Translating proof to products

REC-1245

First-in-class RBM39 degrader



REC-1245: Novel biology with early clinical activity

Phase 1 monotherapy results support expansion at 45 mg once daily

Novel mechanism with broad potential

Oral RBM39 degrader targeting vulnerabilities in hard-to-treat cancers
Disrupts splicing of transcripts associated with stress-response and DNA repair

Platform-derived biological insight

RBM39 phenocopies CDK12 loss while sparing CDK13-associated liabilities
204 compounds screened to development candidate in 18 months

Early clinical activity supports expansion cohorts

3 partial responses[1]
2 endometrial, 1 HCC

91.7% DCR (11/12)[2]
At 8 weeks, doses ≥45 mg

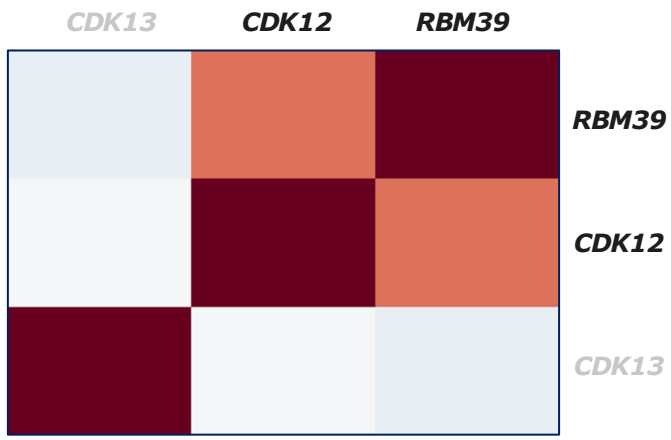
45 mg QD selected for expansion cohort
No serious TRAEs or dose reduction reported in the 45 mg cohort

1. PRs at doses ≥45 mg: Confirmed (n=2), unconfirmed (n=1); note that for one of 2 confirmed PRs, confirmatory scan has been reported by the site and entered into the EDC after the 21 August 2026 data cutoff 2. Overall DCR at 8 weeks across doses: 66.7% (14/21).
Note: N=30 safety evaluable across all dose groups; N=12 efficacy evaluable at doses ≥45 mg (participants in follow-up who haven't reached their first efficacy assessment are excluded)

Recursion

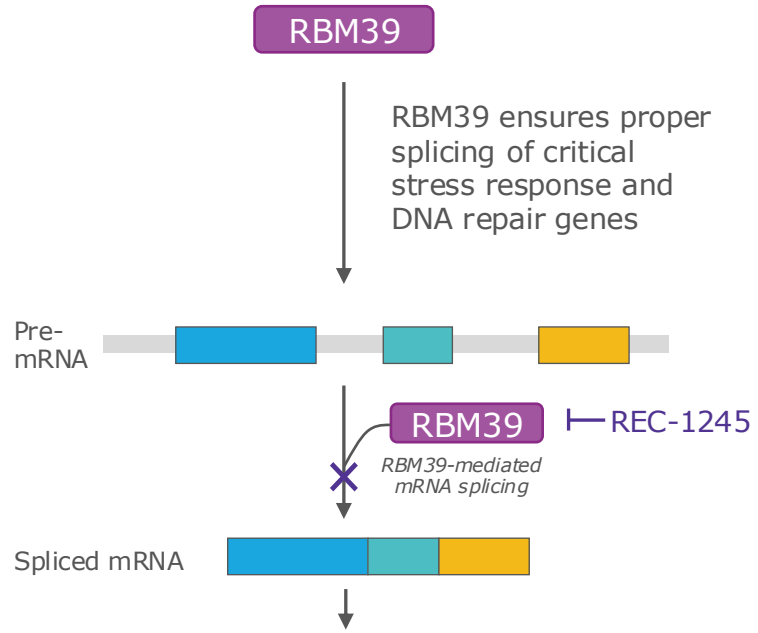
RBM39: Oncology target with broad potential based on highly relevant mechanism in multiple tumor types

Recursion OS Insight



- Biological insight converted into a novel molecular glue degrader
- RBM39 phenocopies CDK12 loss while sparing CDK13-associated liabilities
- Advanced from **204 compounds to candidate in 18 months**

