response.
Clinical benefit: Combination treatment across lunresertib-sensitizing alterations and doses

- OR across all genotypes:
  - 33.3% in CCNE1 (n=18)
  - 17.4% in FBXW7 (n=23)
  - 21.4% in PPP2R1A (n=14)

- CBR is promising across genotypes:
  - 44% in CCNE1 (n=18)
  - 35% in FBXW7 (n=23)
  - 50% in PPP2R1A (n=14)

- Treatment ongoing in 16 patients

- Efficacy and tolerability assessments continue to optimize RP2D in tumor- and alteration-selected expansions

* patients with lunresertib-sensitizing co-alterations: 1 each (FBXW7/CCNE1, PPP2R1A/CCNE1, and PPP2R1A/FBXW7). Data represent the efficacy evaluable patient population (≥ post-baseline tumor assessment). CBR, clinical benefit rate; OR, overall response based on RECIST or CODA CA 125 response; PR, partial response; TL, target lesion; RP2D, recommended phase 2 dose.
Significantly higher molecular responses confirm the benefit of combination treatment

Molecular responses were observed across lunresertib-sensitizing molecular alterations\(^1\)

### Lunresertib monotherapy

MRR: 3/30 (10%)

### Lunresertib + camonsertib

MRR: 12/24 (50%)

Molecular response rate in combination therapy was significantly higher than with monotherapy \(p=0.003\)

\(^1\)\text{ASCE gander 2017, Gals et al. Molecular responses: \(\geq 50\%\) decline in mVAF as assessed by Tempos if and Tempos if+ gene panels for patients with detectable somatic alterations in monotherapy and combination therapy, respectively; \text{best mVAF} capped at \(+100\%\). p-values of monotherapy vs. combination therapy determined using chi-squared test. MRR: molecular response rate; mVAF: mean variant allele frequency.}\n
Early response in recurrent FBXW7 mutated colorectal adenocarcinoma

- Overall response: cPR (RECIST)
- RECIST target lesion decrease -43.3%
- Received therapy for 27.6 weeks

<table>
<thead>
<tr>
<th>Left para-aortic lymph node</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
</tbody>
</table>

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

Pre-treatment
On-treatment
ctDNA Dynamics

- Genes: ALR c.1118T
- AKT c.2343T
- FBXW7 c.807T
- NOTCH1 c.3004T

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

Overall response: cPR (RECIST)

RECIST target lesion decrease -70.2%

Therapy ongoing for >21 weeks

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

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

CA-125 dynamics

3/4: 3 days on/4 days off; BID, twice daily; CH, chemotherapy; cPR, confirmed partial response; RECIST, Response Evaluation Criteria in Solid Tumors; QD, once daily; RP2D, recommendd phase 2 dose; TA, tumor assessment.
Conclusions & Lunresertib Development Plan
Maria Koehler, MD, PhD, Chief Medical Officer
**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**
**Lunresertib + camonsertib combination therapy (additional data)**

**MYTHIC is a dose finding Phase 1 study: Preliminary RP2D range identified, schedule optimization ongoing.** RP2D is important; only 18 pts were treated at preliminary RP2D range.

**Anemia is the primary tolerability issue to alleviate.** Our experience and our emerging understanding of the anemia promises a range of simple solutions for patients.

**Gynecological cancers are the largest trial population with strongest signal so far.** We expect a robust signal at refined dose and schedule with increasing patient numbers.

