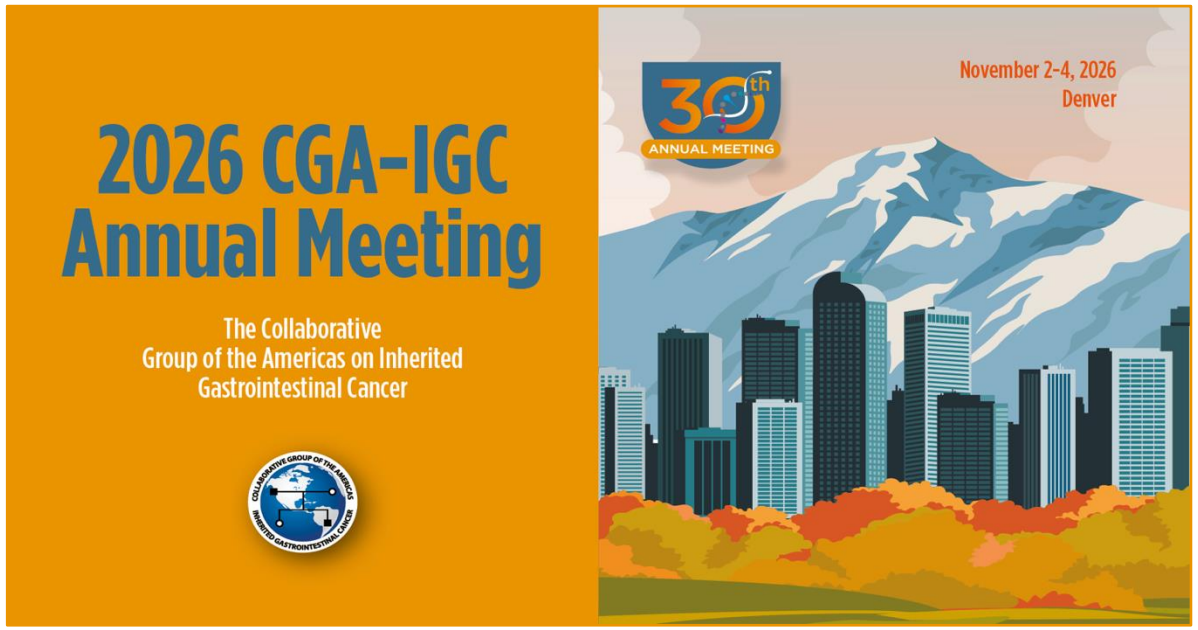
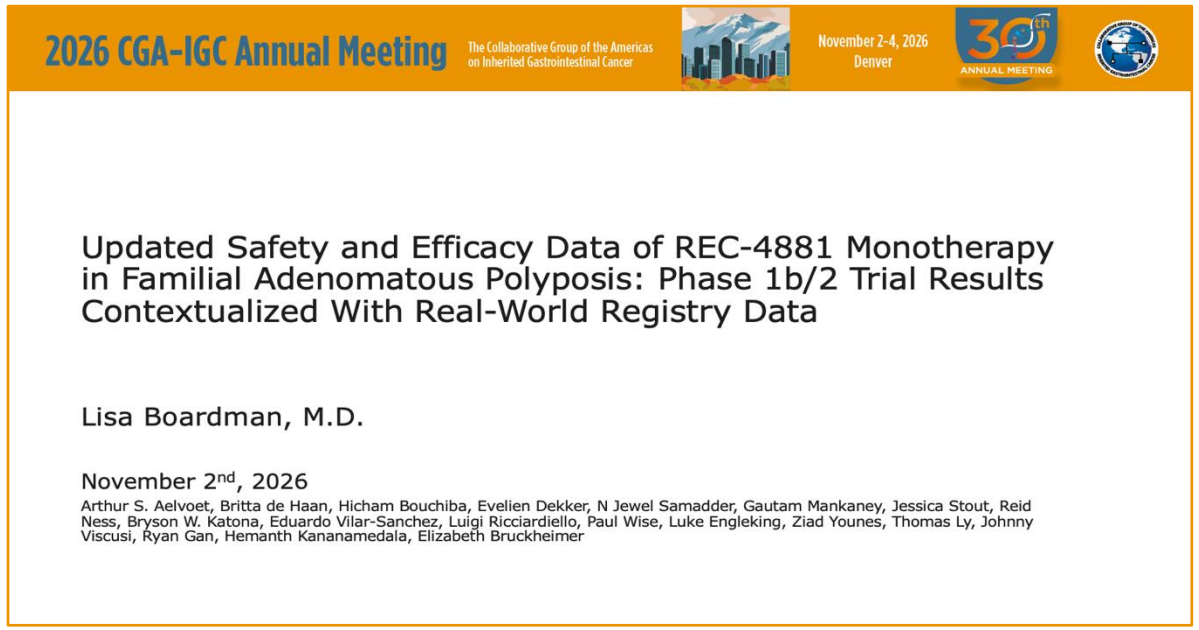
Translating proof to products

REC-4881

MEK1/2







30th CGA-IGC Annual Meeting, Denver

- Leading annual meeting dedicated specifically to **hereditary GI cancer syndromes** including FAP
- Highly targeted audience: **Connects the entire care ecosystem** including gastroenterologists, surgeons, genetic counselors, and researchers

