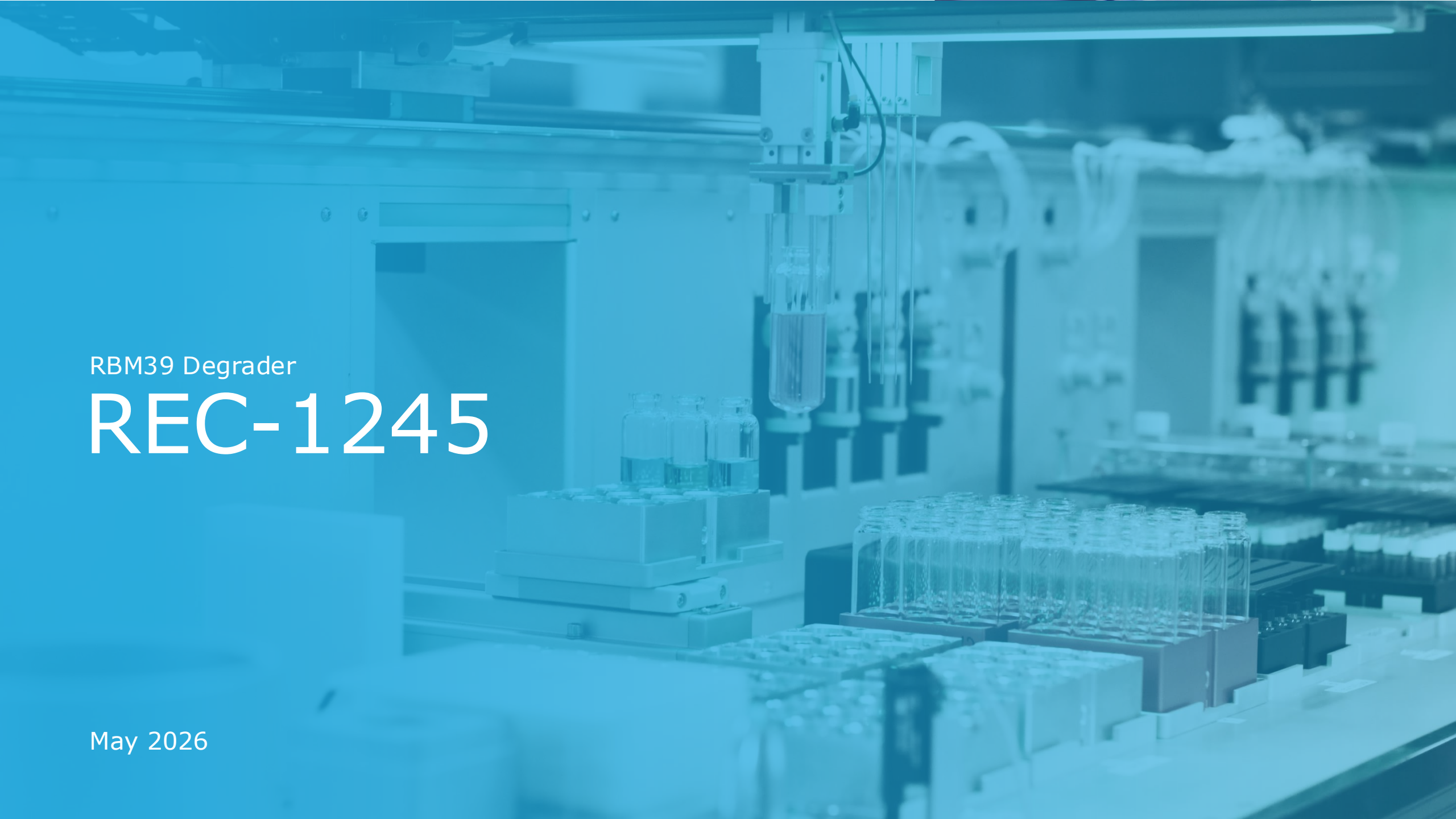


RBM39 Degrader

REC-1245

May 2026

REC-1245: RBM39 degrader

A highly selective RBM39 degrader for biomarker-enriched solid tumors and lymphoma

Program Status	• Potential **first-in-class** RBM39 degrader in solid tumors • First patient dosed in **4Q24** • Additional Phase 1 dose escalation data expected **2H26**
Mechanism of Action	• **Molecular glue** that degrades RBM39 via E3 ligase adaptor DCAF15 • **Disrupts RNA splicing** to downregulate cell cycle checkpoints and DDR networks
Thesis & Differentiation	• **RBM39 phenotypically mimics CDK12** and is **distinct** from **CDK13** in Recursion OS • **Novel approach** to target DDR biology via RBM39 **avoids on-target toxicities** associated with cell cycle checkpoint inhibitors (e.g., CDK12, WEE1, ATR, ATM, PLK1) • **Selective** RBM39 degrader with **minimal ITGA2 liability** to limit thrombocytopenia
Unmet Need[1]	• **>100,000 patients** with solid tumor or lymphoma experience disease progression while on frontline therapies • Potential to be used as a **single agent or in combination** with chemo/IO