**We are highly interested in multiple other tumors.** Numerous opportunities and nothing is off the table.

---

## Treatment at preliminary RP2D increases efficacy

Gynecologic cancers provide most robust example of criticality of sufficient exposure

<table>
<thead>
<tr>
<th>Gynecologic Cancers Only:</th>
<th>RP2D (N=10)</th>
<th>Non-RP2D (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response (RECIST/CA-125)</td>
<td>6 (60.0%)</td>
<td>4 (25.0%)</td>
</tr>
<tr>
<td>RECIST response (confirmed+unconfirmed) **</td>
<td>5 (50.0%)</td>
<td>2 (12.5%)</td>
</tr>
<tr>
<td>CBR</td>
<td>7 (70.0%)</td>
<td>8 (50.0%)</td>
</tr>
<tr>
<td>Therapy Ongoing Without PD</td>
<td>5 (50%)</td>
<td>5 (31.3%)</td>
</tr>
</tbody>
</table>

Most doses were below daily RP2D exposure
More patients still ongoing at RP2D level
Patient split between RP2D and Non-RP2D reflects thorough dose finding; only most recent patients at RP2D exposures.
Enrollment now open in multiple tumor expansions with RP2D optimization

**additional endometrial cancer with uPR after data base lock for total of 6 RECIST responders.
Anemia likely a result of synergistic combination effect

Mostly a sole, manageable event, suggestive of narrow bone marrow effect

Dose optimization and individualized patient management now in place:

1) Maintain RP2D weekly in patients without anemia
2) Early onset: schedule adjustment
3) Late onset: “on demand” modifications

Gr 3 anemia at RP2D reflects higher risk population

- 8/9 pts w Gr3 anemia entered study w anemia; median Hb = 10.7 g/dL
- Median age 59y, 3 were >70 years old
- Median previous therapies was 4

Assessment of this approach and dose/schedule optimization is ongoing
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 (n=1 post-baseline tumor assessment). CBR, clinical benefit rate; OR, overall response based on RECIST v1.1 or sRECIST CA-125 response; MRR, molecular response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; Gynecologic Cancer InterGroup (GCIG); RP2D, recommended phase 2 dose.
Opportunity across multiple tumor types: emerging signals from Phase 1 trial – non gynecologic tumors

Multiple development options: Additional investigation ongoing

Small #pts in 11 different tumors

1/3 of patients with NSCLC have 10m PFS
1/3 of patients with upper GI cancer have 10m PFS
1/2 of patients with cholangio: cPR
1/3 of patients with breast cancer: uPR, continuous target lesion shrinkage

CRC of keen interest: N=13, only 4 at RP2D, one cPR, 4 treated >16 weeks, including one for >1 year
Evolving broad trial program: sponsored and collaborative

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

**Lunresertib Combination Therapy**

- **MAGNETIC:** + Gemcitabine
- **MYTHIC:** + Camonsertib
- **MINOTAUR:** + FOLFIRI
- **IST:** + CCTG¹
- **IST:** + Carbo/paclitaxel²

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

¹ Canadian Clinical Trial Group (CCTG) collaborations include NCT06605500 and NCT05601440.
² SOC for 1st-line ovarian cancer is carboplatin/liposomal (Platinol). PARP maintenance therapy or carboplatin/liposomal with bevacizumab + bev maintenance therapy; this IST supports potential 1st line combination studies as triplet therapy in patients with CCNE1 amplified tumors.
MYTHIC trial: Key takeaways and next steps

- Validated lunresertib mechanism of action and SNIPRx preclinical patient selection approach

- Safety, tolerability, early efficacy signals confirmed in camonsertib combination therapy

- 50% RECIST response observed in camonsertib combination in 10 pts in largest cohort (gynecological tumors) at preliminary RP2D, underscoring high opportunity in other tumor types we are now enrolling

- Clear understanding of anemia pattern facilitates patient friendly, simple management; Update 2024

- MYTHIC trial expanded to evaluate combination therapy in patients with select tumor types and genomic alterations; Expect to report additional data in 2H 2024

- Oncology and patient communities taking high interest in emerging data accelerating the expansion of lunresertib development as MYTHIC moves ahead
Upcoming Catalysts
Lloyd M. Segal, President & CEO
# Upcoming milestones