REC-4881 Data Summary

- Reductions in larger, higher-risk polyps observed
- Combined findings support activity across the upper and lower GI tract
- No new safety signals observed in the updated data

A registrational study of REC-4881 in FAP is expected to begin in 2H 2027

Note: Registrational study initiation pending outcome of ongoing FDA discussions

REC-4881: Potential to transform FAP care

Study eligibility expanded to adults 18 years and older

Rapid reductions that persist off treatment

- **87%**[1] with reductions in total polyp burden[2]
- **1 in 3** achieved ≥65% reduction after 12 weeks of treatment (**47%** median reduction)
- **85%** (11 of 13) maintained reductions below baseline after 12 weeks off-treatment
- **Reductions in larger, higher-risk polyps**

Deep reductions in upper GI polyp burden

- **92%** had reductions in upper GI polyp burden[4]
- **~1 in 2** achieved ≥65% reduction in upper GI polyp burden
- **92%** (11 of 12) maintained reductions below baseline 12 weeks off treatment

Oral therapy with a favorable safety profile

- **Favorable safety profile**[5] with 15.4% Gr 3 TRAEs and no TRAEs above Gr3
- **Durable benefit** off therapy may allow for flexible dosing potential

On REC-4881's rapid activity

"I think it's very impressive… there's no study before that showed these kind of regressions."

- Gastroenterology physician-scientist, European AMC

On upper GI activity

"This would make a big difference for the patient… it would lower the cancer risk, would lower the surgery risk and it would maybe lower the number of endoscopies."

- Practicing gastroenterologist, US AMC

1. Efficacy Evaluable (n=16); Efficacy-evaluable population defined as participants with measurable disease (non-zero polyp burden) at baseline endoscopy, who received at least 75% of study drug, and had at least one post-baseline on-study endoscopic assessment. At Week 13, n=15 efficacy evaluable patients, as 1 patient did not have a Week 13 endoscopy. At Week 25, n=13 efficacy evaluable patients, as 2 patients did not have Week 25 results at the data cutoff and 1 patient discontinued the study after Week 13
2. Polyp burden defined as the sum of all polyp diameters; percent change from baseline is measured at the Week 13 and Week 25 endoscopies
3. Fewer polyps >5 mm at Week 13 in 6 of 8 patients with at least one polyp >5 mm at baseline
4. Upper GI: n=13; 2 patients had no upper GI anatomy and 1 patient did not have a Week 13 endoscopy
5. Safety evaluable (n=26; 5 Ph 1b and 21 Ph 2). Of the 21 Ph 2, 16 are efficacy evaluable per the definition noted above

Recursion

FAP: a serious, lifelong chronic disease with zero approved therapies

~$15B

'26 Total Addressable FAP market (US + EU5)[6]

EPIDEMIOLOGY

>50K **Diagnosed FAP patients**

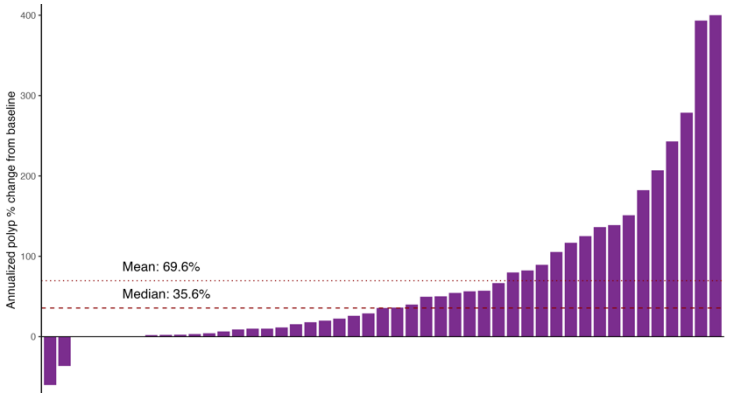
US + EU5[5]

Inherited APC-driven disease

Characterized by precancerous polyps

Real world data show persistent polyp growth over time

Amsterdam UMC registry (n=47, ~20-year follow-up)[4]



85%

of evaluated patients had annual polyp-burden increase

UNMET NEED & BURDEN OF CARE

0 approved therapies

No approved pharmacologic treatments for FAP-associated duodenal polyposis

Lifelong chronic disease

Most penetrant driver of GI cancer[1]
Multiple major surgeries and a lifetime of surveillance[2]

Upper GI: greatest unmet need

Complex polyp removal; advanced disease may require major surgery

Psychological burden

Patients develop anxiety and/or PTSD, ongoing cancer threat concerns, repeated procedures and life-altering interventions[3]

