LSD1 Inhibitor

REC-4539

May 2026

LSD1 Inhibitor: REC-4539

Unmet Need

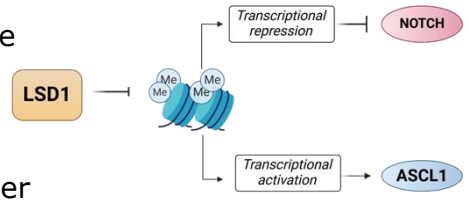
Potential in solid tumors (e.g. SCLC) hematology oncology (e.g. AML)

>45,000

Treatable US + EU5[1]

Mechanism of Action

- **Reversible** LSD1 inhibitor that can selectively upregulate NOTCH signaling
- **Promotes differentiation** of neuroendocrine cancer cells



Development Strategy

H1 2026

Phase 1
Monotherapy
Dose Escalation

EXPECTED STAGES

Phase 1
Combination
Dose Escalation

Phase 1
Combination
Dose Expansion

Differentiation

- Potential **best-in-class** LSD1 Inhibitor
- **Shorter-predicted half-life** plus **reversible MOA** to manage **on-target AEs**

Lower Predicted Thrombocytopenia

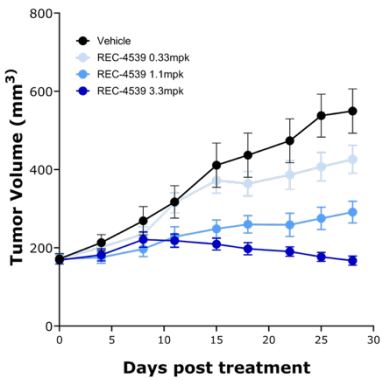
Shorter Half-Life

Optimal CNS Exposures

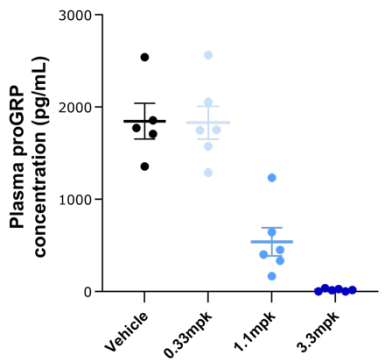
Key Preclinical Data

- **Dose-dependent** efficacy in SCLC human xenograft model
- Well tolerated with limited impact on platelet levels

CDX Model: H1417[3]



Plasma ProGRP[4]



Recursion Approach

- Precision design using **active learning**, combining reversibility with **CNS penetration**

414

Novel compounds synthesized to candidate ID

What's Next

- Early safety and PK from monotherapy trial **2H 2027**

1. EvaluatePharma Epidemiology 2023 (US and EU5). 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer V.3.2025. 3. Payne et al. AACR, (2023). 4. Data on File

Recursion

REC-4539: LSD1 inhibitor

A precision designed unique LSD1 inhibitor with CNS penetrance

Program Status	• Potential **best-in-class** LSD1 inhibitor
Mechanism of Action	• **Reversible LSD1 inhibitor** that can selectively upregulate NOTCH signaling • Promotes **differentiation of neuroendocrine cancer cells** • **Impairs DNA repair pathways** sensitizing SCLC cells to immune checkpoint inhibitors
Thesis & Differentiation	• LSD1 inhibitor designed to be **reversible** and **brain penetrant** • **Shorter-predicted half life** versus competitors to manage **on-target toxicity** • **Highly selective** to reduce **off-target toxicity** • Preclinical data shows therapeutic exposures have minimal effects on platelets, suggesting potential **reduced risk of thrombocytopenia**
Unmet Need[1]	• **>45,000 patients** with treatable extensive stage SCLC • Limited treatment options post progression on frontline therapies

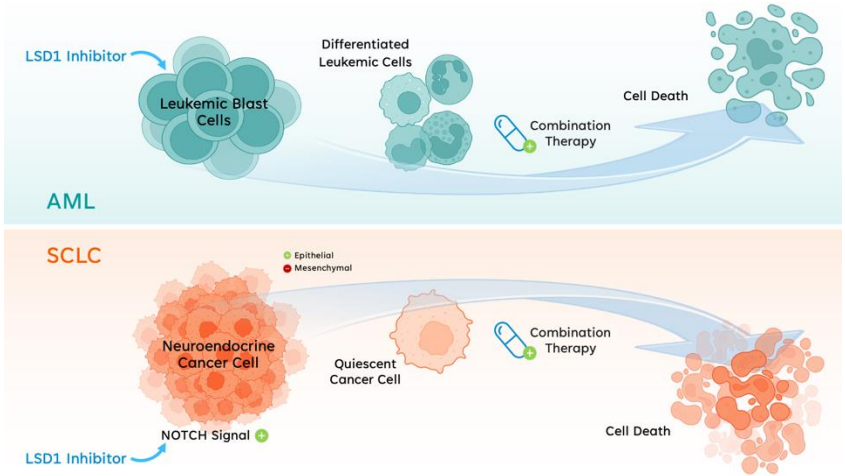
Recursion Approach

- **Precision design** using **active learning to select most information rich compounds**
- 414 novel compounds synthesized to candidate ID
- Used multiparameter optimization to design a unique candidate combining reversibility with CNS penetration

