# REC-617

## CDK7 inhibitor

Recursion

# **REC-617:** Potential best-in-class oral CDK7 inhibitor

### Biological Insight

**Combining** CDK7 inhibitors with agents **targeting complementary pathways** may achieve a more comprehensive anti-tumor response

### Design

AI-powered precision design to optimize PK/PD to **maximize potential therapeutic index** with **minimal** off-target effects

### In Vivo Data

Demonstrates **potent tumor regressions** with no body weight changes and favorable PK

### Clinical

Early monotherapy dose escalation data suggests **potential best-in-class** with a manageable safety profile and preliminary clinical activity

## What's Next

- Recruitment ongoing for **monotherapy & combination dose-escalation**
- Preliminary **ovarian combination data in 2027**

# **REC-617:** Phase 1/2 ELUCIDATE ongoing

Monotherapy Ph 1/2 ongoing; combination Ph 1 ongoing

## REC-617 Monotherapy

**Phase 1 Dose-Escalation**

✓ MTD achieved in advanced solid tumors

- Alternative dosing schedules ongoing

**Phase 2 Dose-Expansion**

- 2L+ platinum-resistant ovarian cancer with 10 mg REC-617 ongoing

## REC-617 Combinations

**Phase 1 Dose-Escalation – initiated 2H25**

- 2L+ platinum-resistant ovarian cancer with REC-617 in combination with standards of care
  - Bevacizumab and paclitaxel or
  - Pegylated liposomal doxorubicin (PLD)
- Potential to add additional tumor types in combination with standard of care

## Clinical Update

- Recruitment ongoing for all cohorts
- Preliminary ovarian combination data in **2027**

# **ELUCIDATE:** Monotherapy MTD for QD regimen identified in Phase 1/2 clinical trial of REC-617 in advanced solid tumors

**Key inclusion criteria**
- Unresectable, locally recurrent, or metastatic cancer
- Progressed following, or intolerant to, available SoC treatments
- ECOG PS 0-1

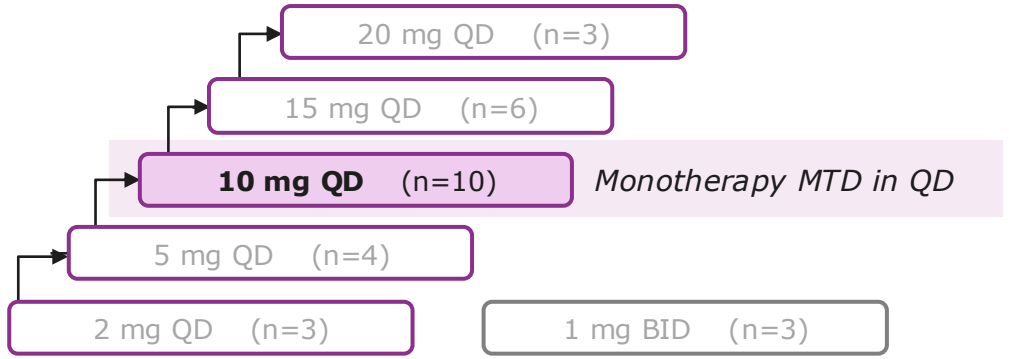
**Primary objective**
- PK and safety

**Secondary objective**
- Anti-tumor activity

**Data Cutoff Date:** 2025-09-29

| Patient Characteristics[1] | N=29 |
|---|---|
| **Median age (years)** | 60 |
| Range | 30-79 |
| **Tumor type** | |
| Breast carcinoma ($HR^+/HER2^-$)[2] | 4 (14%) |
| Colon adenocarcinoma | 13 (45%) |
| Non-small cell lung cancer (NSCLC) | 4 (14%) |
| Epithelial ovarian carcinoma | 7 (24%) |
| Pancreatic adenocarcinoma | 1 (3%) |
| **Median prior lines of prior systemic regimens** | 4 |

**Phase 1 Monotherapy Dose-Escalation**
*Continuous once-daily dosing summary*




- **10 mg continuous daily dosing established as MTD**
  - Manageable safety profile
  - Target coverage consistent with preclinical potency
  - Preliminary clinical activity observed
- Phase 1 combination escalation enrolling at 5 mg QD [MTD-1]



1. Data-cut off: 29 September 2025. All data shown as n (%) unless otherwise specified
2. All patients received CDK4/6 inhibitors in prior lines

Recursion

# **Phase 1 safety:** REC-617 monotherapy continues to show a manageable safety profile supporting best-in-class potential

Data Cutoff Date: 2025-09-29

| Adverse Event[1], n | | N=29 | |
|---|---|---|---|
| | | **All Grade** | **Grade ≥3** |
| **Treatment-Related Adverse Event (TRAE)** | | 26 (90%) | 8 (28%) |
| **Most Common TRAEs (≥20%)** | | | |
| *GI related* | **Diarrhea** | **20 (69%)** | 4 (14%) |
| | **Nausea** | **12 (41%)** | 1 (3%) |
| | **Vomiting** | **8 (28%)** | 1 (3%) |
| *Non-GI related* | Fatigue | 13 (45%) | 0 |
| | Decreased appetite | 9 (31%) | 2 (7%) |
| | Thrombocytopenia | 8 (28%) | 2 (7%) |
| **Other Class TRAEs** | | | |
| *Non-GI related* | Weight decreased | 5 (17%) | 0 |
| | ALT increased | 4 (14%) | 1 (3%) |
| | AST increased | 3 (10%) | 0 |
| | Stomatitis | 3 (10%) | 0 |