1. Ferrandon et al, Fam Cancer. 2025; doi: 10.1007/s10689-025-00479-3, NCI BRCA1 and BRCA2: Cancer Risks and Management (PDQ®). 2. EMA/NORD and Orphanet based Epi estimate adjusted for colectomy rate (Syngal S, et al. Am J Gastroenterol 2015;110(2):223–62. DOI 10.1038/ajg.2014.435) and long term surveillance rate (Tatsuta et al. PLoS One. 2026 Feb 13;21(2):e0339401. 3. Mol MJ, et al. Psychooncology. 2025;34(5):e70176. 4. Natural History Analysis evaluated data from ~200 FAP patients. The analysis shown is a subset of 47 patients aged ≥55 with a history of colectomy and measurable polyp burden at baseline endoscopy, matching TUPELO's original eligibility criteria. Each bar represents one patient. The analysis is intended to contextualize the TUPELO single-arm data and to better understand the background natural history of FAP disease progression. Limitations include potential variability in polyp count estimation between endoscopies; endoscopies are typically conducted annually in routine care, while the TUPELO data represent polyp burden at Week 13. These data are not intended for direct comparison with clinical trial data. 5. US: Burke et al. (2026). ACG Clinical Guideline: Diagnosis and Management of Adenomatous Colorectal Polyposis Syndromes. Range of [1 in 2,800 to 1 in 18,000] -> A single prevalence of 1 in 10,000 is applied to both the US and EU5. FAP shows no significant racial, ethnic or geographic variation (BMJ Best Practice), and no founder effect was found in population-based study (Gut 2002). Diagnosis rates: Danish diagnosed point prevalence divided by Danish birth frequency = 82.7%, Karstensen JG et al. Endoscopy 2019; 6. Based on company estimates, modeled total addressable market, pre and post colectomy FAP (not realized or forecasted sales): Based on rare-disease oral net price (benchmark GOMEKLI ~$30k/mo for adults); assumes 10% gross-to-net discount and EU5 price as 0.7x of US price

Recursion

Disease challenge: Upper GI is the greatest unmet need in FAP

The majority of polyp burden in post-colectomy patients is found in the upper GI

No approved therapies

Management relies on lifelong surveillance and repeated endoscopy, with frequency increasing as disease severity progresses

Complex endoscopic polyp removal

Thin duodenal walls and challenging anatomy increase the risk of bleeding and perforation during polyp removal[1]

High-morbidity, high-risk surgery

Advanced disease may require removal of the duodenum, with high complication rates and prolonged recovery

Highest cancer risk

Upper GI cancers remain a major cause of cancer-related death after colectomy

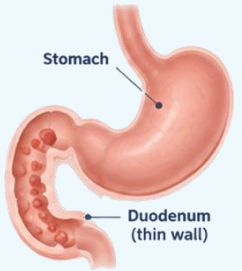
Polyp shape and thin duodenal walls complicate upper GI polyp removal



Sessile polyp in upper GI[2]



Peduncular polyp in lower GI[3]



> [Removal of the duodenum] has a lot of complications – way more than the colon… 50% got a severe complication… [hospital stays that] could be four months. So this is really surgery you want to prevent.
>
> - Gastroenterology physician-scientist, European AMC

1. Lim, C. H., & Cho, Y. S. (2016). Nonampullary duodenal adenoma: Current understanding of its diagnosis, pathogenesis, and clinical management. World journal of gastroenterology 2. Lee, J.H., Chung, W.C. (2018). Duodenal Tumors. In: Chun, H., Yang, SK., Choi, MG. (eds) Clinical Gastrointestinal Endoscopy 3. Kuipers, E., Rösch, T. & Bretthauer, M. Colorectal cancer screening—optimizing current strategies and new directions. Nat Rev Clin Oncol 10, 130–142 (2013)

REC-4881 | Potential to transform $15B FAP market opportunity

US + EU5 FAP ADDRESSABLE MARKET[1]

Estimated prevalence ~67,100

Diagnosed prevalence[2] ~55,700

POST-COLECTOMY[3]

~37,200

67% | Immediate focus

→

PRE-COLECTOMY[3]

~18,500

33% | Future expansion

~$10B[4]

Post-colectomy opportunity

→

~$5B[4]

Pre-colectomy expansion

POTENTIAL LIFETIME IMPACT OF REC-4881

Reduce repeated interventions

Potential to reduce surveillance frequency and repeated endoscopic procedures

Patient benefit Less treatment burden, travel and time away from work

Avoid high-morbidity complications

Potential to reduce major upper GI surgery, cancer, and complications associated with endoscopic resection

System benefit Hospital capacity, caregiver burden and follow-up costs

On REC-4881's polyp burden reduction

"This would make a big difference for the patient… it would lower the cancer risk, would lower the surgery risk and it would maybe lower the number of endoscopies."

- Practicing gastroenterologist, US AMC

1. US: Burke et al. (2026). ACG Clinical Guideline: Diagnosis and Management of Adenomatous Colorectal Polyposis Syndromes. Range of [1 in 2,800 to 1 in 18,000] -> A single prevalence of 1 in 10,000 is applied to both the US and EU5. FAP shows no significant racial, ethnic or geographic variation (BMJ Best Practice), and no founder effect was found in population-based study (Gut 2002).
2. Per company calculations, diagnosed share is calculated as Danish diagnosed point prevalence divided by Danish birth frequency: 6.11 per 100,000 ÷ 7.39 per 100,000 (1 in 13,528) = 82.7%, rounded to 83%; Karstensen JG et al. Colorectal cancer in individuals with familial adenomatous polyposis, based on analysis of the Danish Polyposis Registry. Endoscopy 2019;51(04):S127
3. Per company calculations, the post-colectomy share is the midpoint of the US rate and the Danish rate: (80.65% + 53%) ÷ 2 = 66.8%. The US rate averages two cohorts (82.7% and 78.6%); Feldman D et al. Dis Colon Rectum. 2025; J Gastrointest Surg. 2019, Utah registry; Beck SH et al. Am J Gastroenterol. 2024
4. Based on rare-disease oral net price (benchmark GOMEKLI ~$30k/mo for adults); assumes 10% gross-to-net discount and EU5 price as 0.7x of US price, per company calculations

