



Ongoing Phase 1b/2 Trial of the Allosteric MEK1/2 Inhibitor REC-4881 as Monotherapy in Familial Adenomatous Polyposis (FAP):

Updated Safety and Efficacy

December 8, 2025



Forward Looking Statements

This presentation discusses an investigational product whose safety and efficacy have not been established.

This document contains information that includes or is based upon “forward-looking statements” within the meaning of the Securities Litigation Reform Act of 1995, including, without limitation, those regarding the early and late stage discovery, preclinical, and clinical programs; licenses and collaborations; prospective products and their potential future indications and market opportunities; Recursion OS and other technologies; business and financial plans and performance; and all other statements that are not historical facts.

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From platform discovery to positive clinical data: REC-4881's emerging potential for treatment of familial adenomatous polyposis

High Unmet Need in FAP

- **>50,000 patients** in US/EU5
- **Lifelong** surveillance and **life altering surgeries**
- **No approved** pharmacotherapy

Rapid Polyp Burden Reduction

- **Meaningful polyp reduction** at 4 mg in **majority of patients** after 12 weeks of treatment

Safety Data Update

- **Most common TRAEs in line with MEK1/2 class effect** (*incl. dermatitis acneiform, CPK increase, rash*)
- **Most Grade 1/2, low rates of Grade 3, no grade 4/5**

First Platform to Clinical Proof of Concept

- Recursion's **unbiased AI-driven phenotypic approach** uncovered MEK1/2i as a mechanism that rescues APC-deficient cells
- First to clinically investigate **MEK1/2 inhibition for FAP**

Durable Polyp Burden Reduction

- **Significant polyp burden reduction** maintained in **most patients** after 12 weeks off-treatment

Path Forward

- **Engage FDA** to define a potential registration path (1H 2026)
- Expand population from **≥55 to 18 years old** and further optimize **dosing** schedule

Recursion momentum: Delivering pipeline advancements and partnership value

**>\$500
million**

in total cash inflows
achieved across all our
partnerships
and collaborations



- ✓ **6 Phenomaps:** 4 GI oncology, 2 neuroscience
- ✓ **1 program** initiated in GI onc indication



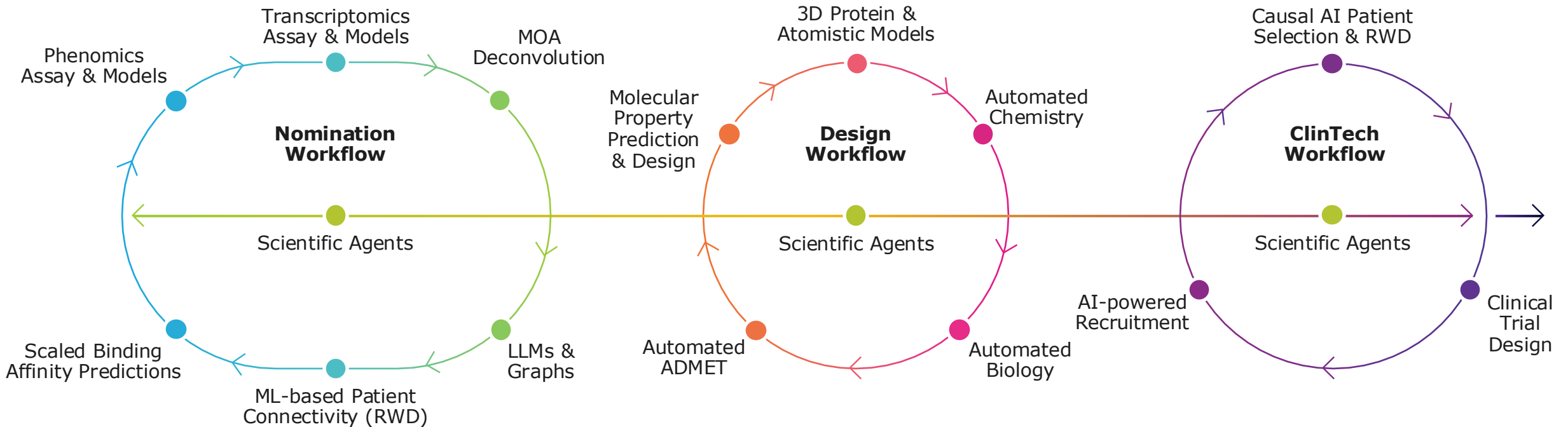
- ✓ **4 milestones** achieved in 18 months
- ✓ Portfolio of projects **continuing to expand**
- ✓ **Potential upcoming milestones** (e.g., development candidate, lead series)

Recursion OS 2.0: Efficiently delivering novel insights, precision design, and optimized clinical trials

AI-powered
Biological Insights

AI-enabled
Precision Design

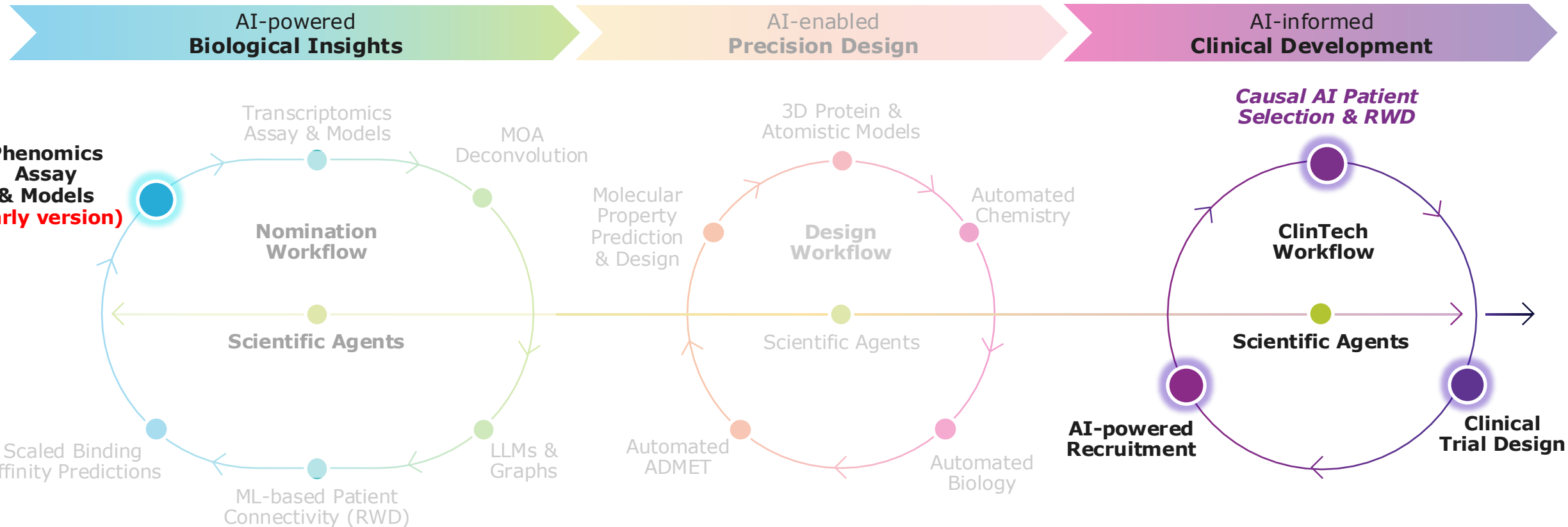
AI-informed
Clinical Development



Supported by BioHive-2

The **fastest, most powerful supercomputer** wholly-owned and operated by a pharma or biotech company
~65PB of data including 40PB of proprietary data

REC-4881: In-licensed based on novel insights from Recursion OS V0.1; now leveraging V2.0 platform to advance clinical development