Recursion Approach

- **Unbiased ML-aided genomics screen** to identify biological signature and relate cellular phenotypes
- Progressed REC-1245 from target biology to IND-Enabling studies in **under 18 months (vs. 42 months in industry[2])**

1. *Internal company estimates. Assumes US+EU5 addressable incidence with biomarker-enriched solid tumors and other select histologies.*
2. *Paul et al, Nat Rev Drug Discov (2010).*

Recursion

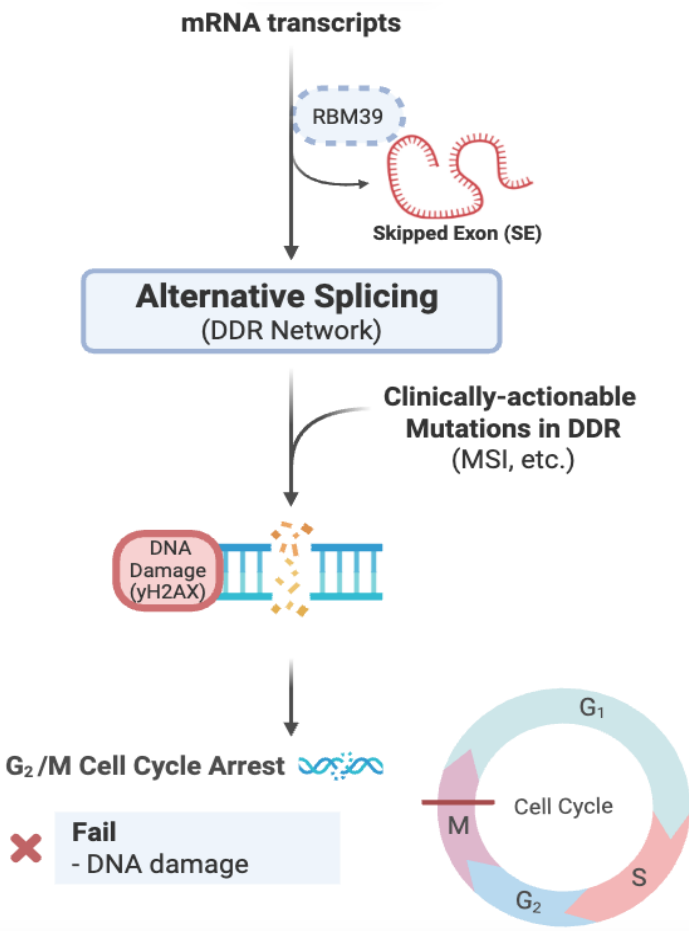
RBM39 Degrader: Selective degradation of RBM39 impairs splicing, compromising DDR pathways and transcriptional regulation

Biological Rationale

- **RBM39 is a splicing factor essential for DDR network** and a c-Jun/ER/PR transcriptional coactivator
- **Overexpression of RBM39** in many solid tumors is **linked to poor survival**, highlighting it as a **key cancer driver**[1]
- REC-1245-induced RBM39 degradation leads to **DNA damage and cell death** in several genetic backgrounds / tumor types such as those w/ DDR deficiency

REC-1245 Opportunity

- REC-1245 is a **highly potent, first-in-class RBM39 degrader**
- **>100,000** addressable patients across US & EU5 - **solid tumor indications and lymphoma**[2]
- **Currently no RBM39 degraders approved by the FDA**

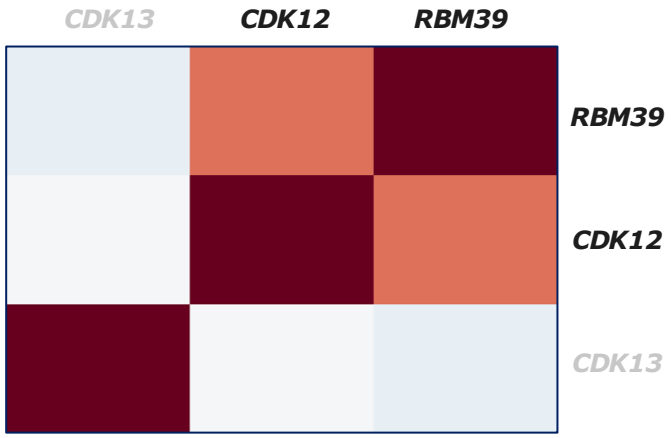


1. Cui F et al. RBM39 is a potential prognostic biomarker with functional significance in hepatocellular carcinoma. Transl Cancer Res. 2024 Apr 30;13(4); Zhang R et al. Systematic pan-cancer analysis identifies RBM39 as an immunological and prognostic biomarker. J Cell Mol Med. 2022 Sep;26(18):4859-4871
2. Multiple biomarkers being explored