Recursion

Recursion's platform uncovered a novel therapeutic opportunity in FAP

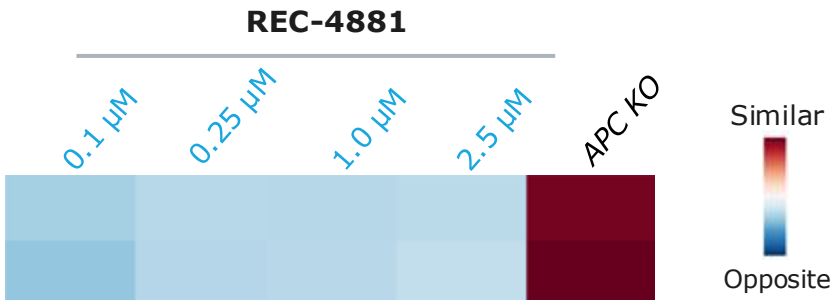
Novel insight uncovered by platform

Unbiased phenotypic screening

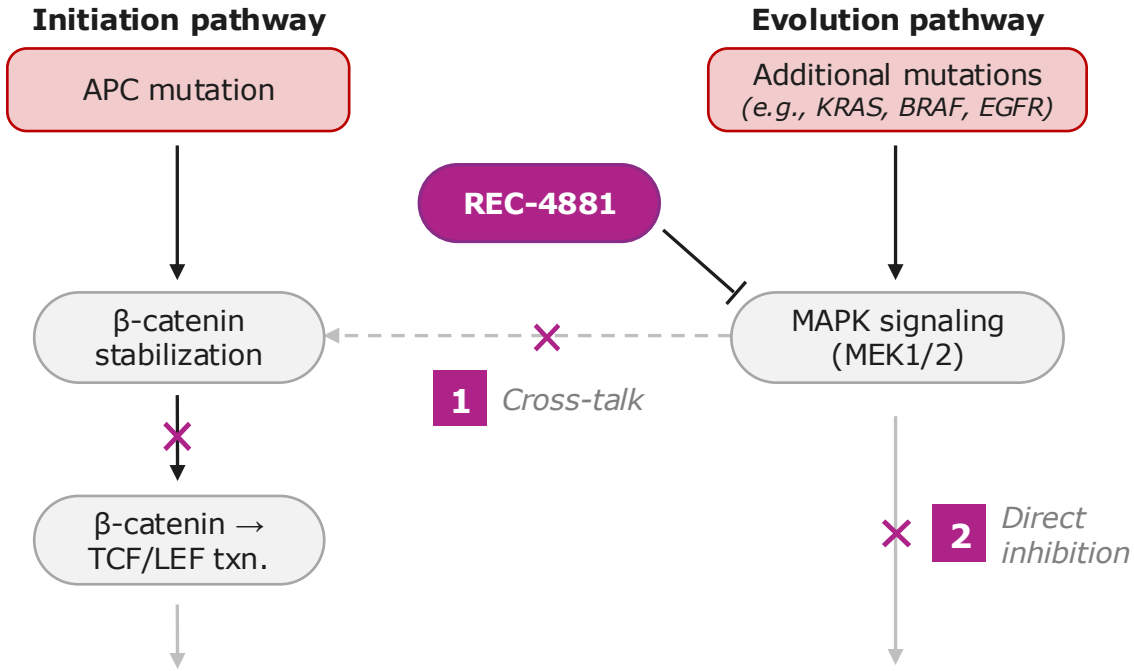
Proprietary AI foundation models analyzed cellular images to identify relationships between genetic and compound perturbations

Unexpected biological insight

MEK1/2 inhibition emerged as a potential way to reverse cellular phenotypes associated with APC loss – unappreciated synthetic rescue relationship



Mechanistic rationale for REC-4881



Sources: Fujishita T, et al. Cancer Sci. 2015;106(6):692–699; Blaj C, et al. Cancer Res. 2017;77(7):1763–1774; Guardavaccaro D, Clevers H. Sci Signal. 2012;5(219):pe15; Cheng YT, et al. Part Fibre Toxicol. 2026;23:4; Georgopoulos NT, et al. J Cell Sci. 2014;127(13):2967–2982.