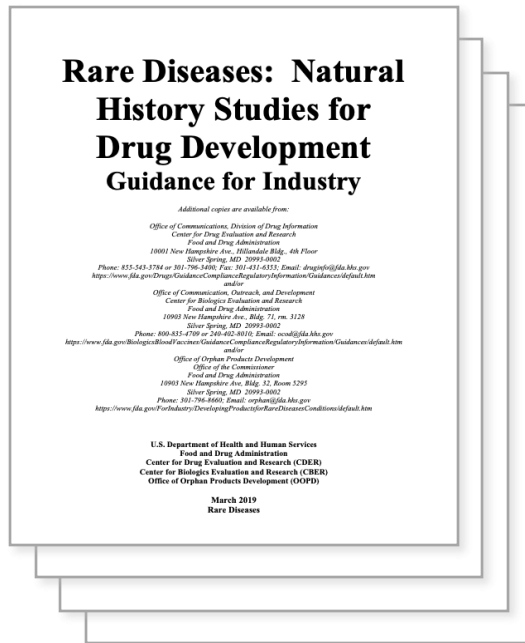


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Natural history RWE: Quantifying FAP disease progression to contextualize TUPELO program and inform regulatory path

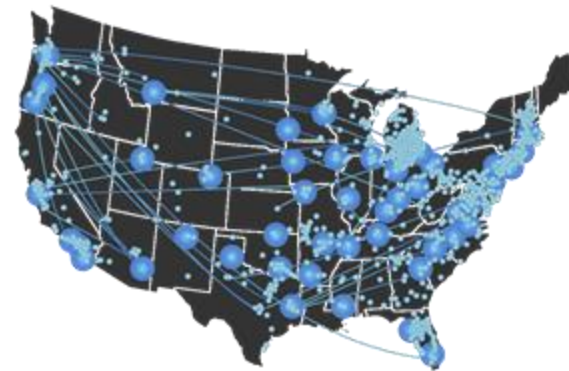
Natural history data generation is critical in rare disease drug development, and noted by health authorities in numerous guidances¹



Leveraged our ClinTech platform and academic partnerships to run **large-scale real-world evidence (RWE) analytics** to contextualize TUPELO program

1. Understand FAP burden in US and inform future trial design

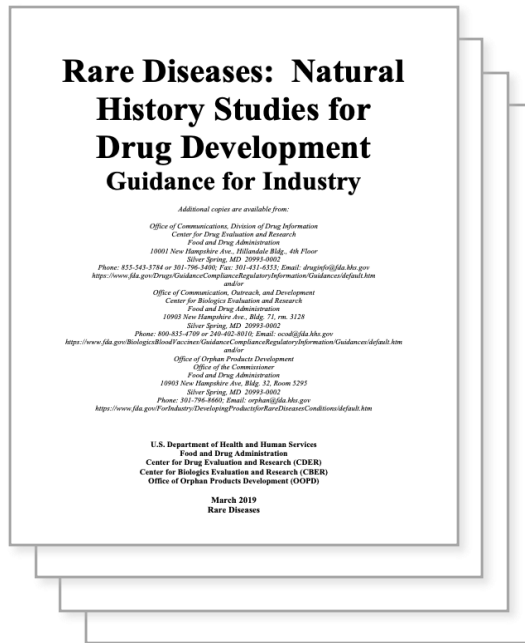
- Analyzed more than 1,000 US FAP patients and 250,000 physician notes
- Custom LLM-based pipeline to assess disease progression and treatment patterns



1. Supported by multiple guidances including: U.S. Food and Drug Administration. Rare Diseases: Natural History Studies for Drug Development (Draft Guidance for Industry) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2019 Mar; U.S. Food and Drug Administration. Rare Diseases: Considerations for the Development of Drugs and Biological Products (Guidance for Industry) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2023 Dec; U.S. Food and Drug Administration. Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products (Guidance for Industry) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2023 Aug; and others

Natural history RWE: Quantifying FAP disease progression to contextualize TUPELO program and inform regulatory path

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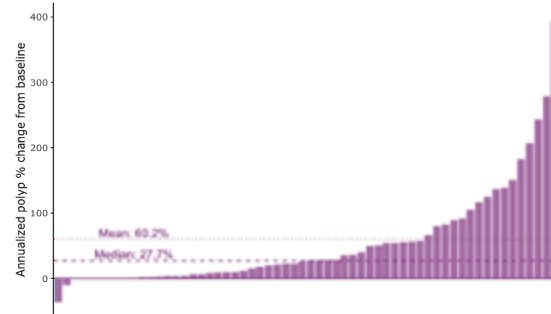


Leveraged our ClinTech platform and academic partnerships to run **large-scale real-world evidence (RWE) analytics** to contextualize TUPELO program

2. Contextualize efficacy in TUPELO relevant population

- Registry from one of the largest and longest running real-world FAP cohorts with ~200 patients with ~20 years of follow up
- Quantify natural change in polyp burden

Annualized % change in polyp burden in a natural history cohort
Amsterdam University Medical Center FAP registry (N=55)



In collaboration with Amsterdam University Medical Center

1. Supported by multiple guidances including: U.S. Food and Drug Administration. Rare Diseases: Natural History Studies for Drug Development (Draft Guidance for Industry) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2019 Mar; U.S. Food and Drug Administration. Rare Diseases: Considerations for the Development of Drugs and Biological Products (Guidance for Industry) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2023 Dec; U.S. Food and Drug Administration. Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products (Guidance for Industry) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2023 Aug; and others

Fireside chat: Today's speakers



Elizabeth Bruckheimer, PhD

*VP of Clinical Development
Recursion*

- Highly accomplished executive with ≥ 20 years of industry experience, **directing all phases of drug development from preclinical to clinical execution**
- Former VP and CSO Panbela Therapeutics / Cancer Prevention Pharmaceuticals **leading largest FAP Phase 3 trial**



Jessica Stout, DO

*Assistant Clinical Professor
University of Utah School of Medicine*

- Double board-certified in **Internal Medicine and Gastroenterology**
- Specializes in **complex gastrointestinal disease management** incl. long-term, multi-organ **management of FAP**



David Mauro, MD, PhD

*Chief Medical Officer
Recursion*

- Former CMO **Codiak BioSciences & Checkmate Pharmaceuticals**
- Former ED of Oncology **Merck**
- Over 20 years of experience in **oncology drug development**, incl. spearheading early- and late-stage development for **more than 25 INDs** over the past decade



Alfred M. Cohen, MD, FACS, FASCRS

*Former Chief of Colorectal Service
Memorial Sloan-Kettering Cancer Center*

- Former CMO **Cancer Prevention Pharmaceuticals**
- Former Director, CEO at Lucille P. Markey Cancer Center at **University of Kentucky**
- >50 years of experience in **CRC treatment & research**, with clinical **focus on QoL** in patients with CRC, Lynch syndrome, and **FAP**

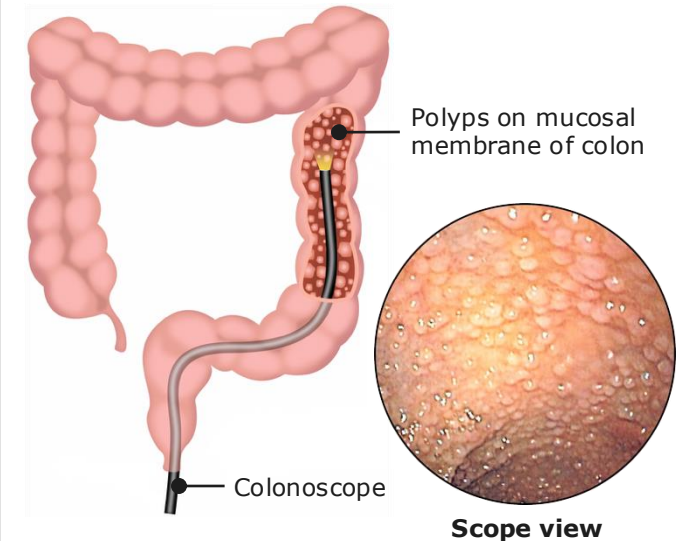
REC-4881 Program

Elizabeth Bruckheimer, PhD | *VP, Clinical Development*

Disease context: FAP is a rare disease characterized by extensive polyps in the GI tract, with no approved pharmacotherapies