Recursion

REC-1245: Novel platform derived insight to unlocking comprehensive genomic instability vulnerabilities

Recursion OS Insight

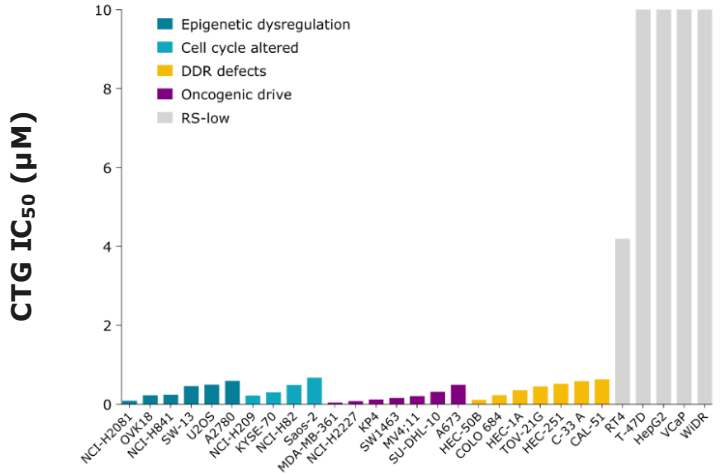


Platform-derived novel target and degrader

- RBM39 loss phenocopies CDK12 deficiency
- RBM39 degrader: advanced from **204 compounds to candidate in 18 months**
- Translates phenomic insight into mechanism, with **rapid and potent RBM39 degradation in human PBMCs within 24 hours**[1]

Preclinical Insight

In vitro: Cell viability with REC-1245[2]

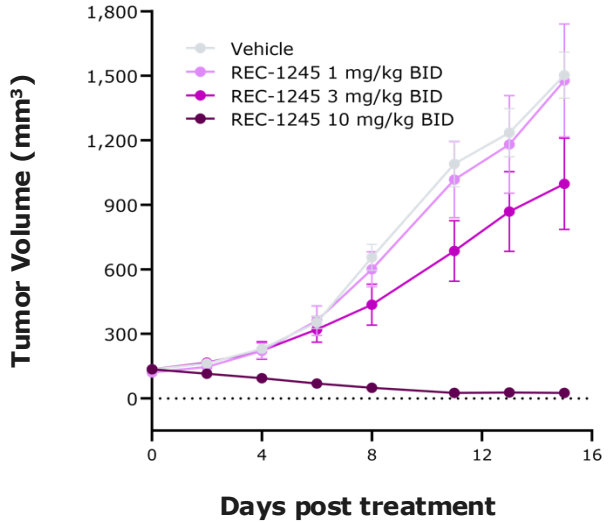


Potential REC-1245 sensitivity based on genomic instability

- Emerging preclinical data uncover **replication stress and DNA repair vulnerability** as potential signatures for REC-1245 sensitivity

Preclinical Data

Ovarian CDX Model: OVK18 (MSI-H)



REC-1245 induces significant tumor regressions in an ovarian CDX

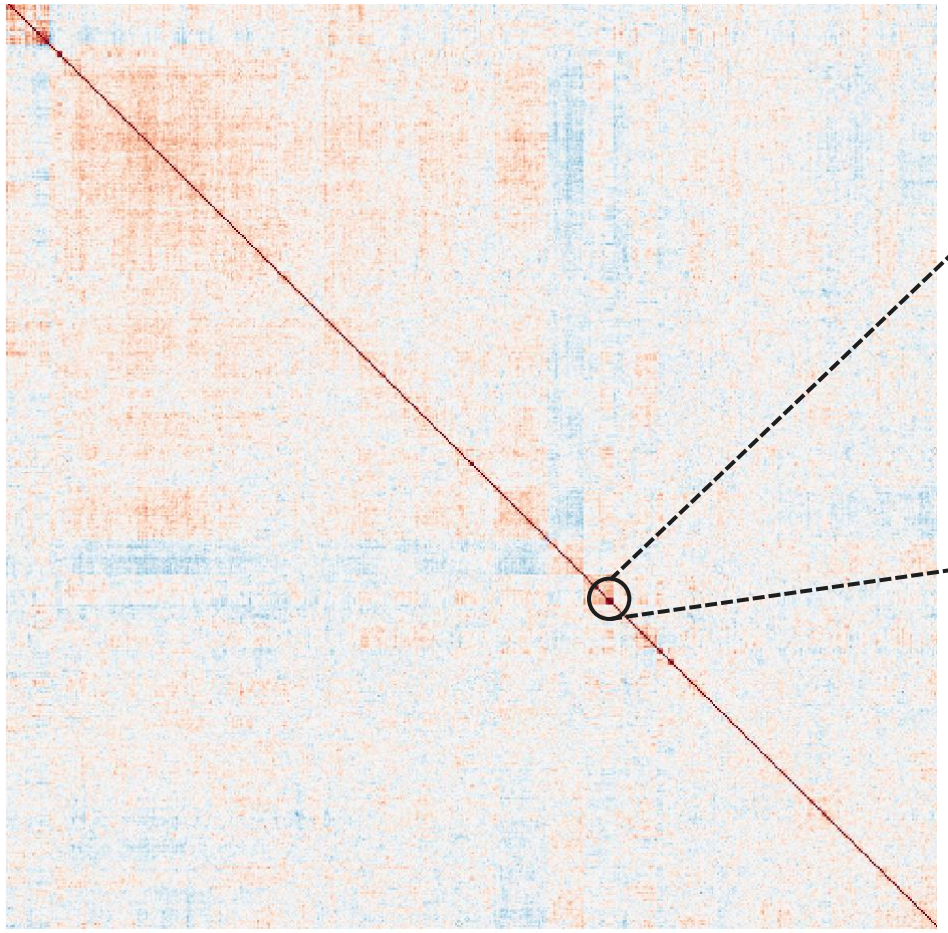
- Model driven by elevated replication stress