Recursion

Week 13 polyp burden reduction | REC-4881 drives significant reductions in total polyp burden after 12 weeks of treatment

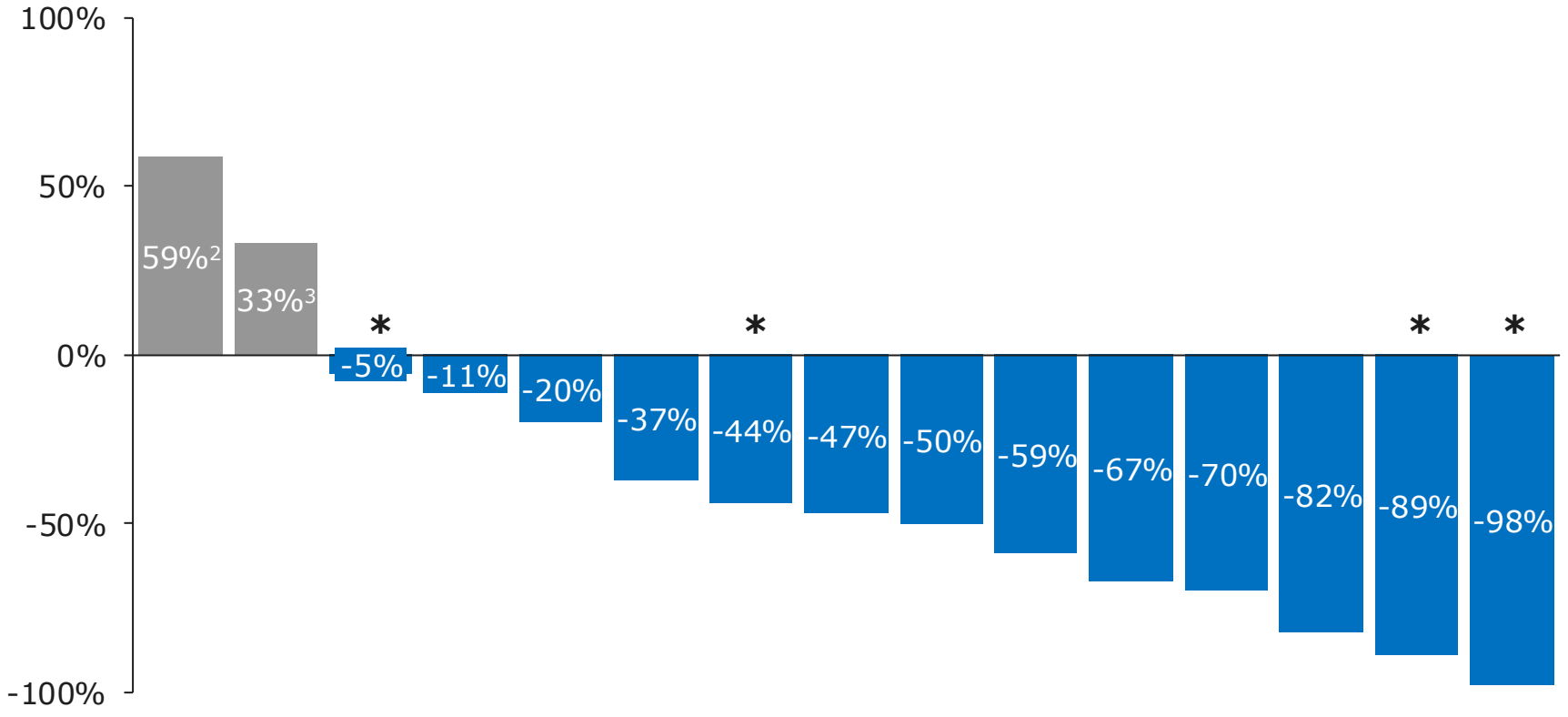
Study eligibility expanded to adults 18 years and older

87%
Had a reduction in total polyp burden

≥65%
Polyp burden reduction in 1 in 3 patients

47%
Median total polyp burden reduction

Week 13 total polyp burden reduction relative to baseline (n=15[1])



*Additional patients since previously reported data cutoff (November 25, 2025)

1. 15 of 16 efficacy evaluable patients are shown, as 1 patient did not have a Week 13 endoscopy
2. The site corrected baseline polyp burden to exclude polyps excised for biopsy at screening; this correction revised the previously reported increase from 32% to 59%
3. Baseline polyp burden of 3 mm (2 polyps), increasing to 4 mm (1 polyp) at Week 13, all in the lower GI