Disease Background

- **Orphan disease** caused by autosomal dominant **inactivating mutations in APC¹**
- **One of the most clinically significant hereditary colorectal cancer syndromes**
- Majority of patients will develop 100s-1000s of colorectal adenomas with **near-100% CRC risk** by age ~40 in absence of surgery or excisions
- Adenomas **progressively accumulate** with **limited evidence of spontaneous regression**, driving disease burden throughout life
- Lifetime of endoscopic surveillance, frequent excisional interventions, **life-altering surgeries**, and poor QoL, morbidity and mortality



Scope view source: Samir at the English-language Wikipedia, CC BY-SA 3.0, via Wikimedia Commons

High Unmet Need

- **>50,000** addressable patients in US + EU²
- **Surgery** as the only standard-of-care
- Current medical therapies have **no impact on slowing disease progression**
- **REC-4881** may be positioned to fill a significant unmet need with **no approved pharmacotherapies**

Patient journey: FAP is a lifelong continuum of disease progression and intervention, driven by chronic polyp growth

100s of polyps develop in adolescence; progress to CRC by age 40 if left untreated

Colectomy typically occurs in the early 20s to prevent malignant transformation¹

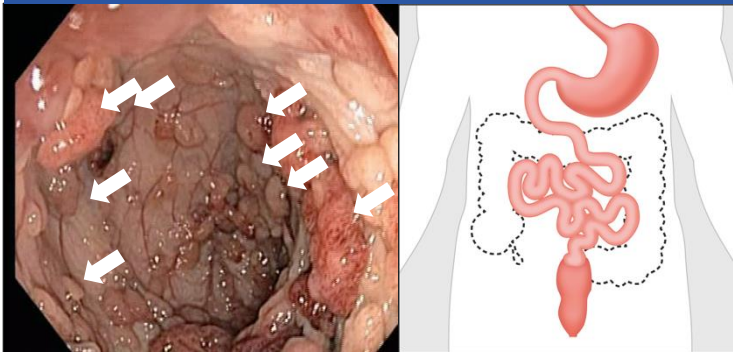
Retained rectum/neo-rectum continue to develop **progressive polyposis**

~50% of patients require rectum or pouch removal due to uncontrolled polyps, while others remain at high risk²

~90% of FAP patients develop duodenal adenomas, often progressive

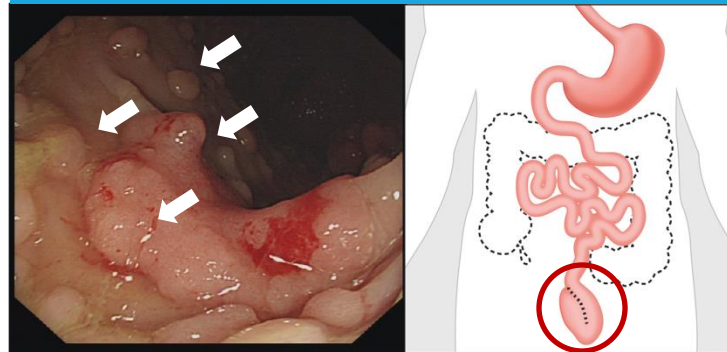
6% eventually undergo duodenectomy — one of the most complex GI surgeries³

Adolescence to early adulthood: Colectomy: colon removal



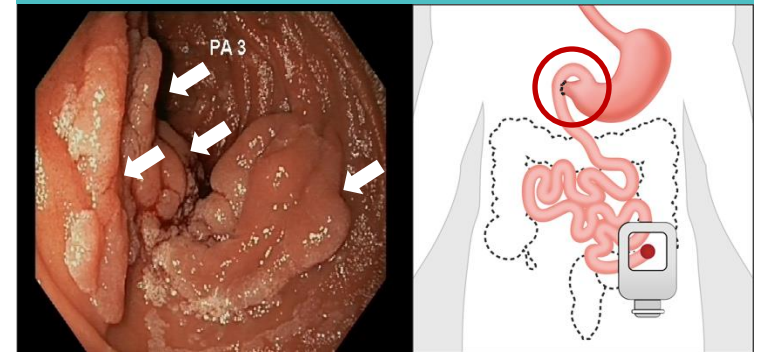
Eliminates immediate cancer risk in colon but does not stop ongoing polyp formation in the rectum/pouch or duodenum

Post colectomy disease: Removal of rectum & high-risk polyps



Life-altering surgery that affects continence, fertility, and long-term GI function

Upper GI progression: Duodenectomy: duodenum removal



High-morbidity intervention performed solely to control polyp growth

Note: There is a high degree of variability in SOC across practices and/or regions

1. Vasen HFA et al. Optimizing the timing of colorectal surgery in patients with Lynch syndrome: A review. Scand J Gastroenterol. 2019 May;54(5):541-8

2. Aziz O et al. Meta-analysis of observational studies of ileorectal versus ileal pouch-anal anastomosis for familial adenomatous polyposis. Br J Surg. 2006 Apr;93(4):407-17.

3. Karstensen JG et al. Endoscopic indicators in patients with familial adenomatous polyposis undergoing duodenal resections – a nationwide Danish cohort study with long-term follow-up. Fam Cancer. 2024 Nov;23(4):607-615.

ClinTech insights: Real-world US electronic health records and physician notes highlight disease progression in FAP patients

1,068 FAP patients and 256,000 physician notes were analyzed during period of 2017-2025¹

“No polyps were removed given there were an **innumerable amount (>300)** and removal would not be endoscopically feasible.”

“[they] had **greater than 10 surgeries and multiple revisions** of [their] colectomy and resection of [their] small bowel.”

“[they] underwent a Whipple procedure because the **duodenal and ampullary polyp burden was too high.**”

- Patients commonly had disease **progression and continuous intervention**
 - Limited evidence of spontaneous polyp burden reduction in any FAP patient
- Frequent polypectomies with **at least 5 polyps removed per patient per year**²
 - Advanced excisions are associated with **risk of complications** such as perforation and bleeding^{3,4}
- At least **75% of patients had a major FAP-related surgery** documented⁵

Note: all reported rates are adjusted for variable follow up time. Data analysis includes unstructured physician notes and structured components of EHRs such as billing codes for phenotype definitions.

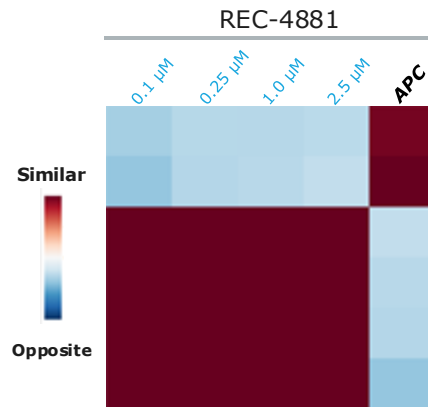
1. Notes were processed using a custom NLP pipeline with Recursion-built and operated supercomputer, BioHive-2
2. Polypectomy rates are expected to be under-estimated due to documentation practices in routine clinical care
3. Amoyel M, Belle A, Dhooge M, et al. Outcomes of endoscopic mucosal resection for large superficial non-ampullary duodenal adenomas. *Sci Rep.* 2022;12:14592.

doi:10.1038/s41598-022-18528-7

4. Lemos Garcia J, Rosa I, Pereira da Silva J, Lage P, Claro I. Endoscopic Approach to Duodenal Adenomas in Familial Adenomatous Polyposis: A Retrospective Cohort. *GE Port J Gastroenterol.* 2023;30:430-436. doi:10.1159/000527209
5. Major surgeries were defined as ileal pouch-anal anastomosis, colectomy, proctocolectomy, Whipple, ileostomy, and ampullectomy. Analysis captures documentation of “history of” such procedures. Major surgeries are expected to be underestimated due to limited follow up period and potential underreporting of patient medical history.