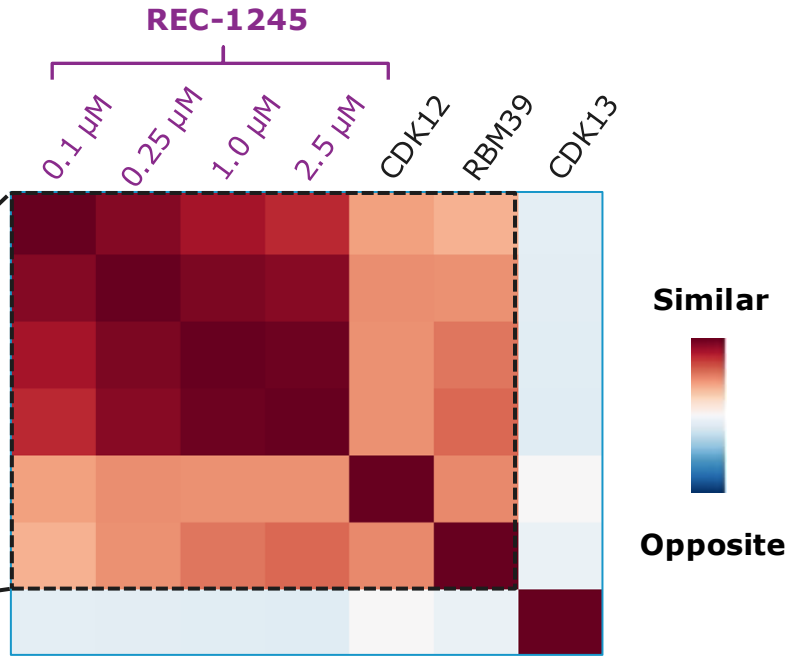
1. Data not shown.
2. Cell lines were assigned to broad pathway dysregulation contexts based on 1 or more documented alteration from CCLE/GSDC databases

Recursion

REC-1245 (RBM39 degrader): Platform inferred a functional similarity between RBM39 and CDK12 biology suggesting a novel approach to potential DDR modulation

Recursion OS Novel Insight





Gene: Gene Relationship: Genetic KO of *RBM39* and *CDK12* found to be phenotypic similar with neither genes demonstrating a relationship to *CDK13* genetic KO

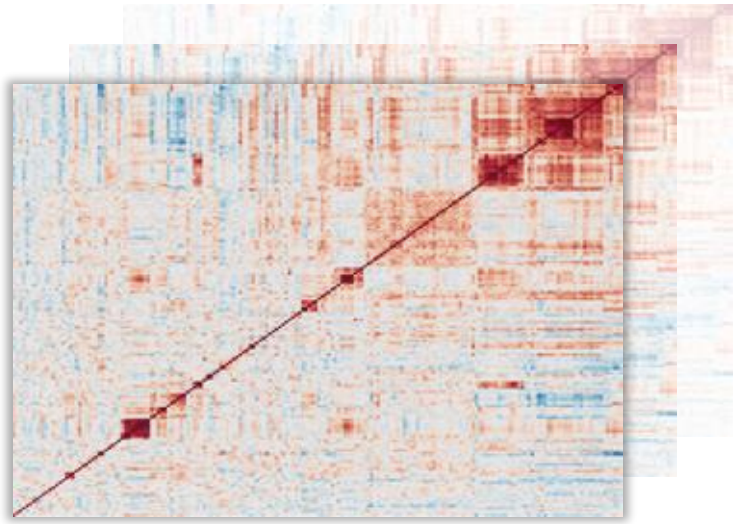
Gene: Compound Relationship: REC-1245 demonstrates phenotypic similarity to RBM39 and CDK12 genetic KO but not CDK13, in line with inferred hypothesis