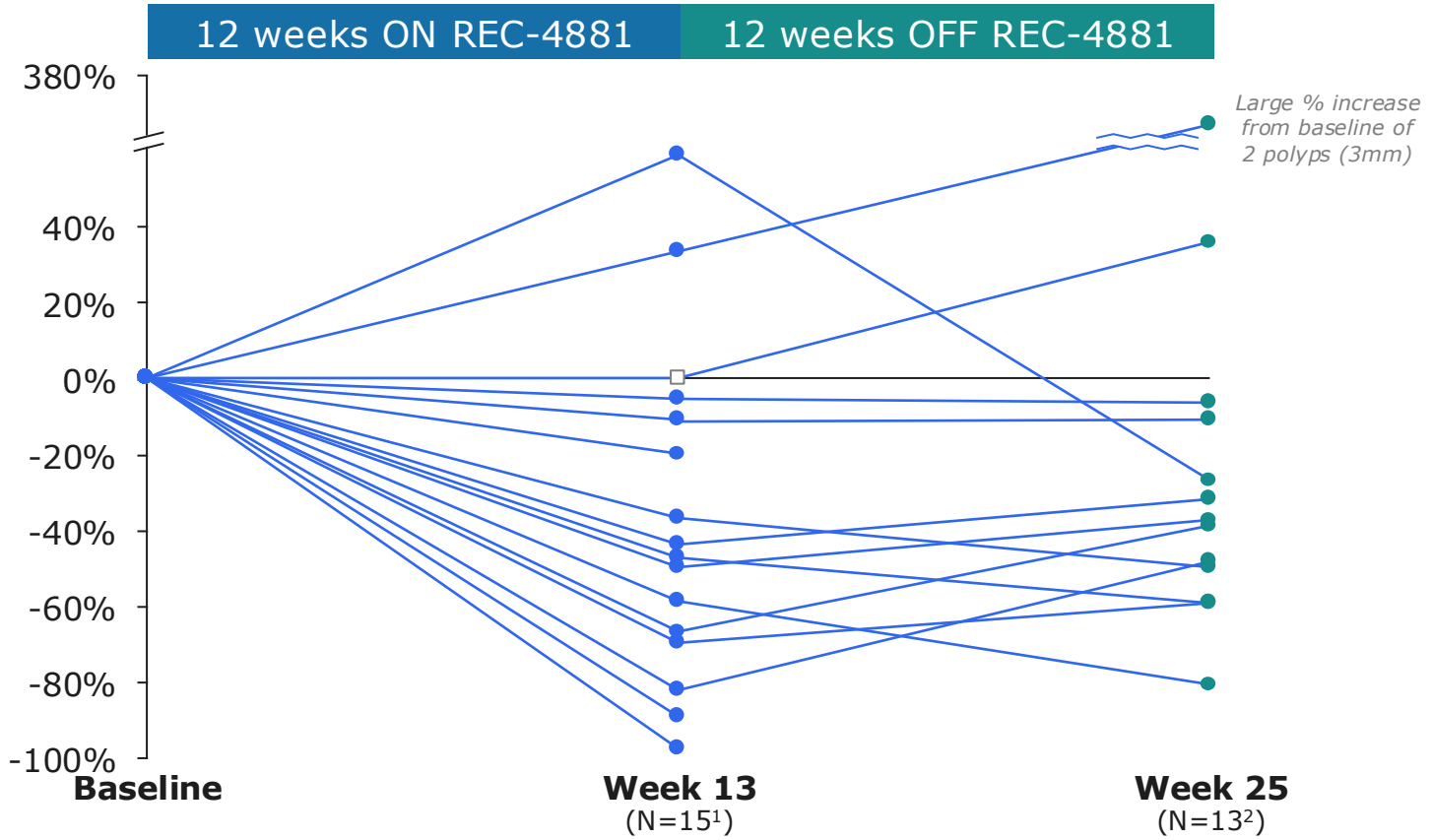
Note: Efficacy Evaluable (n=16); Efficacy-evaluable population defined as patients with measurable baseline polyp burden, ≥75% study drug exposure, and ≥1 post-baseline endoscopic assessment
Note: Results reflect the 10-Sep-2026 data cutoff. Data review since the last presentation also updated 2 patients after minor corrections of <5mm: -48% to -47% and -69% to -67%

Recursion

Week 25 polyp burden reduction | Treatment effect persists after 12 weeks off treatment

11 of 13 patients remained below baseline at Week 25

% change from baseline in total polyp burden in post-colectomy patients at Wk. 13 and Wk. 25



85%

11 of 13 patients remained below baseline after 12 weeks off treatment

- Sustained activity despite 12 weeks without treatment
- Durability may allow for dosing flexibility, which may be important in the context of long-term disease management

1. 15 of 16 efficacy-evaluable patients, 1 patient did not have a Week 13 endoscopy and is shown at Week 13 as an open square
2. 13 of 16 efficacy-evaluable patients; 2 patients did not have Week 25 results at the data cutoff, and 1 patient discontinued the study after Week 13

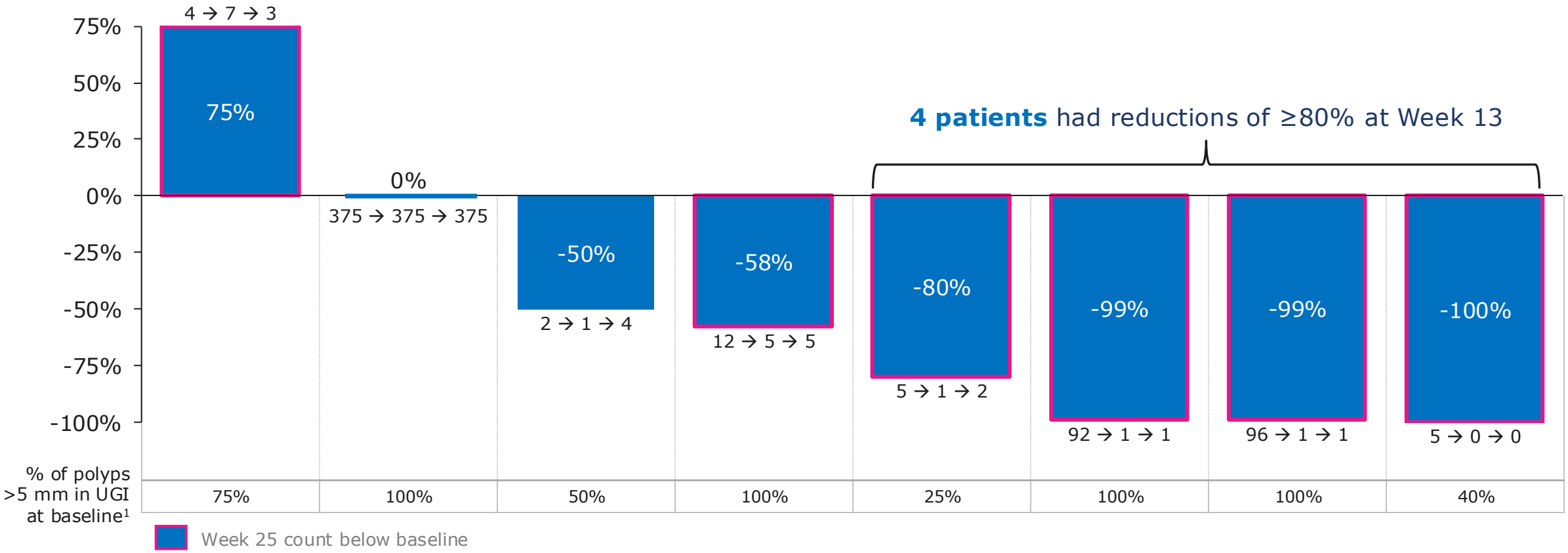
Note: For any excisions at the week 13 endoscopy, the excised polyp burden was added back to the week 25 polyp burden beforecalculating the change from baseline