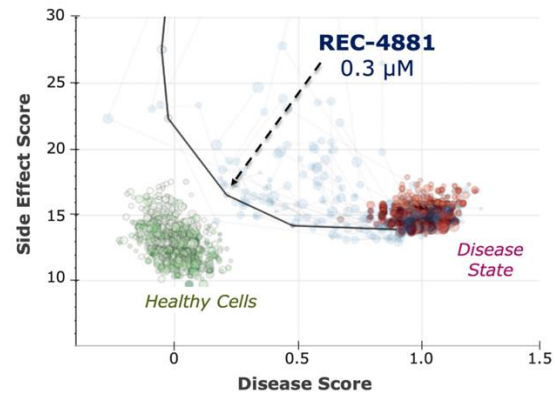
Platform insight: Unbiased AI-driven phenotypic discovery identified MEK1/2 inhibition as a novel APC-rescue mechanism, positioning REC-4881 for FAP

Identified by **phenotypic discovery** platform to rescue APC LoF



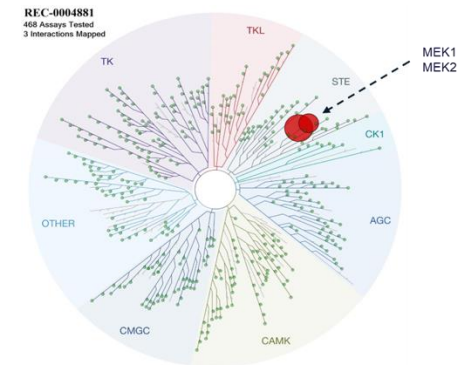
- Platform screened **thousands of compounds** in APC mutant rescue assays
- **REC-4881 strongly clusters with APC rescue signature**, indicating reversal of APC LoF induced phenotypes
- Identified a **novel, mechanistically grounded therapeutic entry point** for FAP; a disease driven by APC inactivation

REC-4881 **suppresses disease-inducing effect** of APC mutations



- In disease-model systems, **REC-4881 shifts APC-mutant cells toward healthy-state biology**
- Demonstrates **suppression of disease-inducing ERK/MAPK hyperactivation**
- **Precision mechanism aligned** with the underlying **genetics of FAP**

REC-4881 is a **potent and selective** allosteric MEK1/2 inhibitor



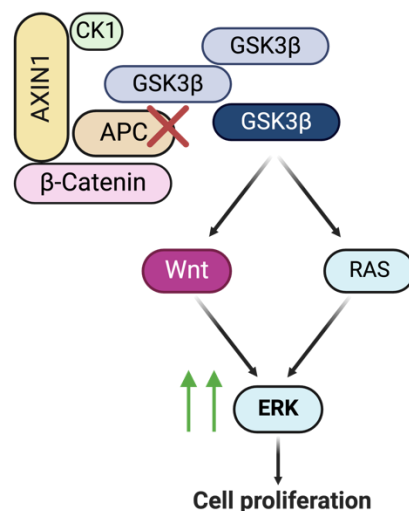
- From 468 kinases, **only 3 had inhibition >65% at 1 μ M**
- **No significant binding inhibition (>50%)** across 71 **receptors or ion channels** at 10 μ M
- Selectivity profile supports a **clean, targeted approach**

Guided by this novel insight, **Recursion in-licensed REC-4881 from a major pharmaceutical company¹ and redirected REC-4881 as a mechanistically aligned therapeutic candidate for FAP**

REC-4881 profile: A precision MEK1/2 inhibitor uniquely suited to the biology and anatomy of FAP

Mechanism of Action

- **APC loss-of-function drives FAP** through hyperactivation of Wnt/ β -catenin and MAPK signaling, leading to uncontrolled adenoma formation
- **REC-4881 selectively blocks ERK activation (MAPK pathway)**—a key downstream consequence of APC inactivation and a driver of adenoma proliferation
- **Precision mechanism aligned with the underlying genetics** of FAP



Differentiation

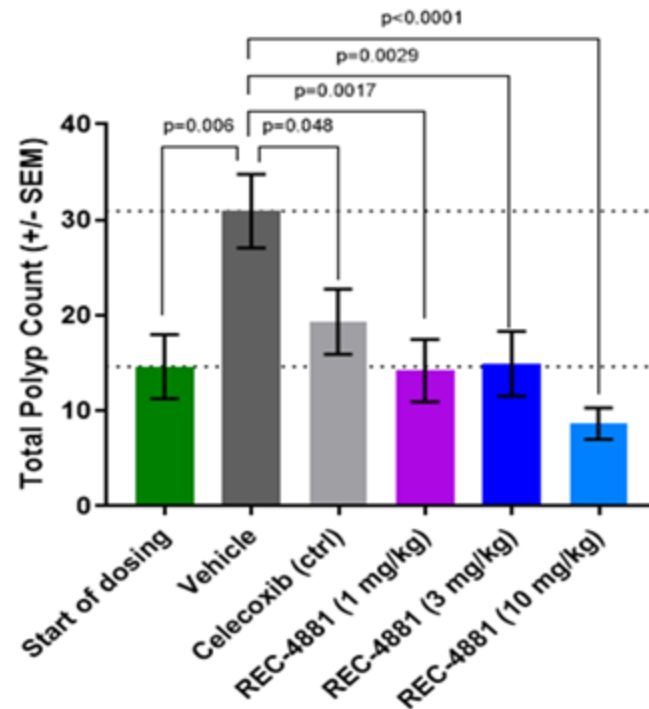
- Potential **first-in-disease** and **best-in-class** for FAP
- **Potent, non-competitive, allosteric** MEK1/2 inhibitor
- Oral 4 mg dose is **pharmacologically active** with meaningful target engagement
- PK/PD profile supports **localized GI activity enriching at the disease site**

| | REC-4881 ¹ |
|---|-----------------------|
| Half-Life (hr) | 48-60 |
| Dose Regimen | 4 mg QD |
| COLO-205 Cells ² In Vitro (nM) | 0.54 |
| MEK1 IC ₅₀ (nM) ³ | 3 |
| Mean Clinical Concentration (unbound nM) | 0.37 |
| Unchanged Fecal Percent of Dose (%) | 17 |

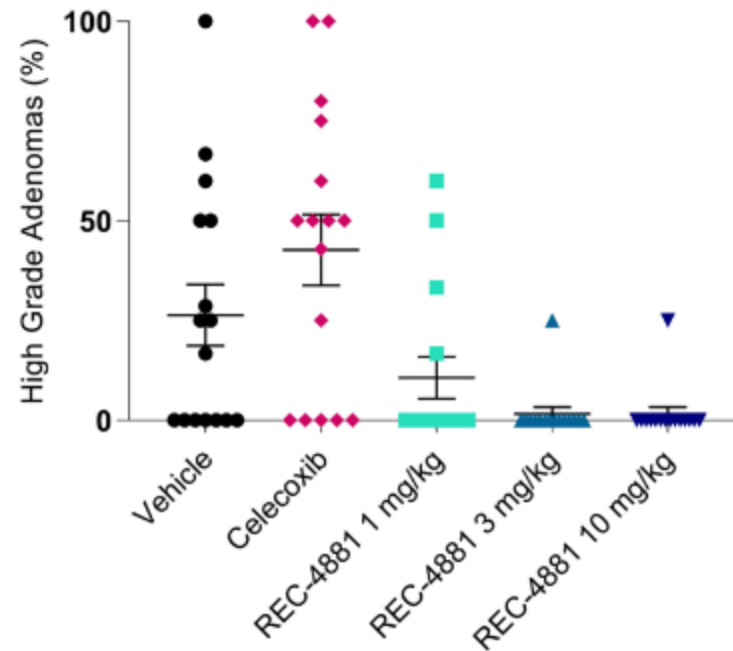
REC-4881's high GI excretion and long half-life supports targeted exposure at GI adenomas — the primary sites of disease in FAP

Preclinical data: REC-4881 reduced total polyps and high-grade adenomas in APC^{min/+} FAP models

Mean Polyps Per Group¹



% Pre-Cancerous Polyps²



Preclinical Summary

APC^{min/+} Mouse Model of FAP

- **Significant reduction in polyp count**, outperforming celecoxib at clinically relevant exposures³
- Decreases both **polyp number** and **pre-cancerous adenomas**

1. Mean GI polyp count after oral administration of indicated dose of REC-4881, celecoxib or vehicle control for 8 weeks. Polyp count at start of dosing reflects animals sacrificed at the start of study (15 weeks of age). P < 0.001 for all REC-4881 treatment groups versus vehicle control.