1. *Data on File.*

Recursion

Platform links RBM39 biology to CDK12, a key regulator of DNA damage response genes (DDR) and replication stress (RS)

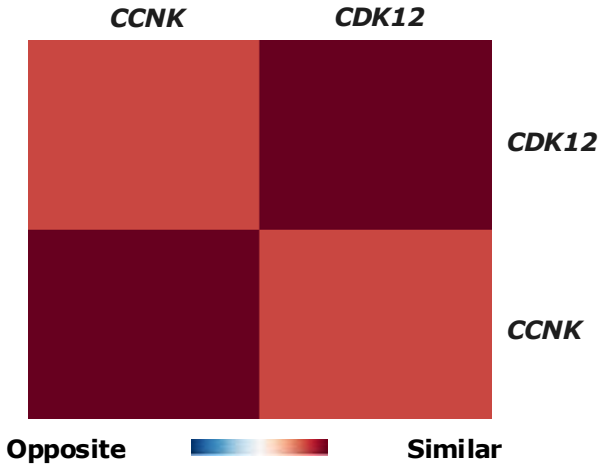
AI-guided Multimodal Mapping



Deep genome coverage across major DDR pathways in HUVEC PhenoMap[1]

- **Whole genome CRISPR** knockouts; close to **1 million** compounds profiled
- **Vast** DDR network resolution **unattainable** with single-readout screens

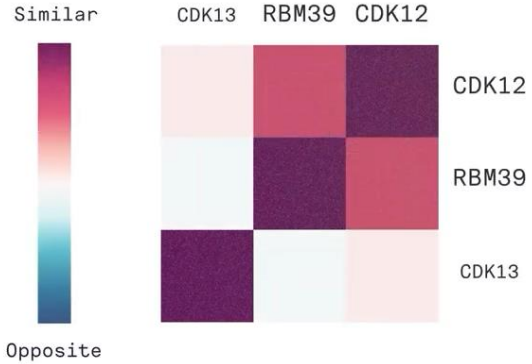
CDK12 Axis Recapitulated



CDK12 and cyclin K (CCNK) share a similar signature in phenomic readout

- CDK12 kinase activity **requires** CCNK binding, a **well-established** dependency
- **Validates** approach and potential for novel **AI-**driven **mechanistic** and **patient** insights

Genetic-Chemical Convergence



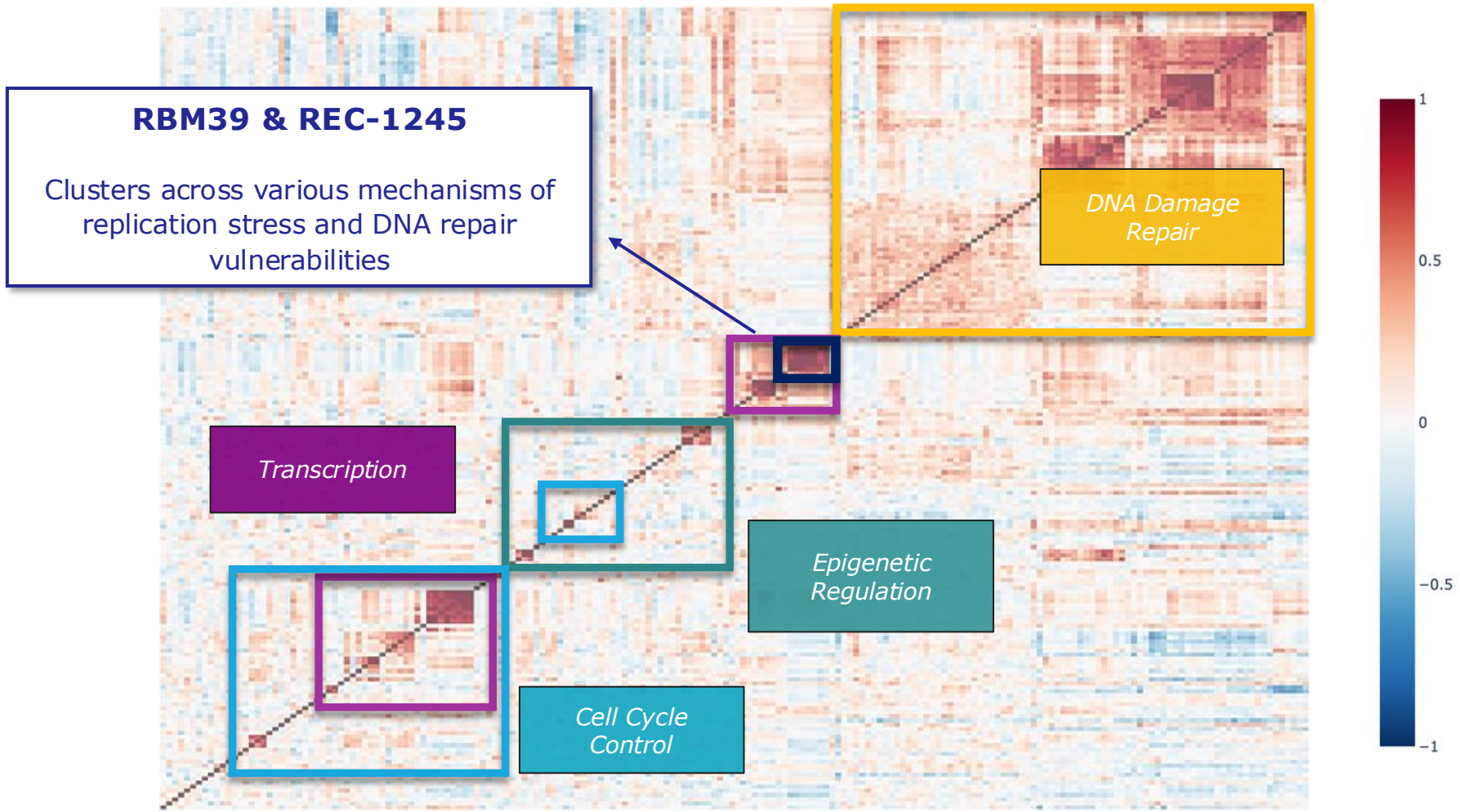
RBM39 loss mimics CDK12 inhibition, providing a druggable potential analog