<table>
<thead>
<tr>
<th>2H 2023</th>
<th>1H 2024</th>
<th>2H 2024</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camonsertib Phase 2 TAPISTRY trial initiation</td>
<td>RP-1664 clinical trial initiation</td>
<td>RP-3467 (Polθi) clinical trial initiation</td>
</tr>
<tr>
<td>Lunresertib + carboplatin/paclitaxel combination Phase 1 IST initiation</td>
<td>Initial lunresertib + FOLFIRI combination Phase 1 data</td>
<td>Lunresertib + gemcitabine combination Phase 1 data</td>
</tr>
<tr>
<td>RP-1664 and RP-3467 (Polθi) focused investor event</td>
<td></td>
<td>Lunresertib + camonsertib combination Phase 1 data (expansion cohorts)</td>
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</tbody>
</table>
Insight that enriches. Precision that empowers.

Lunresertib MYTHIC Clinical Trial Update
October 13, 2023
Insight that enriches. Precision that empowers.
Disclaimer

Statements contained in this presentation regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as “anticipates,” “believes,” “expects,” “intends,” “plans,” “potential,” “projects,” “would” and “future” or similar expressions are intended to identify forward-looking statements. Each of these forward-looking statements involves substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by such forward-looking statements. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including specifically our clinical trials of lumaresant (RP-6306) and camorresant; the expected timing of program updates and data disclosures; the timing of filing INDs and other regulatory documents; the timing and likelihood of seeking regulatory approval for our product candidates; the competitive landscape for our product candidates; our ability to identify and develop additional product candidates using our SNIPRx platform; and our estimates regarding expenses, future revenue, capital requirements, cash runway and needs for additional financing.

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 August 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
Targeting the un-targetable through synthetic lethality

Genetic Alterations in Cancer

<table>
<thead>
<tr>
<th>Current Treatment Paradigm</th>
<th>Next Generation Therapeutics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Targetable</strong></td>
<td><strong>SNIPRx identifies and targets necessary genes to induce synthetic lethality</strong></td>
</tr>
<tr>
<td>Gain-of-function</td>
<td>- Highly targeted &amp; tumor-type agnostic approach</td>
</tr>
<tr>
<td>~29%</td>
<td>- Exploiting cancer cell genomic instability, including DNA damage repair</td>
</tr>
<tr>
<td><strong>Un-targetable</strong></td>
<td><strong>Platform validated with established and expanding clinical-stage pipeline</strong></td>
</tr>
<tr>
<td>Loss-of-function</td>
<td></td>
</tr>
<tr>
<td>~54%</td>
<td></td>
</tr>
<tr>
<td><strong>Un-targetable</strong></td>
<td></td>
</tr>
<tr>
<td>Gain-of-function</td>
<td></td>
</tr>
<tr>
<td>~17%</td>
<td></td>
</tr>
</tbody>
</table>
Enabling target identification & patient insights through SNIPRx®

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

![Diagram showing the process of target identification and patient insights through SNIPRx®](image-url)

- CANCER-ASSOCIATED GENETIC LESION
- NORMAL CELL
- Lethal
  - Viable
  - POTENTIAL SL DRUG TARGETS
  - Small molecule inhibitor (clinical candidate)
  - Viabl
  - Lethal SL genetic lesion
  - STEP² genetic alterations

Predicted responders
Predicted non-responders
### 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 (RP-3500/ RG6526)</td>
<td>ATM + 10 STEP2 lesions</td>
<td>ATR</td>
<td>Ph2 TAPESTRY</td>
<td>Ph1/2 Morphine-Lung</td>
<td>Ph1/2 TRES: Mono + PARP (olaparib) Combo</td>
<td>Ph1/2 ATTAC: PARP (olaparib/vinblastine) Combo</td>
<td>Ph1/2 TRES: Gemcitabine Combo</td>
</tr>
<tr>
<td>Lunresertib (RP-6306)</td>
<td>CCNE1, FBXW7 + others</td>
<td>PKMYT1</td>
<td>Ph2 CCGA 87’s</td>
<td>Ph1 MYT1: Mono + Camonsertib Combo</td>
<td>Ph1 MAGNETIC: Olaparib/Haplo Combo</td>
<td>Ph1 WINTAM: FPAR Combo</td>
<td>Ph1 Carboplatin/paclitaxel Combo IBT</td>
</tr>
<tr>
<td>RP-1664</td>
<td>Undisclosed</td>
<td>Undisclosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RP-3467 Pol I Inhibitor</td>
<td>BRCA1/2 + others</td>
<td>PolI</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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<td></td>
</tr>
<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