Recursion

REC-4881 reduced number of >5 mm polyps in 6 of 8 patients

% change from baseline to Week 13 in count of polyps >5 mm across entire GI tract (n=8)

Patients with at least one polyp >5 mm at baseline



Baseline → Wk13 → Wk25: Absolute counts of polyps >5 mm shown above each bar

Not shown: 1 patient with no polyps >5 mm at baseline had 4 polyps >5 mm at Week 13 and 2 polyps >5 mm at Week 25

1. Proportion of total polyps >5 mm found in the Upper GI at baseline
Note: Polyps >10 mm were not separately measured and are included in the totals for polyps >5 mm

Recursion

Data Cutoff Date: 10-Sep-2026

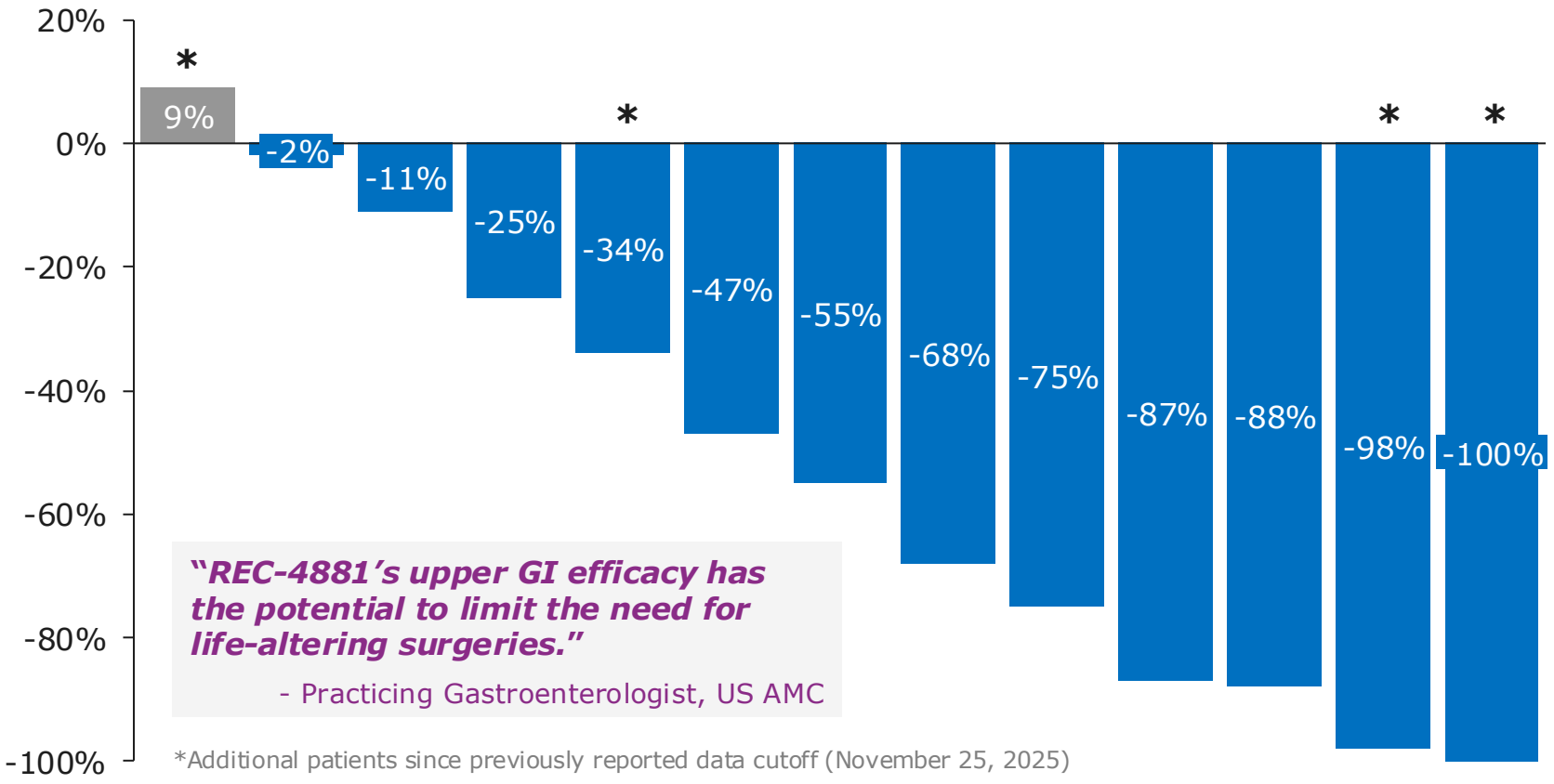
Week 13 - upper GI | Nearly 1 in 2 (46%) patients achieved ≥65% reductions in upper GI polyp burden