- Suppresses DDR networks and cell-cycle pathways
- Potential for **tumor-selective** activity with a **wider** therapeutic index

1. *List of DDR genes and pathways obtained from Knijnenburg 2018*

Recursion

Multi-omics insights link RBM39 dependency to transcription-replication stress and DNA repair vulnerabilities



Recursion

Target tumors characterized by drivers of genomic instability arising from replication stress potentially linked to RBM39 dependency

Broad patient subsets with replication stress and DNA repair vulnerabilities[1]

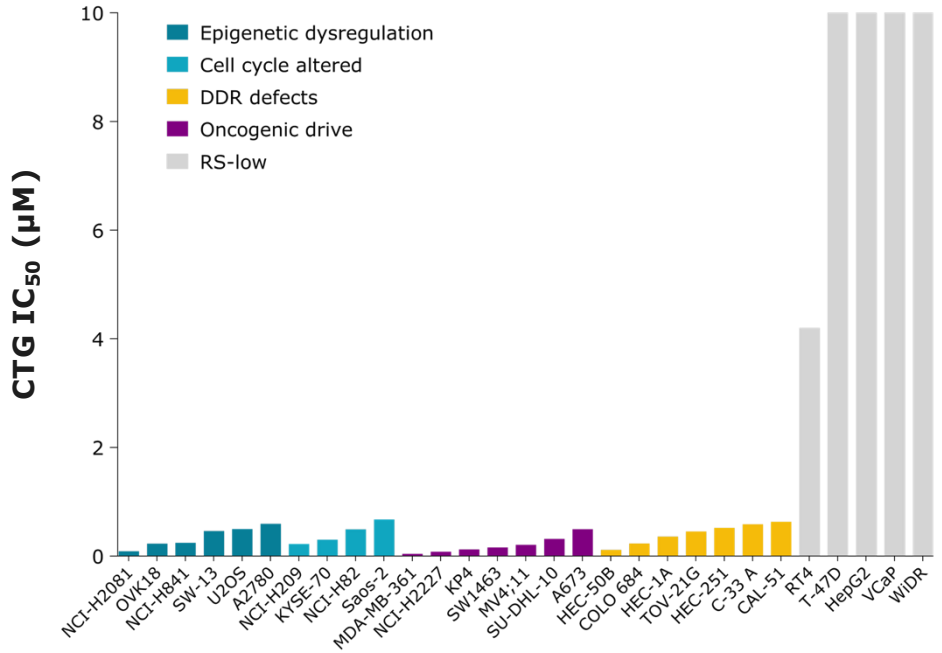
Epigenetic Dysregulation	Cell Cycle Alterations	DDR Defects	Oncogenic Drivers

>100,000 patients in US & EU5 per year[2]

Replication stress and DNA repair vulnerabilities span several solid tumors and blood cancers

- Including colorectal, endometrial, lung, breast, sarcoma, bladder, ovarian, pancreatic, DLBCL and AML
- Correlates with clinically actionable alterations
  - E.g., MYC/MYCN amplification, SWI/SNF loss, MSI-H, HRR defects
- Potential to meaningfully expand beyond initial patient population

In vitro: cell viability with REC-1245[3]



Emerging preclinical data uncover replication stress as a potential signature for REC-1245 sensitivity