**Integrated safety analysis in all patients**

- Most TRAEs were **low grade** (Grade 1/2). **No Grade 4 or Grade 5**
- Most common DLTs were thrombocytopenia and nausea
- **7%** (N=2) discontinued due to a TRAE
  - 1 Grade 3 ALT increased[2]
  - 1 Grade 3 nausea

Safety and tolerability profile support **best-in-class** potential

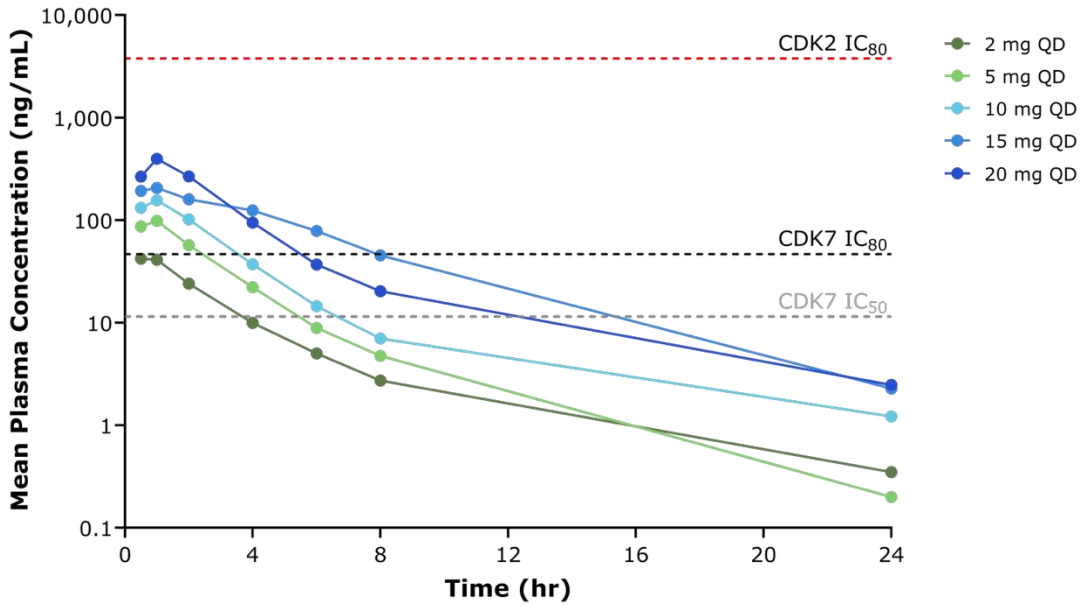
- Previously reported drug-related GI AEs from Phase 1 study of samuraciclib[3]
  - **Diarrhea (82%)**
  - **Nausea (77%)**
  - **Vomiting (80%)**



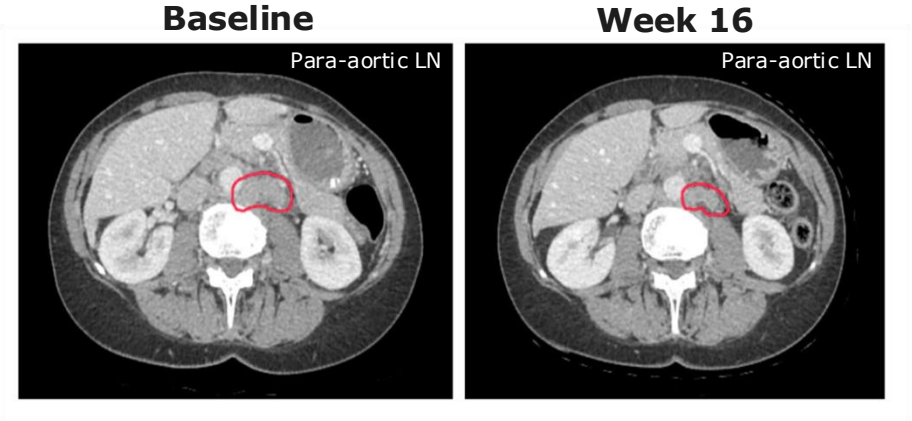
1. Data-cut off: 29 September 2025. All data shown as n (%) unless otherwise specified
2. Ovarian cancer patient with baseline liver metastases and history of liver resection
3. Coombes, RC, Nat Comms (2023). Phase 1 monotherapy dose escalation data (N=44), Supplementary Table 8