2. Same data displayed in A shown for individual animals on study suggests that at lowest dose tested (1 mg/kg) REC4881 demonstrates maximum efficacy

3. Estimate celecoxib dose used equivalent to 400 mg BID human dose based on estimated water intake at 100mg/kg

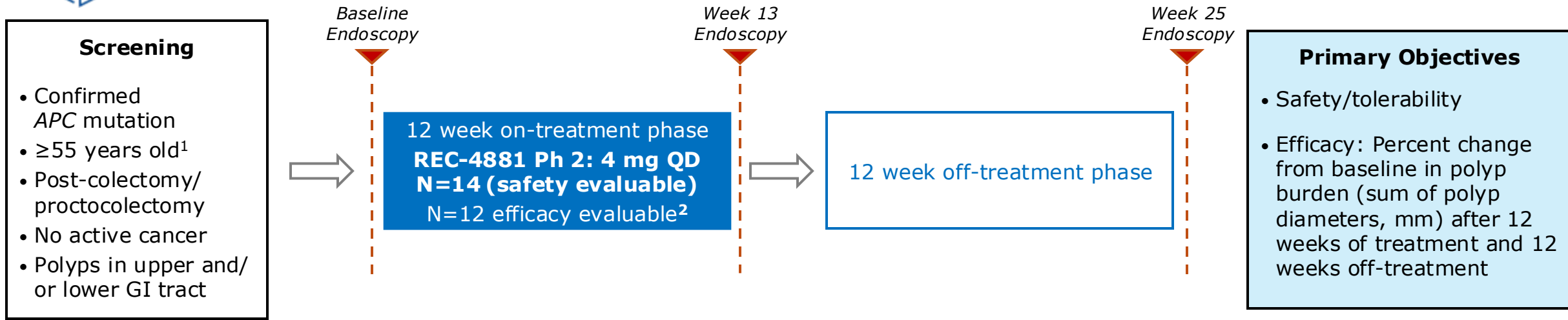


TUPELO

Ongoing Phase 1b/2 Updated Results & Natural History Analysis

Phase 2: REC-4881-201 study design & objectives

Safety, tolerability, PK/PD, and efficacy of once-daily REC-4881 for 12 weeks in FAP



*In parallel, **Natural History Study** conducted analyzing RWD from ~200 FAP patients with ~20 years of follow-up³*

Note: REC-4881 Ph 2 was also tested N=2 patients in 8 mg QD. One patient was excluded due to: less than 75% drug exposure (N=1) and the other patient was excluded due to having zero polyp burden at baseline (N=1)

1. After analysis in Phase 1b, the eligibility criteria was shifted to enroll only patients 55+ years of age to minimize TRAEs associated with MEK1/2 inhibition
2. Efficacy Evaluable Population: Defined as all participants who have measurable disease (non-zero polyp burden) at end of baseline endoscopy, received at least 75% of study drug, and have at least one post-baseline on study endoscopic assessment. For 4 mg QD group, of 14 patients, 12 were efficacy-evaluable. Two were excluded due to: lack of Week 13 endoscopy and less than 75% drug exposure (N=1) and less than 75% drug exposure (N=1)
3. In collaboration with Amsterdam University Medical Center

Phase 2: Baseline demographics and clinical characteristics

Study enrolled a clinically relevant FAP population with significant residual disease burden despite prior surgeries

Phase 2 patients in the safety evaluable population at baseline¹

| Characteristic | Ph 2 REC-4881 4 mg (N=14 safety evaluable) ² |
|---|---|
| Age, years | 61.9±4.8 |
| Sex, n (%) | |
| Female | 8 (57.1) |
| Male | 6 (42.9) |
| Race, n (%) | |
| White | 14 (100) |
| FAP Disease Primary Site, n (%)³ | |
| Duodenum | 11 (78.6) |
| Rectum/Pouch | 3 (21.4) |
| Spigelman Stage at Baseline, n (%)⁴ | |
| Stage 0 | 0 |
| Stage I | 1 (8.3) |
| Stage II | 2 (16.7) |
| Stage III | 7 (58.3) |
| Stage IV | 2 (16.7) |
| Unknown | 2 (16.7) |
| Total Polyp Burden at Baseline, mm | 814.5±2376.7 |
| Median | 132.0 |

Note: Plus-minus values are means ± SD. Percentages may not total 100 due to rounding

1. Only patients from Phase 2 have FAP-related information since no endoscopy assessments were performed for Phase 1b participants

2. N=14 safety evaluable patients, N=12 efficacy evaluable patients in Phase 2

3. N=1 No LGI anatomy; N=2 No UGI anatomy

4. Spigelman Staging System is used to assess the severity of duodenal polyposis in patients with FAP. The stage is determined based on polyp number and size, histology, and dysplasia severity

Phase 1b and Phase 2: REC-4881 summary of adverse events

REC-4881's safety profile is consistent with the MEK inhibitor class

| Event, n (%) | REC-4881 Ph 1b and 2 4 mg (N=19 safety evaluable) ¹ |
|--|---|
| Any TEAE related to study drug (TRAE) | 18 (94.7) |
| Grade 4/5 TRAE | 0 |
| Grade 3 TRAE | 3 (15.8) |
| Discontinuation due to TRAE | 4 (21.1) |
| Dose interruption due to TRAE | 2 (10.5) |
| Dose modification due to TRAE | 0 |

REC-4881 Safety

4 mg dose: Safety profile **consistent with MEK1/2 inhibition**

- **Most common TRAEs Grade 1/2:**
 - Dermatitis acneiform (57.9%; 52.6% Grade 1/2, 5.3% Grade 3)
 - Blood CPK increase (36.8%; 26.3% Grade 1/2, 10.5% Grade 3)
 - Rash (31.6%; all Grade 1/2)
 - Diarrhea (26.3%; all Grade 1/2)
 - LVEF decrease (10.5%; Grade 2)²
- **Low rates of Grade 3 TRAEs, no Grade 4/5 events:**
 - Grade 3 (n=3): Dermatitis acneiform (5.3%, n=1), blood CPK increase (10.5%, n=2)
- **Discontinuations (n=4) due to:**
 - Grade 1 (n=1): 1 diarrhea
 - Grade 2 (n=3): 1 retinopathy, 1 rash, 1 hypertension
- **92% common TRAEs are Grade 1/2**
- 72% common TRAEs resolved within 12 weeks³