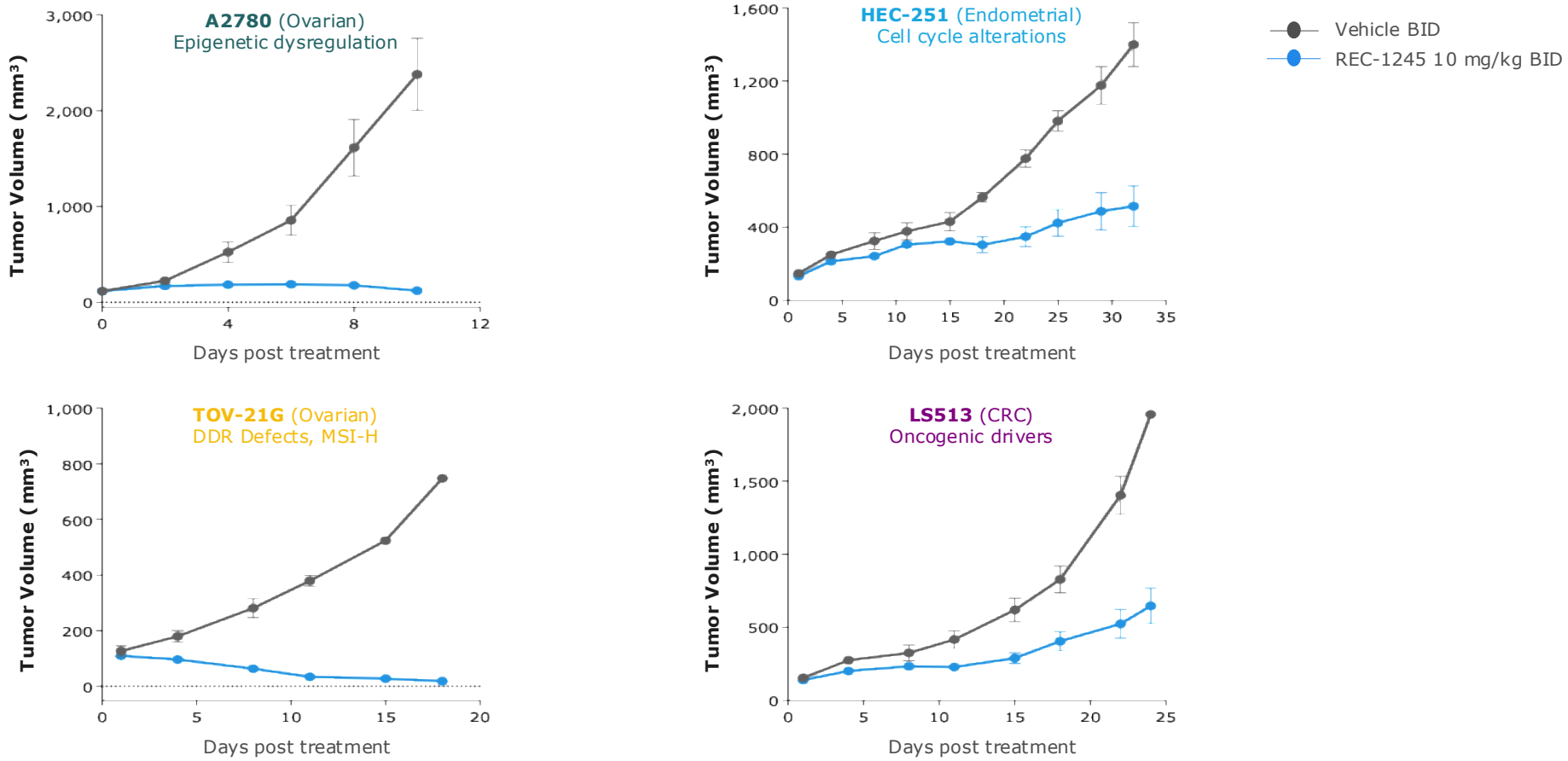
- REC-1245 also demonstrates concentration-dependent increases in γH2AX in high replication stress driven human cancer cells in vitro *(data not shown)*

1. *da Costa 2022, NRDD*
2. *Internal company estimates. Assumes US+EU5 addressable incidence with biomarker-enriched solid tumors and other select histologies.*
3. *Cell lines were assigned to broad pathway dysregulation contexts based on 1 or more documented alteration from CCLE/GSDC databases*

Recursion

Emerging preclinical data suggests greater sensitivity with REC-1245 in high replication stress and DDR vulnerable tumors

REC-1245 demonstrates reduction in tumor volume across different tumors with high-RS signatures and DNA repair vulnerability[1]



1. *N=4 mice per group.*

Phase 1 Dose Escalation Update: Early data from monotherapy dose escalation with REC-1245

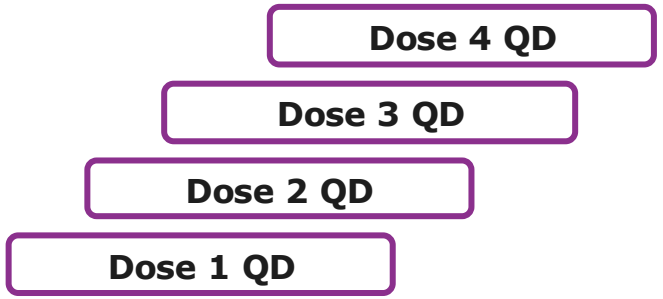
Key inclusion criteria

- **Unresectable, locally recurrent, or metastatic select solid tumors or select relapsed/refractory lymphoma**
- Progressed following, or intolerant to, available SoC treatments