1. EvaluatePharma Epidemiology 2023 (US and EU5)

LSD1i: Promising oncology target historically blocked by class-limiting on-target toxicity and poor CNS exposure

- Overexpression of LSD1, a pivotal epigenetic master regulator, promotes **tumor progression and immune evasion**
- Potential to **address high-impact indications** by targeting LSD1, where current therapies often fall short
  - E.g., small cell lung cancer (SCLC) and acute myeloid leukemia (AML)
- Opportunity to address **~45,000 patients** with treatable ES-SCLC in US+EU5 currently with **limited treatment options** post-progression



Challenges

Prior LSD1 inhibitors have had safety liabilities and limited CNS penetrance:

- On-target, dose-limiting thrombocytopenia linked to irreversible MOAs and long half lives
- Limited brain penetrance impacting >50% of SCLC patients who develop brain metastases

Opportunity

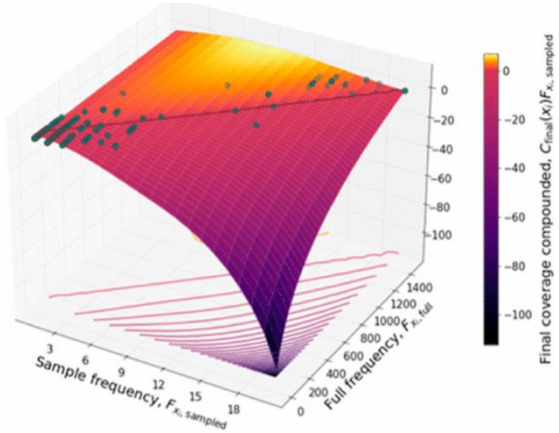
Overcome the **treatment-limiting clinical toxicity** observed with prior LSD1 inhibitors, **improving safety & maximizing efficacy:**

- By combining **reversibility** and **short half-life**
- With **CNS penetrance** to combat metastasis

Recursion

REC-4539: AI-enabled precision design to overcome class-limiting toxicity issues

Recursion OS Insight



414 novel compounds
to candidate ID

Precision designed to combine improved safety with CNS penetrance

- Leveraged AL-methods like Coverage Score[1] to select unbiased, information rich hits suitable for rapid multi-parameter optimization to design a unique candidate

Preclinical Insight

Assay	DC Criteria	Competitor 1	Competitor 2	REC-4539
Brain : Plasma Ratio	>0.5			
MDCK-MDR1 Efflux Ratio (Pgp)	<2			
Predicted Human Half-life	QD dosing			

Meets or exceeds criteria | Minor deviation | Major deviation

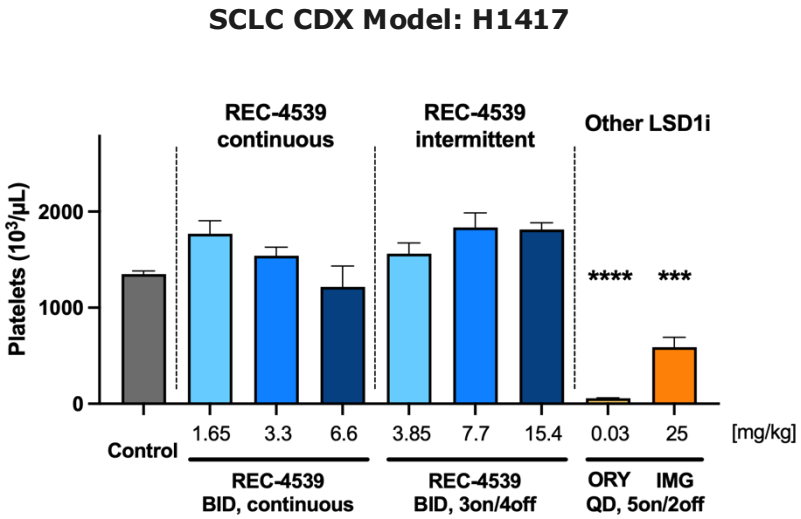
Development Candidate (DC) Criteria:

- **Brain:plasma ratio:** green >0.5; red <0.5
- **MDCK-MDR1 efflux ratio (Pgp):** green <2; yellow >2-<10; red >10
- **Predicted half-life:** green <24 hours; yellow 24-48h hours; red >48 hours

Potential best-in-class LSD1i, with reduced risk of on-target toxicity

- Shorter-predicted human half-life vs competitors plus reversible MOA to manage on-target AEs (e.g. thrombocytopenia)
- Sufficient CNS exposures vs competitors

Preclinical Data



REC-4539 has minimal impact on platelets in an SCLC CDX

- Well-tolerated, with similar preclinical efficacy to competitors[2]

1. Coverage Score: A Model Agnostic Method to Efficiently Explore Chemical Space, *J. Chem. Inf. Model.* 2022, 62, 18, 4391–4402. 2. Efficacy data not shown.