### Roche

**Global development and commercialization collaboration for Camonsertib**

- $135M upfront
- ~$1.2B potential milestones
- High single-digit to high-teens royalties
- 50/50 U.S. co-development, profit/cost share and co-promotion option

### Bristol Myers Squibb

**Multi-target discovery collaboration leveraging SNIPRx® discovery platform**

- $65M upfront
- ~$3B potential milestones
- Royalties
- Both SL targets and “undruggable” targets outside our focus
Proven experience in drug discovery and development

Leadership Team

Lloyd M. Segal  
President & CEO

Steve Forte, CPA  
Chief Financial Officer

Michael Zinda, PhD  
Chief Scientific Officer

Maria Koehler MD, PhD  
Chief Medical Officer

Cameron Black, PhD  
Head of Discovery

Philip Herman  
Chief Commercial, Portfolio Development Officer

Kim A. Seth, PhD  
Chief Business Officer

Daniel Bélanger  
Head of Human Resources

Scientific Founders

Daniel Durocher, PhD  
- Developed CRISPR SL platform  
- Deep DNA repair knowledge  
- Lerner-Van Tienstraub Research Institute (LTRI) & professor at University of Toronto

Agnel Sfeir, PhD  
- DDR and cancer pathway investigator  
- Pioneer in Polβ, genome instability  
- Professor, MSKCC

Frank Sicheri, PhD  
- Globally recognized structural biologist, expert in eukaryotic cell signaling, drug mechanism of action  
- LTRI & professor at University of Toronto
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

Initially identified CCNE1 amplification sensitive to PKMYT1 inhibition

STEPP² 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>Tumor Type</th>
<th>Prevalence of Genes of Interest</th>
<th>Eligible Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine</td>
<td>3.8% 12.2% 7.6% 4.7% 28.9%</td>
<td>7,000</td>
</tr>
<tr>
<td>Ovarian</td>
<td>3.3% 19.0% 26.0%</td>
<td>6,300</td>
</tr>
<tr>
<td>Stomach</td>
<td>10.2% 6.4% 17.7%</td>
<td>9,000</td>
</tr>
<tr>
<td>Colorectal</td>
<td>13.1% 14.7%</td>
<td>24,500</td>
</tr>
<tr>
<td>Bladder</td>
<td>5.6% 6.3% 12.2%</td>
<td>6,200</td>
</tr>
<tr>
<td>Cervical</td>
<td>9.1% 11.8%</td>
<td>1,300</td>
</tr>
<tr>
<td>Esophageal</td>
<td>7.1% 3.3% 11.5%</td>
<td>4,500</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>7.1% 7.8%</td>
<td>1,200</td>
</tr>
<tr>
<td>Lung Squamous</td>
<td>4.7% 7.6%</td>
<td>5,300</td>
</tr>
</tbody>
</table>

* Based on estimated number of pts treated in 1st line, advanced setting for diagnosed and new recurrent patients (CancerMktcl. Treatment Architecture. United States, 2021; accessed 6/19/20) 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

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

**Lunresertib Combination Therapy**
- **MAGNETIC:** + Gemcitabine
- **MYTHIC:** + Camosertib
- **MINOTAUR:** + FOLFIRI
- **IST:** + CCTG
- **IST:** + Carbo/paclitaxel