ALL PATIENTS	N=16
Age (median)	**65**
Range	57-77
Advanced solid tumors	**16**
Tumor biomarker	
MSI-H and/or dMMR	7
MSS	9
Prior systemic therapy lines (median)	**4.5**

Ph 1A Monotherapy Dose-Escalation
Continuous once-daily dosing summary

Additional dose levels enrolling



Primary objective
- PK and safety

Secondary objective
- Anti-tumor activity

→ **ClinTech:** Ongoing RWE efficacy contextualization leveraging high-fidelity longitudinal EHR and claims data

Note: Data-cut off date 2026-03-31

Recursion

Preliminary Safety Data: REC-1245 well-tolerated with no DLTs across all evaluated doses to date

Treatment-Related Adverse Event (TRAE)	
	Patients (n=16)
Patients with **Any TRAE**	**10 (62.5%)**
Grade 1-2	9 (56.3%)
Grade 3	1 (6.2%)
Grade 4-5	0 (0.0%)

Preliminary safety and tolerability summary

- REC-1245 was **well-tolerated**
- **No DLTs reported** across evaluated doses to date
- **No serious TRAE** was reported
- **90%+ of TRAEs were Grade 1 or 2**
  - Most common GI-related: constipation (12.5%, n=2), nausea (12.5%, n=2), vomiting (12.5%, n=2)
  - Most common non-GI related: fatigue (18.8%, n=3)
- 6.2% (n=1) of patients experienced Grade 3 nausea and vomiting

Note: Data-cut off date 2026-03-31; All data summaries are reported for Safety Evaluable Population

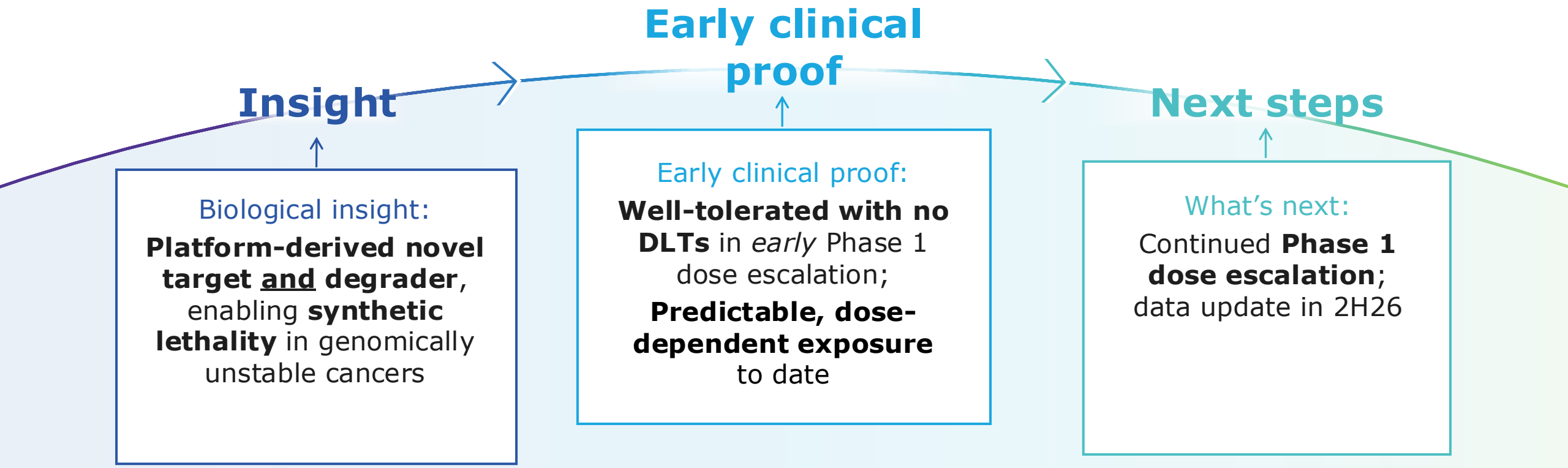
Preliminary PK/PD summary

Early data suggests REC-1245 has **predictable, dose dependent exposure**

- **Predictable, dose-dependent exposure** across evaluated patients to date
- **PK is supportive of QD dosing** and exposures continue to increase with dose
- Expect to **achieve exposures consistent with tumor regression** in mice **within the next two dose levels**
- Pharmacodynamic assessments demonstrate **target engagement**

Note: Data-cut off date 2026-03-31; N=16

REC-1245 (RBM39): Insight → early proof → next steps



Recursion