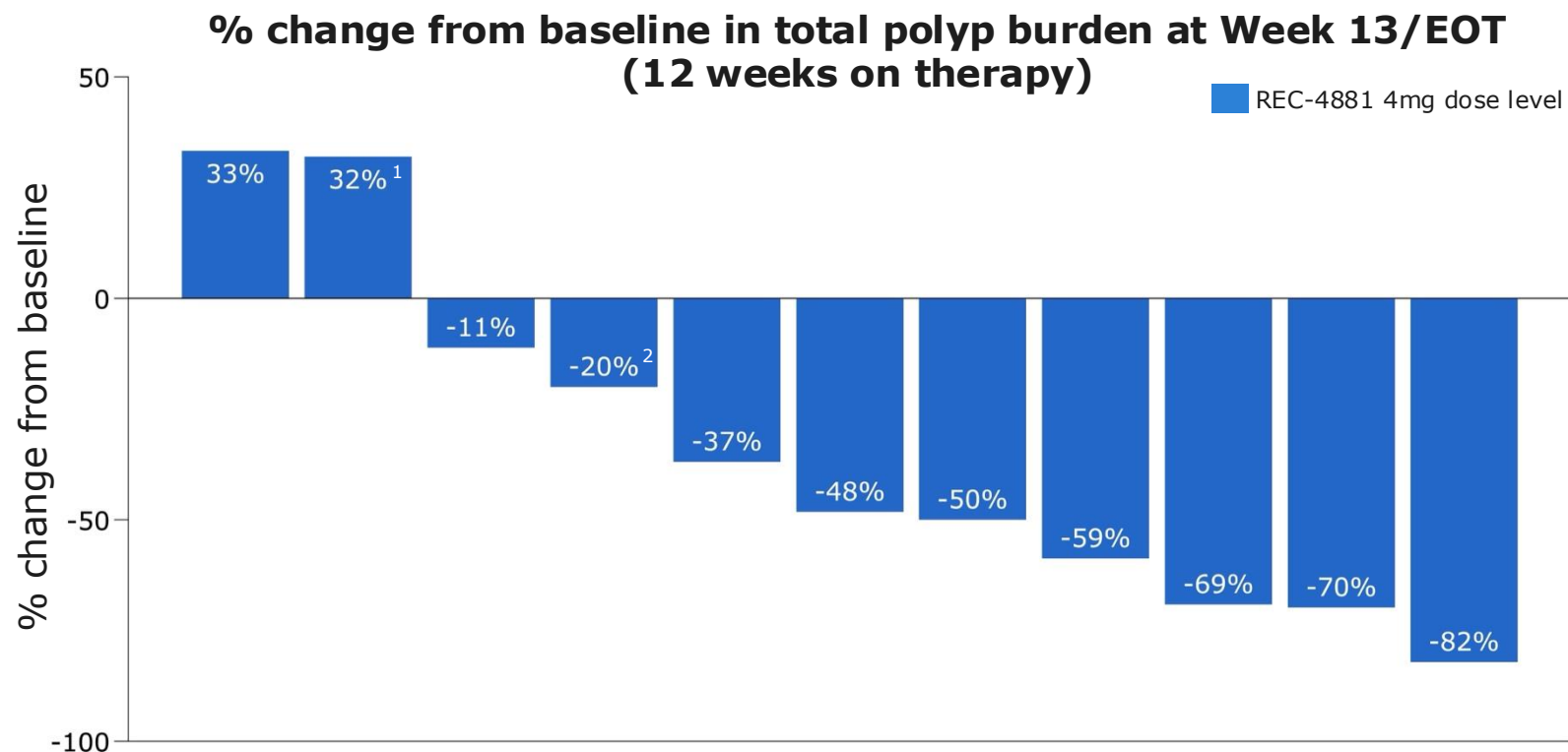
Note: For 8 mg (N=2, only 1 efficacy evaluable), N=1 (50%) exhibited Grade 2 TRAEs (rash), no Grade 3 TRAEs

1. For 4 mg, N=5 patients in Phase 1b and N=14 patients in Phase 2 were dosed; safety data cutoff date of 2025-11-25

2. Decrease was transient, patients were asymptomatic and 1 recovered following drug withdrawal. Based on using absolute percent change in LVEF, which is the widely used approach to measure changes in trials, for MEK inhibitors, etc.

3. Resolved: 96% Grade 1/2, 4% Grade 3; Unresolved: 71% Grade 1/2, 29% Grade 3 (e.g., CPK, Dermatitis Acneiform, rash)

3 months on-treatment: Rapid polyp burden reductions with REC-4881, 75% of patients responding



Percent (%) change from baseline calculates the change between post-resection value from screening visit to the pre-resection value at Week 13/EOT visit. Subjects with absolute value of 0 at baseline are not displayed.

REC-4881 Efficacy

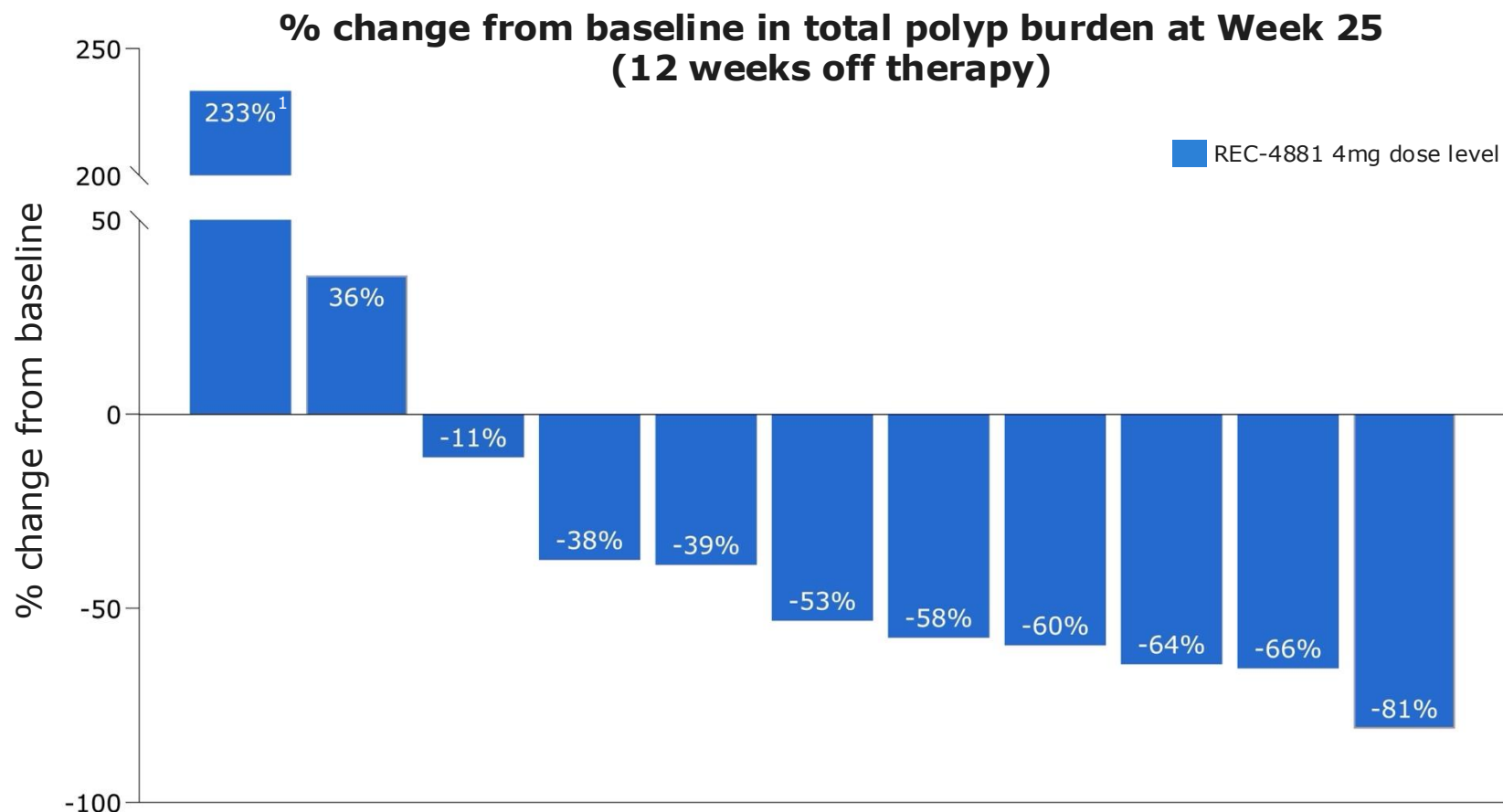
- **Majority (9/12, 75%) of evaluable patients showed reductions in polyp burden by Week 13**
- **Polyp burden reduction³: 43% median (32% mean) at week 13**
- **Signal across UGI & LGI polyps**
 - **Upper GI burden (n=10): 52% median (46% mean) reduction** in UGI polyp burden
 - **Lower GI burden (n=9): 57% median (36% mean) reduction** in LGI polyp burden
- Responses seen across a wide range of baseline burdens

Note: N of 12 patients were efficacy evaluable, 1 patient missed Week 13 assessment

Note: Polyp burden defined as the sum of all diameters of polyps in the GI

1. Following the March data cut, a quality review identified suboptimal bowel preparation at baseline. To ensure an accurate, like-for-like assessment, polyp burden was re-evaluated using video review restricted to the clean distal LGI segments matched to the same anatomical regions at Weeks 13 and 25
2. Patient reached W25 but did not perform W25 Assessment
3. Efficacy Evaluable Population (n=12): Defined as all participants who have measurable disease (non-zero polyp burden) at end of baseline endoscopy, received at least 75% of study drug, and have at least one post-baseline on study endoscopic assessment. One patient was efficacy evaluable after completion of W25 assessment but did not complete W13 assessment, baseline measurement carried forward for W13 assessment per SAP for missing data. Therefore, this patient contributed 0% polyp burden reduction at W13 and not shown in figure.