RBM39 is a master splicing factor



Cancer cells rely on accurate splicing of stress response and DNA repair genes for survival

RBM39 degradation disrupts RNA splicing and expression of stress response and DNA damage repair genes

REC-1245

- **Potential first-in-class** molecular glue degrader
- Oral, **highly bioavailable**, and **highly selective**
- Hits **multiple oncogenic drivers** achieving synthetic lethal cancer cell killing
- Drives rapid and potent **RBM39 degradation** in human PBMCs within 24 hours and induces **significant tumor regressions** in multiple xenograft models driven by replication stress[1]

1. Data available but not shown

RBM39: A broad opportunity in hard-to-treat cancers

>100k

Total addressable patients/yr (US + EU5)[1]

Targeting RBM39 is relevant across multiple indications

Hard to treat tumors
Including endometrial, hepatocellular (HCC) and ovarian cancers

Transcriptionally driven cancers
Including pediatric tumors (Ewing sarcoma and neuroblastoma)

Two complementary development strategies

Intrinsically primed and vulnerable tumors[2,3]

Create vulnerabilities and deepen efficacy in earlier lines with REC-1245 + SoC

Monotherapy Opportunity

- **Clinical status:** Phase 1 dose escalation in multiple tumor types ongoing; dose expansion actively recruiting in endometrial cancer and other prioritized indications[4]

Combination Opportunity

- **Development strategy:** Identify rational combinations with potential to support earlier-line use alongside SoC

1. Company estimate based on undisclosed solid tumor indications with strong mechanistic rationale, including some biomarker-defined populations. Addressable patients/year reflects estimated annual incidence of potentially relevant populations in the US and EU5 (UK, France, Germany, Italy and Spain) 2. Preclinical evidence: Kohsaka et al., npj Precis. Oncol. 2024;8:117. 3. Singh et al., Sci. Adv. 2021;7:eabj5405; Lyu et al., Eur. J. Med. Chem. 2026;314:118921. 4. DAHLIA Phase 1/2 study, NCT06678659.

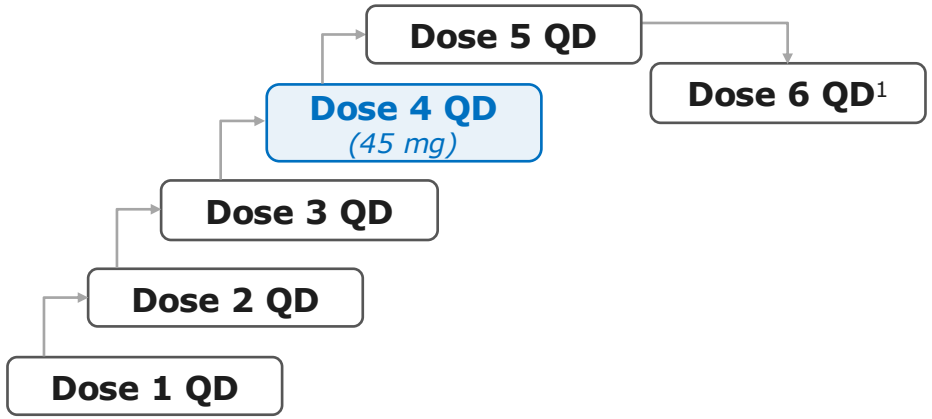
Recursion

REC-1245 Phase 1 dose escalation update

Early activity from monotherapy dose escalation

Phase 1A monotherapy

Continuous once-daily dosing



Key inclusion criteria

Unresectable, locally recurrent or metastatic select solid tumors, or select relapsed/refractory lymphoma

Progressed following, or intolerant to, available standard-of-care treatments

Primary objective	**Secondary objective**
PK and safety	Anti-tumor activity

Emerging response and safety data

- **Multiple partial responses at doses ≥45 mg***
- **Activity across tumor types**
  - Heavily pretreated population
  - 3 PRs (median 5 prior lines of therapy)
- **Data support expansion cohorts (45 mg)**
  - Monotherapy expansion at an active dose with an acceptable safety profile
  - First expansion into endometrial actively enrolling (45 mg QD)