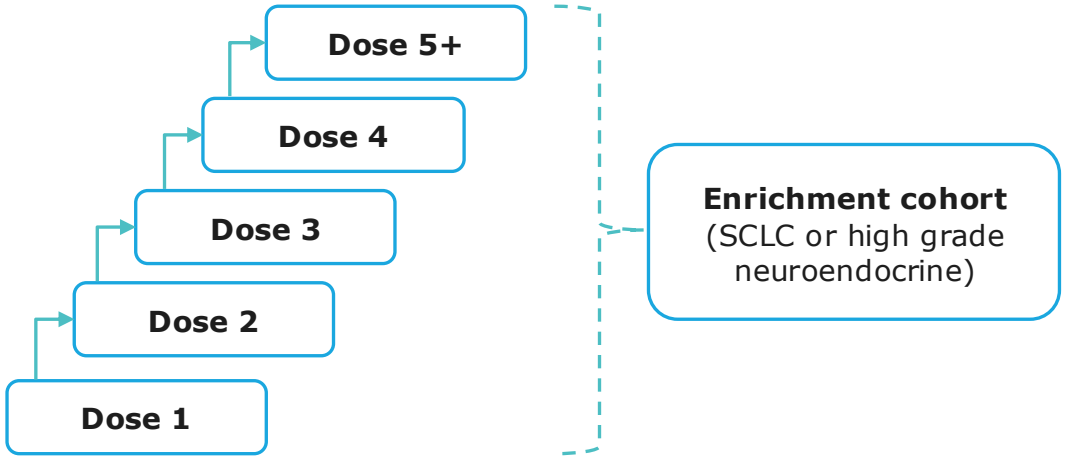
Recursion

FPD in Phase 1 Dose Escalation: ENLYGHT Phase 1 trial in patients with select solid tumors including SCLC

Phase 1 Dose Escalation

ENLYGHT patient population; N = ~25

- Patients with solid tumors including SCLC and high grade neuroendocrine or small cell carcinomas non-lung origin[1]



- **Rapid data-driven program go/no-go** based on clinical safety profile observed in solid tumors
- REC-4539 **precision designed** to **avoid on-target thrombocytopenia** observed with competitor LSD1 inhibitors

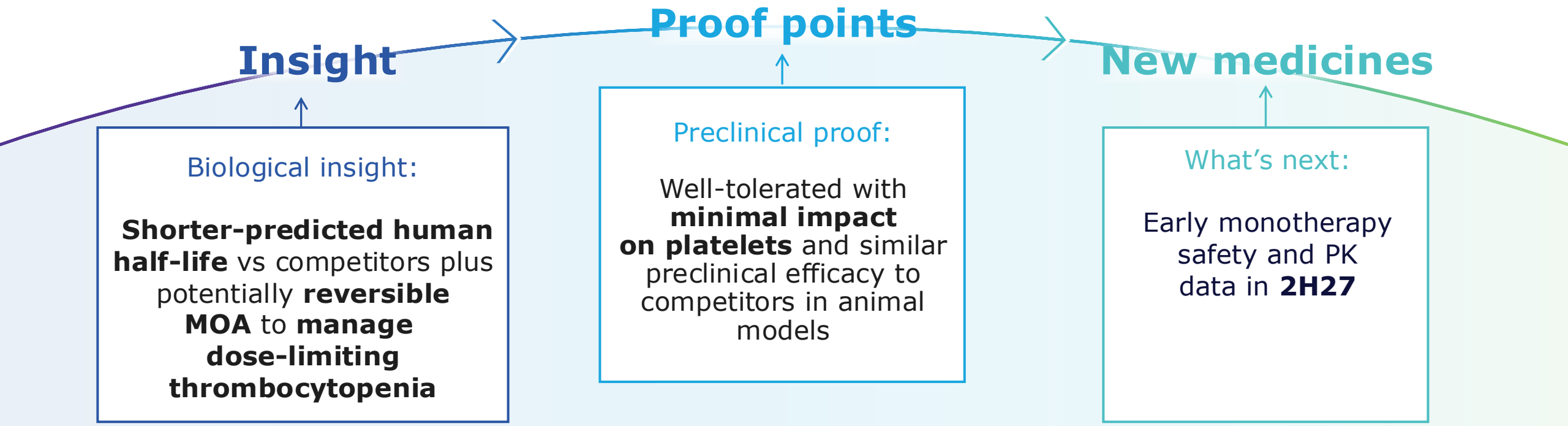
Next steps

- Early safety and PK from monotherapy trial in 2H27

ENLYGHT: Dose Determining Study of EXS74539 (REC-4539) in Participants With Select Solid Tumors; NCT07517198

1. Other solid tumor types include: Non small cell lung cancer, triple negative breast cancer, squamous cell carcinoma liver cancer, prostate, ovarian, renal, head and neck, and gastric cancers.

REC-4539 (LSD1): What's next



Recursion