After 3 months off-treatment: Durable polyp burden reductions with REC-4881, with 82% of patients responding



Percent (%) change from baseline calculates the change between post-resection value from screening visit to the pre-resection value at Week 25/EOT visit.

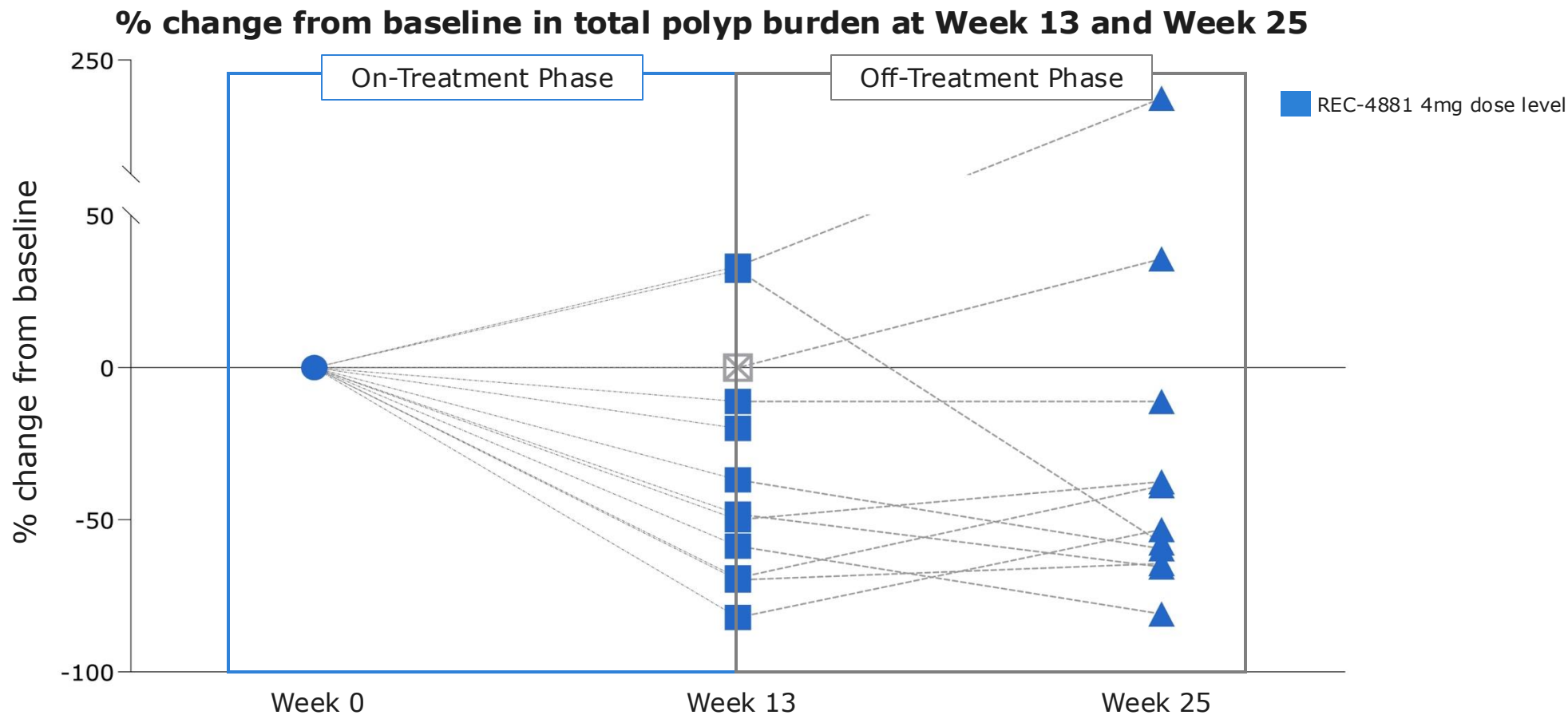
REC-4881 Efficacy

- **11 patients** on 4 mg efficacy evaluable²
- **82% of patients responded** (>0% reduction)
- **73% achieved durable ≥30% reductions** through Week 25
- **53% median** (18% mean) reduction in total polyp burden at Week 25 assessment
- Deep responses observed across a wide range of baseline polyp burdens

Note: Polyp burden defined as the sum of all diameters of polyps in the GI

1. Non-responder with 233% increase – polyp burden increased from 3mm to 10mm due to one polyp growth at Week 25
2. Efficacy Evaluable Population: Defined as all participants who have measurable disease (non-zero polyp burden) at end of baseline endoscopy, received at least 75% of study drug, and have at least one post-baseline on study endoscopic assessment. One patient who had a week 13 endoscopy did not have a Week 25 endoscopy

3 months on and 3 months off-treatment: REC-4881 produces durable reductions in polyp burden through Week 25

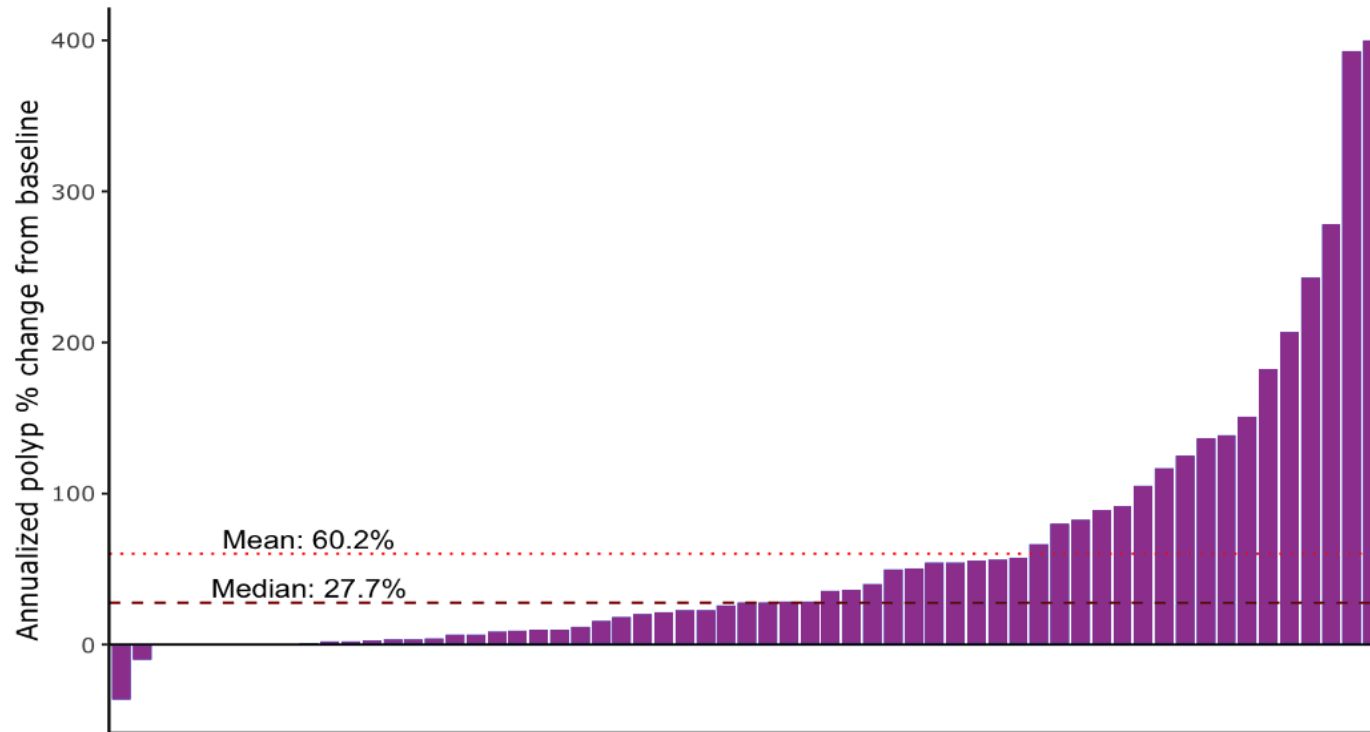


Week 25 results show that REC-4881's biological effect persists after dosing ends, with most patients maintaining meaningful reductions in polyp burden