*Confirmed (n=2), unconfirmed (n=1); note that for one of 2 confirmed PRs, confirmatory scan has been reported by the site and entered into the EDC after the 21-Aug-2026 data cutoff.
1. DL5 had DLTs, DL6 explored a dose between dose level 4 and 5

Recursion

REC-1245: Safety & treatment-related adverse events (TRAEs)

All doses (N=30)		
TRAE	**Any grade**	**Grade ≥3**
Any TRAE	22 (73.3%)	8 (26.7%)
Fatigue	9 (30%)	0
Anemia	9 (30%)	3 (10%)
Nausea	6 (20%)	1 (3.3%)
Thrombocytopenia	6 (20%)	3 (10%)
Stomatitis	5 (16.7%)	3 (10%)

45 mg QD / DL4 (N=10)		
TRAE	**Any grade**	**Grade ≥3**
Any TRAE	7 (70%)	2 (20%)
Fatigue	3 (30%)	0
Anemia	3 (30%)	0
Nausea	2 (20%)	0
Thrombocytopenia	0	0
Stomatitis	1 (10%)	0

45 mg once daily (N=10)

- No dose-limiting toxicities (DLTs)
- No serious TRAEs
- Most frequent TRAEs: fatigue and anemia (30% each); all Grade 1–2

Dose escalation established the tolerability limit

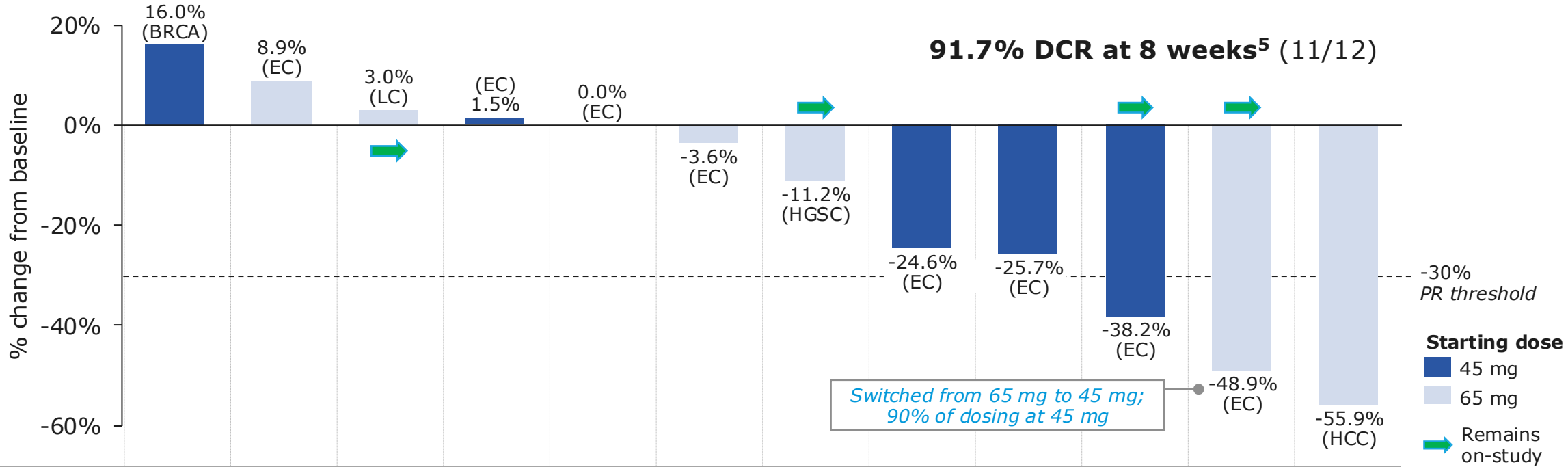
At 65 mg QD, 3 of 4 DLT-evaluable patients experienced dose-limiting toxicities

- DLTs include stomatitis, neutropenia/febrile neutropenia, thrombocytopenia
- MTD was exceeded

Grade 3 TRAEs were elevated creatinine and hypokalemia

REC-1245: Three partial responses in endometrial and liver cancer

Target lesion change by starting dose in response evaluable patients at 45 mg and 65 mg (N=12)