**Future Opportunities**
- Determined RP2D dose/schedule
- Progress to late-stage trials

- 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

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1. Canadian Clinical Trial Group (CCTG) collaborations include NCT06605590 and NCT06601440.
2. SODC for 1st line ovarian cancer is carboplatin/paclitaxel (6 cycles) + PARP maintenance therapy or carboplatin/paclitaxel with bevatinomab + bev maintenance therapy; 1st IST supports potential 1st line combination studies as triplet therapy in patients with CCNE1 unamplified tumors.
**Lunresertib:**

MYTHIC Preliminary Phase 1 Trial Results
(M1: Monotherapy)
(M2: Camonsertib Combination Therapy)

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**MONOTHERAPY**

Safe, well tolerated, and anti-tumor activity established (N=67)

Recommended Phase 2 dose: 80 to 100mg twice daily in intermittent schedule

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**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
--- | ---
Right paratracheal LN | Overall response: cPR (RECIST)
Left external iliac chain LN | RECIST target lesion decrease -41%

Further, 7 patients with <30% tumor shrinkage, and 2 patients with PFS > 6 and 14 months, respectively

BID-I, twice daily; intermittent; cPR, confirmed partial response; LN, lymph node; RECIST, Response Evaluation Criteria in Solid Tumors; PFS, progression-free survival; RP2D, recommended phase 2 dose; TA, tumor assessment.
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.

ATR activation (through CHK1-mediated inhibition of CDC25) results in inactive CDK1.
## 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>
</tr>
<tr>
<td></td>
<td>PPP2R1A/CCNE1</td>
<td>cPR</td>
<td>-53.0</td>
<td>18.1</td>
<td>2/Y</td>
</tr>
<tr>
<td></td>
<td>FBXW7</td>
<td>cPR*</td>
<td>-100.0</td>
<td>11.1+</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td>FBXW7</td>
<td>uPR</td>
<td>-39.6</td>
<td>16.0</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td>FBXW7</td>
<td>uPR*</td>
<td>-44.7</td>
<td>11.4+</td>
<td>3/Y</td>
</tr>
<tr>
<td></td>
<td>CCNE1</td>
<td>cPR</td>
<td>-70.2</td>
<td>21.4+</td>
<td>2/Y</td>
</tr>
<tr>
<td></td>
<td>CCNE1*</td>
<td>cPR*</td>
<td>-30.8</td>
<td>12.6+</td>
<td>3/Y</td>
</tr>
<tr>
<td>Ovarian</td>
<td>CCNE1</td>
<td>CA-125</td>
<td>-16.9</td>
<td>29.0+</td>
<td>9/Y</td>
</tr>
<tr>
<td></td>
<td>CCNE1</td>
<td>CA-125</td>
<td>-23.1</td>
<td>37.0+</td>
<td>2/Y</td>
</tr>
<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>
</tr>
<tr>
<td>Colorectal</td>
<td>FBXW7</td>
<td>cPR</td>
<td>-43.3</td>
<td>27.6</td>
<td>3/Y</td>
</tr>
<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 cut-off date as of Oct. 6, 2023. Relevant patient tumor co-exist.

† BRCA1 rearrangement and ‡ BRCA1 deleterious. + Treatment ongoing. BL, baseline; uPR, unconfirmed partial response; RECIST, Response Evaluation Criteria in Solid Tumors; TL, target lesion; Tx, treated; cPR, confirmed 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)

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*Efficacy evaluable patients only (1st 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 wks 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%)

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

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

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

Male 63 years old

Recurrent colorectal adenocarcinoma

FBXW7 Mutant

TP53 mut

3 prior lines of therapy

Lunr 240mg QD 3/4
Cam 80mg QD 3/4

Left para-aortic lymph node

Baseline TA - 6 weeks TA - 12 weeks

- Overall response: cPR (RECIST)

- RECIST target lesion decrease -43.3%

- Received therapy for 27.6 weeks

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 CCNE1 amplified ovarian cancer