# **Phase 1 preliminary data:** Linear plasma PK profile and early signs of anti-tumor activity

## REC-617: Clinical Drug-Plasma C1D1 Exposure




- REC-617 demonstrates **dose-proportional** exposures **exceeding** CDK7 $IC_{80}$
- **Exposures remain below** CDK2 $IC_{80}$, supporting selective target inhibition[1]




**REC-617 monotherapy demonstrated signs of early anti-tumor activity[2]:**

- **One confirmed, durable partial response** by RECIST 1.1[3]
  - 4L PROC patient; no BRCA 1/2 mutation
  - Initiated therapy at 20 mg QD, dose reduced at Week 4 to 10 mg QD due to transient Grade 3 nausea
  - Patient was treated for approximately 7 months
- Five patients achieved a best response by RECIST 1.1 of stable disease
  - One patient received 2 mg QD
  - Four patients received 10 mg QD

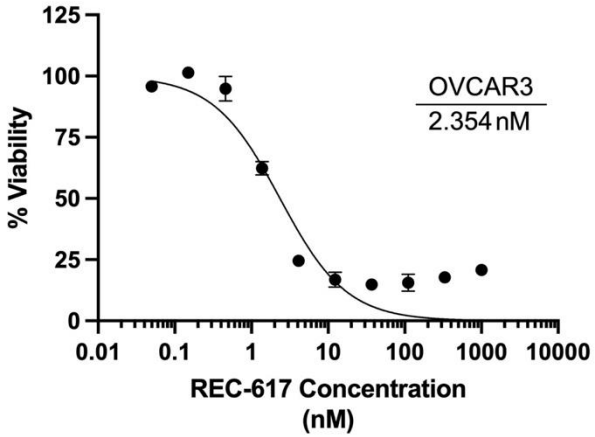


1. In vitro potencies adjusted for plasma protein binding (total-equivalent basis)
2. Data-cut off: 29 September 2025
3. Response evaluation criteria in solid tumors, PR: decrease of more than 30% in the sum of the longest diameters of target lesions + no new lesions + no progression of non target lesions

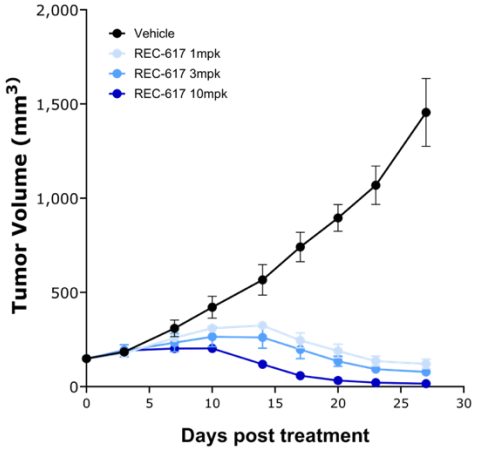
# **Indication selection:** AI-enabled causal inference strengthens preclinical data for indication selection of ovarian cancer for ELUCIDATE

Cell Panels → In Vivo Models → Causal Inference using Omics and Clinical data

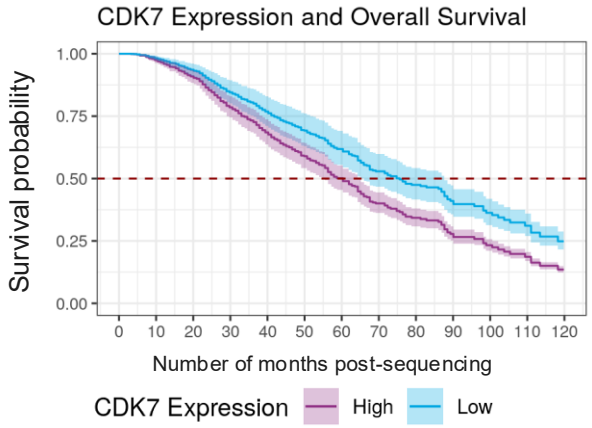
### Cell Line: OVCAR3




### CDX Model: OVCAR[1]




### Patient Data: Ovarian Cancer[2]




### Ovarian cell line sensitive to CDK7 inhibition with REC-617

- Unbiased analysis of over 360 cell lines in glo titer assay

### Potent tumor regression with REC-617 treatment

- 10mpk dose shows complete tumor regression by Day 27
- <10 hours of exposure above CDK7 IC80 to optimize benefit-risk

### CDK7 emerges as a likely driver of poor survival in ovarian cancer

- Based on a causal inference framework leveraging multi-omic and clinical data
- Over ~32K patient records using DNA, RNA, and clinical outcomes

### Impact

- Supports preclinical findings with **causal inference using omics and patient data**
- **1st indication:** 2L+ platinum-resistant ovarian cancer (PROC)

### What's Next

Preliminary **ovarian combination data in 2027**

1. Besnard et al, AACR (2022)
2. Causal inference framework based on a network-informed directed acyclic graph (DAG) to assess CDK7's impact on clinical outcomes. Patients were indexed on their date of NGS sequencing and followed until death or censoring with 10 + years of patient follow available. The model adjusts for relevant clinical and genomic confounders, including BRCA status, treatment history, and tumor genomics.



Recursion