Best overall response[2]	SD	PD	SD	SD	SD	SD	SD	SD	SD	**PR[3]**	**PR**	**PR[4]**
Prior lines of therapy	6	8	3	5	5	2	6	5	3	7	4	5

1. Days receiving 65 mg as a percentage of total elapsed treatment days, including treatment interruptions - remaining time includes lower doses and treatment holds; shown only for patients starting at 65mg 2. Best overall response is the best response recorded on study per RECIST 1.1, including unconfirmed responses 3. Confirmatory scan reported by the site and entered into the EDC after the 21-Aug-2026 data cutoff. 4. Unconfirmed partial response (PR with -48.9% change is confirmed) 5. Disease control rate (DCR) = complete response, partial response, or stable disease among efficacy-evaluable patients (11/12)

Recursion

REC-1245: Confirmed partial response in endometrial cancer

Patient details[1]

- 70-year-old female with recurrent, progressive Stage IV high-grade serous carcinoma of the endometrium
- p53-mutant / HER2 non-amplified, microsatellite stable
- **4 lines of prior therapy including** platinum chemotherapy, tyrosine kinase inhibitor, immunotherapy, and antibody-drug conjugate

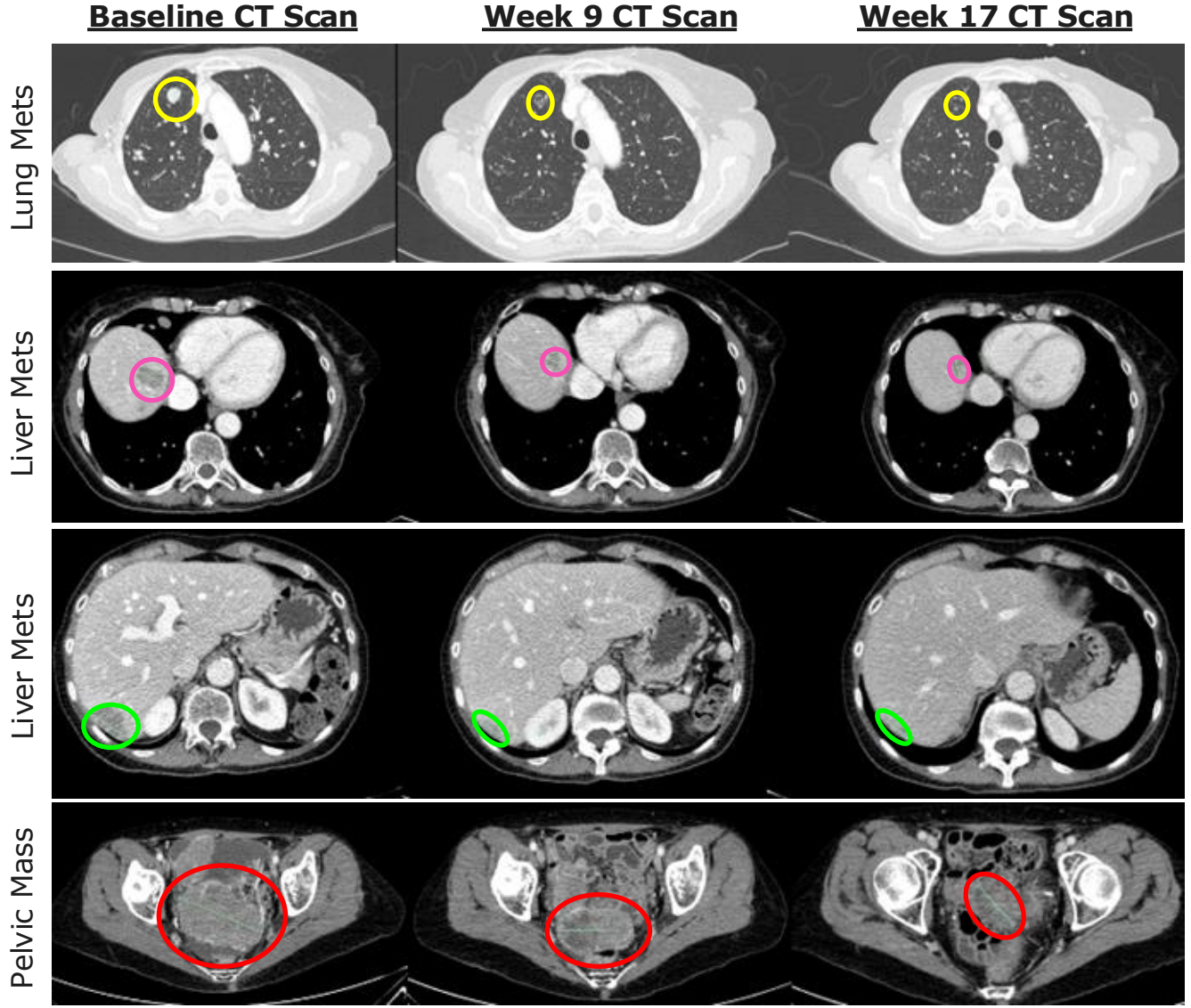
Dosing & clinical response

- **W1D1**: Initiated DL5 @ 65 mg
- **D6-D14**: Interrupted due to G2 oral & abdominal pain
- **D15**: Reduced to 45 mg; tolerated extremely well, abdominal and oral pain resolved

Response summary

- Week 9 Radiographic Assessment: Achieved a **partial response, 32.3% overall decrease.**
- Week 17 Radiographic Assessment: Verified a **partial response, 48.9% overall decrease.**

Patient is **asymptomatic from disease** and **remains on treatment (45 mg)**



1. Prior medical history includes cataracts, neuropathy, compression fracture, and pulmonary embolism

Recursion

REC-1245: Confirmed[1] partial response in endometrial cancer

Patient details[2]

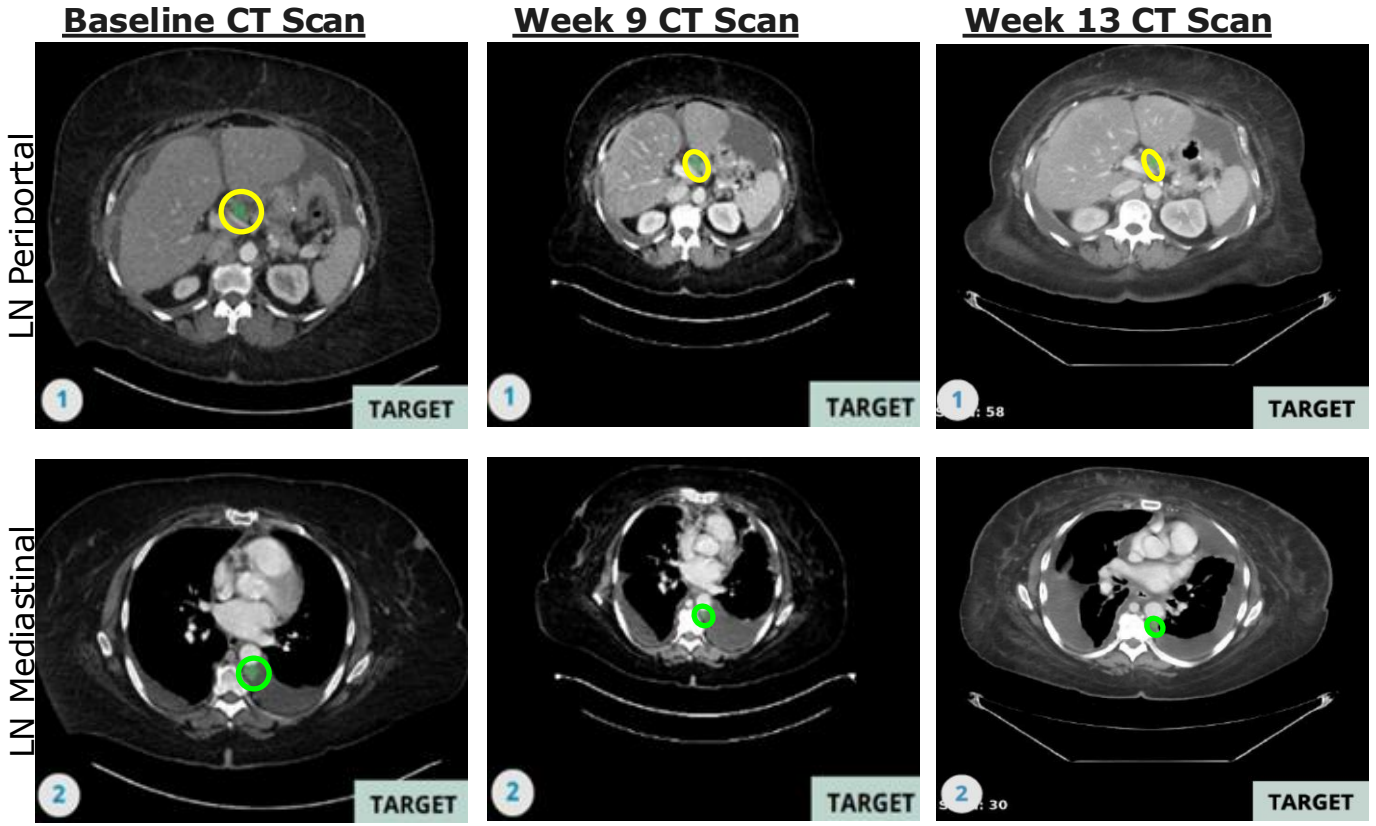
- 54-year-old female with recurrent, progressive Stage IV endometrioid carcinoma of the endometrium
- p53-mutant / HER2 amplified, ER+, PR-, MMR proficient
- **7 lines of prior therapy including,** Platinum/taxane chemotherapy, VEGF inhibitor, HER2-targeted therapy, immune checkpoint inhibitor, tyrosine kinase Inhibitor, antibody-drug conjugate, investigational CAR-T therapy