<table>
<thead>
<tr>
<th>Tumor assessment</th>
<th>Baseline</th>
<th>6 wks</th>
<th>12 wks</th>
<th>18 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vul. Pedunculum</td>
<td>LA: 1.5 cm</td>
<td>LA: 0.7 cm</td>
<td>LA: 0.5 cm</td>
<td>LA: 0.7 cm</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>LA: 2.1 cm</td>
<td>LA: 1.2 cm</td>
<td>No viable lesion reported</td>
<td>No viable lesion reported</td>
</tr>
</tbody>
</table>

CA-125 dynamics

- Overall response: cPR (RECIST)
- RECIST target lesion decrease -70.2%
- Therapy ongoing for >21 weeks

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
MVC amp
TP53 mut

1 prior line of therapy

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

T01 Lymph nodes external iliac left

Tumor assessment

- 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

<table>
<thead>
<tr>
<th>Top 10 Tumor Types* with Highest Prevalence of ATM Deficiency</th>
<th>Top 10 Tumor Types* with Highest Prevalence of ATM Deficiency or STEP² Genomic Alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder Urothelial Carcinoma</td>
<td>Ovarian Serous Cystadenocarcinoma</td>
</tr>
<tr>
<td>Pancreatic Adenocarcinoma</td>
<td>Uterine Corpus Endometrioid Carcinoma</td>
</tr>
<tr>
<td>Lung Adenocarcinoma</td>
<td>Breast Invasive Carcinoma: Basal</td>
</tr>
<tr>
<td>Adrenocortical Carcinoma</td>
<td>Stomach Adenocarcinoma</td>
</tr>
<tr>
<td>Rectum Adenocarcinoma</td>
<td>Bladder Urothelial Carcinoma</td>
</tr>
<tr>
<td>Stomach Adenocarcinoma</td>
<td>Breast Invasive Carcinoma: LumB</td>
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<tr>
<td>Breast Invasive Carcinoma: LumB</td>
<td>Breast Invasive Carcinoma</td>
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<tr>
<td>Breast Invasive Carcinoma: LumA</td>
<td>Lung Adenocarcinoma</td>
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<tr>
<td>Breast Invasive Carcinoma</td>
<td>Colon Adenocarcinoma</td>
</tr>
<tr>
<td>Skin Cutaneous Melanoma</td>
<td>Cervical Squamous Cell Carcinoma</td>
</tr>
</tbody>
</table>

*Source: *TCGA; Not weighted for tumor prevalence

**Notation:**
- ATM: Ataxia Telangiectasia Mutated
- STEP²: Somatic Variation in Pressure

**Footnotes:**
- ATM Deficiency
- STEP² Genomic Alterations
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
**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*

Time on Treatment (wk) – Ovarian

Time to Disease Progression or Death – Ovarian

*Platinum refractory/resistant: progression on platinum or a platinum-free interval of ≤6 mo. CBR: OR or ≥15w on therapy without progression
Clinically relevant benefit in patients with BRCA1/2 mutations with monotherapy

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Description</th>
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<tbody>
<tr>
<td>14%</td>
<td>Overall response in BRCA1/2 (RECIST, 5/37)</td>
</tr>
<tr>
<td>43%</td>
<td>CBR for BRCA1/2 tumors</td>
</tr>
<tr>
<td>48%</td>
<td>CBR for post-PARPi BRCA1/2 tumors</td>
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**Time on Treatment (wk) – BRCA1/BRCA2**

*Module 1 subjects with > 100mg/day dose levels*

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Weeks</th>
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<tbody>
<tr>
<td>BRCA1</td>
<td></td>
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<tr>
<td>BRCA2</td>
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</table>

**Percent change from baseline in target lesions (BRCA1/BRCA2)**

*Module 1 subjects > 100mg/day dose levels*

<table>
<thead>
<tr>
<th>Gene Type</th>
<th>Percent Change from Baseline at Baseline Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td></td>
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<tr>
<td>BRCA2</td>
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</tbody>
</table>

CBR (OR or KL or on therapy without progression) was 40% for BRCA1 population, and 20% for BRCA2 population.
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%)

ORR, overall response rate; CBR, complete benefit rate; CR, complete response; PR, partial response; 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