Note: Percent (%) change from baseline calculates the change between post-resection value from screening visit to the pre-resection value at Week 13/EOT visit and Week 25/EOT. Efficacy Evaluable Population: Defined as all participants who have measurable disease (non-zero polyp burden) at end of baseline endoscopy, received at least 75% of study drug, and have at least one post-baseline on study endoscopic assessment. One patient was efficacy evaluable after completion of W25 assessment but did not complete W13 assessment, baseline measurement carried forward for W13 assessment per SAP for missing data (X box at W13)

Natural history analysis: ~87% show polyp burden increase, while ~10% remained stable, highlighting the disease progression of FAP

Annualized % change in polyp burden in a natural history cohort Amsterdam University Medical Center FAP registry (N=55)



Each bar represents one patient. 6 patients are repeated due to having separate evaluation intervals for lower and upper GI. Data includes 55 patients aged ≥ 55 with history of colectomy and measurable polyp burden at baseline endoscopy. In routine care, endoscopies for lower and upper GI are performed annually with variability. Therefore, polyp burden percent change was annualized. 52 (97%) of the 55 patients had an increase or stable polyp burden. 6 patients had separate endoscopic evaluations for upper and lower GI involvement and have repeated bars.

Natural History Study Summary

- **Key inclusion criteria of the TUPELO trial were applied** to select natural history cohort
- **Natural history** analysis showed:
 - **87% of untreated FAP patients had annual** polyp-burden increase
 - **10%** remained **stable**
 - **3% showed modest decrease**—showing spontaneous regression is rare
 - **Average of 60% polyp burden increase annually**
- Rates were annualized because **endoscopies are administered annually in routine care**
- These data are **not intended for direct comparison** with clinical trial data

Week 13 Spigelman stage: REC-4881 produced Spigelman downstaging in 40% of patients, reflecting UGI disease improvement

| Patient | Spigelman Stage Initial screening -> WK13 -> WK25 |
|---------|--|
| 1 | III -> III -> III |
| 2 | I -> NA ¹ -> II |
| 3 | III -> II -> II |
| 4 | II -> II -> II |
| 5 | III -> II -> II |
| 6 | IV -> IV -> IV |
| 7 | III -> III -> III |
| 8 | III -> III -> NA ² |
| 8 | III -> I -> I |
| 10 | IV -> II -> III |

REC-4881 Efficacy

Improvements reflect **concordant reductions in the upper GI including** polyp burden reduction, polyp count, and Spigelman downstaging

- **WK13:**
 - **4/10 (40%) patients** achieved a ≥ 1 -point change in Spigelman Stage
 - Spigelman **downstaging reflects improvement in duodenal polyposis severity** — a major unmet need with limited therapeutic options.
- **WK25:**
 - **4/10 patients maintained a** ≥ 1 -point change in Spigelman Stage
 - 1 patient had a 1-point increase
 - 1 patient did not have Week 25 endoscopy

Natural history RWD analysis showed **20% of patients experienced an increase in Spigelman stage** between annual endoscopies in routine care. No decrease in Spigelman stage was observed.

AUMC: Amsterdam University Medical Center

Note: N=10 efficacy evaluable for UGI; 2 patients lacked UGI anatomy. Spigelman Stage can be confounded by sampling errors

1. Patient did not perform WK13 endoscopy and so no biopsy collected

2. No biopsy sample collected at WK25 to calculate Spigelman Score

Summary and Next Steps

REC-4881: Phase 1b/2 data review and next steps (I/II)

REC-4881

First Clinical Validation
for Recursion OS Platform

Potential **First-in-Disease**
and **Best-in-Class**

Platform-Generated Novel Mechanistic Insight → First Clinical Proof

- **First clinical validation** of the Recursion OS
- Recursion's phenotypic platform uncovered that **selective MEK1/2 inhibition rescues cells from the loss of APC**, revealing REC-4881 as a **targeted therapeutic** candidate for FAP
- First to **clinically investigate MEK1/2 inhibition for the treatment of FAP**
- Demonstrates Recursion's ability to translate **unbiased phenotypic and mechanistic insights** into potentially differentiated therapeutics

REC-4881: Phase 1b/2 data review and next steps (I/II)

REC-4881

First Clinical Validation
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Potential **First-in-Disease**
and **Best-in-Class**

Rapid and Durable Reductions in Polyp Burden at 4 mg

- **Safety** consistent with MEK inhibitors; low rate of Grade 3 events; no Grade 4/5
- **Rapid and substantial clinical activity** with 43% median reduction in **3 months**; 75% of patients responded
- **Durable effect** with 53% median reduction after **3 months off therapy**; 82% of patients responded despite being off treatment
- **Responses seen in both Upper GI and Lower GI disease**, with 40% Spigelman downstaging by Week 13
- Natural history shows **patients see polyp burden progression when left untreated** with **87% of patients** experience significant **annual polyp growth**, 10% remained stable, and 3% showed modest reduction
- **Current investigational agents** evaluated in separate studies generated approximately **17–29% reduction in polyp burden after 12 months** of treatment. **No off-treatment durability** results were reported¹

REC-4881: Phase 1b/2 data review and next steps (II/II)

REC-4881

First Clinical Validation
for Recursion OS Platform

Potential **First-in-Disease**
and **Best-in-Class**

High Unmet Need in FAP

- FAP affects >**50,000 patients in US/EU5**
- Patients face **life-long polyposis progression** with *near-100%* CRC risk in the absence of surgery with **no approved pharmacotherapies**
- Current sequential surgical treatments lead to **substantial loss in quality of life** and **fail to target the underlying disease biology**

Path Forward

- Expanding population from **≥55 to ≥18 years old** and further **optimizing dosing** schedule
- **Engage FDA** (1H 2026) to **define registration path** informed by leveraging data generated thus far along with RWE assessments
- Continue **follow-up for evaluation of durability**



Thank you to all the trial patients and their families and clinical trial sites

Fireside Chat

Jessica Stout, DO | *Asst Clinical Professor, University of Utah*

AI Cohen, MD, FACS, FASCRS | *Former Chief of Colorectal Service,
Memorial Sloan-Kettering Cancer Center*

David Mauro, MD, PhD | *Chief Medical Officer*

Najat Khan, PhD | *Chief R&D Officer and Commercial Officer, Incoming CEO*

Fireside chat: Today's speakers



David Mauro, MD, PhD
Chief Medical Officer
Recursion

- Former CMO **Codiak BioSciences** & **Checkmate Pharmaceuticals**
- Former ED of Oncology **Merck**
- Over 20 years of experience in **oncology drug development**, incl. spearheading early- and late-stage development for **more than 25 INDs** over the past decade



Jessica Stout, DO
Assistant Clinical Professor
University of Utah School of Medicine

- Double board-certified in **Internal Medicine and Gastroenterology**
- Specializes in **complex gastrointestinal disease management** incl. long-term, multi-organ **management of FAP**



Najat Khan
Chief R&D Officer and Commercial Officer,
Incoming CEO

- Former Chief Data Science Officer & SVP, Global Head of R&D Strategy, Portfolio & Operations at **Johnson & Johnson** Innovative Medicine
- Former Partner & Senior Principal at **Boston Consulting Group**, advising leading biopharma and healthcare organizations on strategy, operations, and innovation



Alfred M. Cohen, MD, FACS, FASCRS
Former Chief of Colorectal Service
Memorial Sloan-Kettering Cancer Center

- Former CMO **Cancer Prevention Pharmaceuticals**
- Former Director, CEO at Lucille P. Markey Cancer Center at **University of Kentucky**
- >50 years of experience in **CRC treatment & research**, with clinical **focus on QoL** in patients with CRC, Lynch syndrome, and **FAP**



Recursion[®]