Dosing & clinical response

- **W1D1**: Initiated Backfill DL4 at 45 mg
- **W4D5:** Interrupted dose due to missed MD appointment
- **W5D1:** Patient restarted drug, tolerating well

Response summary

- Week 9 Radiographic Assessment: Achieved a **partial response, 33.9% overall decrease**
- Week 13 Radiographic Assessment: Verified a **partial response, 38.2% overall decrease**[1]



Patient **remains on treatment (45 mg)**

1. Confirmatory scan reported by the site and entered into the EDC after the 21-Aug-2026 data cutoff.
2. Prior medical history includes Fatigue, Anorexia, Ascites, Pleural Effusions, Depression, Neuropathy, GERD

Note: Images not at consistent scale; based on patient record provided from site

Recursion

Significant opportunity for differentiated oral therapy in **endometrial cancer**

Actively enrolling in endometrial cancer, data expected in 2H27

4th[1]
most common cancer in US women

~68K[1]
estimated new US cases in 2026

~20%[2]
5-year relative survival with distant-stage disease

Limited treatment options in 2L+[3]
for patients relapsing on IO. ADC currently approved only for HER2+

REC-1245: differentiated biology and development rationale:

1. **Disrupts DNA damage repair**[4]
   RBM39 degradation downregulates DNA damage response networks and cell cycle checkpoints

2. **Potential immune priming**[5]
   Missplicing-derived neoantigens provide a mechanistic rationale for immunotherapy combinations

3. **Distinct mechanism from ADCs**[6]
   Target biology provides a rationale to evaluate activity following ADC progression

Exploring additional tumor types in dose expansion

1. US cases and deaths, 2026 estimates: American Cancer Society, Cancer Facts & Figures 2026, endometrial cancer key statistics page, revised 14 January 2026; 2. Stage survival: SEER, as presented by ACS, for people diagnosed 2015 to 2021. Based on SEER stage groups: https://www.cancer.org/cancer/types/endometrial-cancer/detection-diagnosis-staging/survival-rates.html; 3. Only HER2 ADC (for HER2 IHC2+ patients, ~25% of endometrial) currently approved. Lenvatinib + Pembro, dostarlimab often used in 2L but underperforms for patients who have relapsed on ICIs. ADCs such as sac-TMT are expected to enter the market in the near term. 4. Xu et al, Cell Reports Volume 42, Issue 10, 2023; class evidence 5. Lu et al., Cell 2021, doi:10.1016/j.cell.2021.05.038: class evidence 6. Mechanistic hypothesis only. Post-ADC efficacy and absence of cross-resistance remain unestablished for REC-1245. REC-1245 is investigational.

Recursion