92%
Had a reduction in upper GI polyp burden

≥65%
Polyp burden reduction in ~1 in 2 patients

2 pts
Achieved ≥98% reductions

Week 13 upper GI polyp burden reduction (n=13[1])



"REC-4881's upper GI efficacy has the potential to limit the need for life-altering surgeries."

- Practicing Gastroenterologist, US AMC

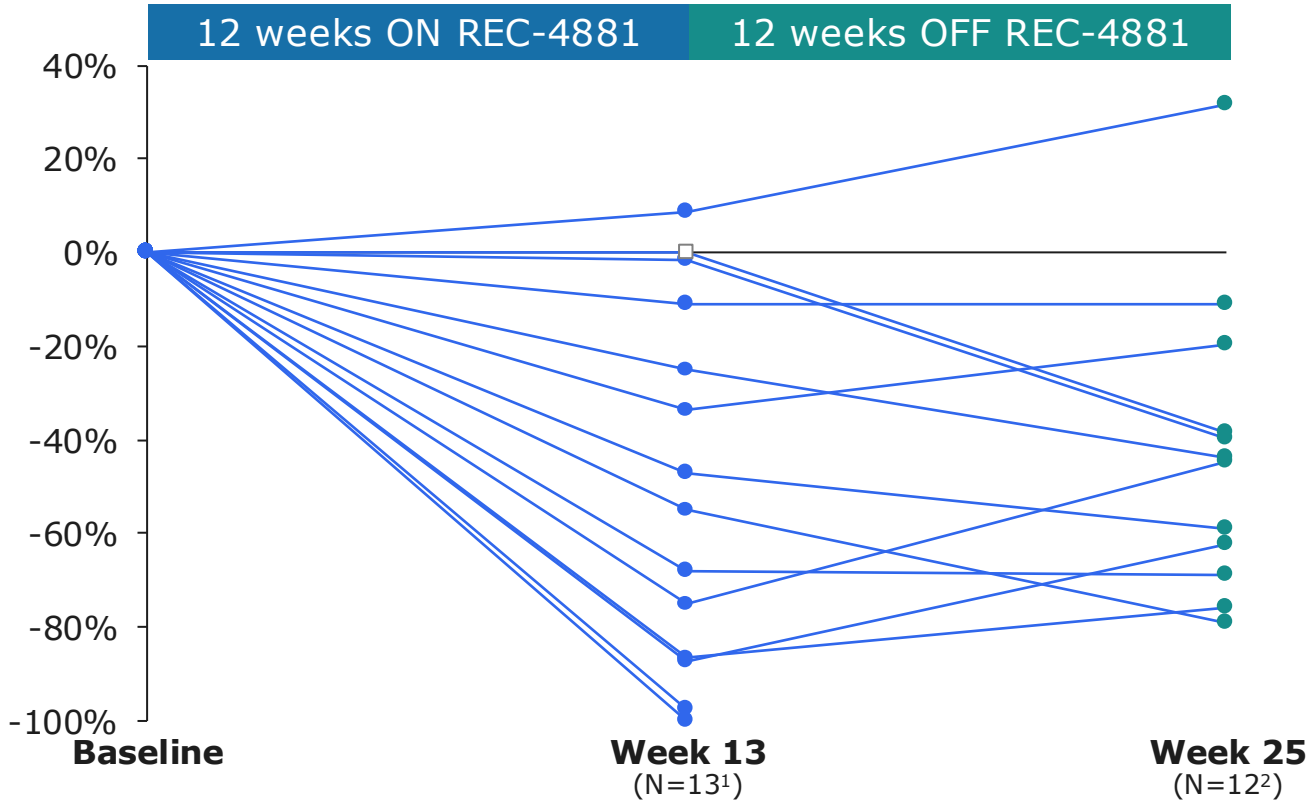
*Additional patients since previously reported data cutoff (November 25, 2025)

1. Upper GI evaluable at week 13: n=13 of 16 efficacy evaluable patients; 2 patients had no upper GI anatomy and 1 did not have a Week 13 endoscopy

Week 25 – upper GI | Polyp burden reductions persist after 12 weeks off treatment

11 of 12 patients remained below baseline at Week 25

% change from baseline in upper GI polyp burden in post-colectomy patients at Wk. 13 and Wk. 25



92%

11 of 12 patients remained below baseline after 12 weeks off treatment

- Sustained activity in the upper GI, where unmet need is greatest
- 6 of 11 patients[3] with equal or greater reductions during the off-treatment period

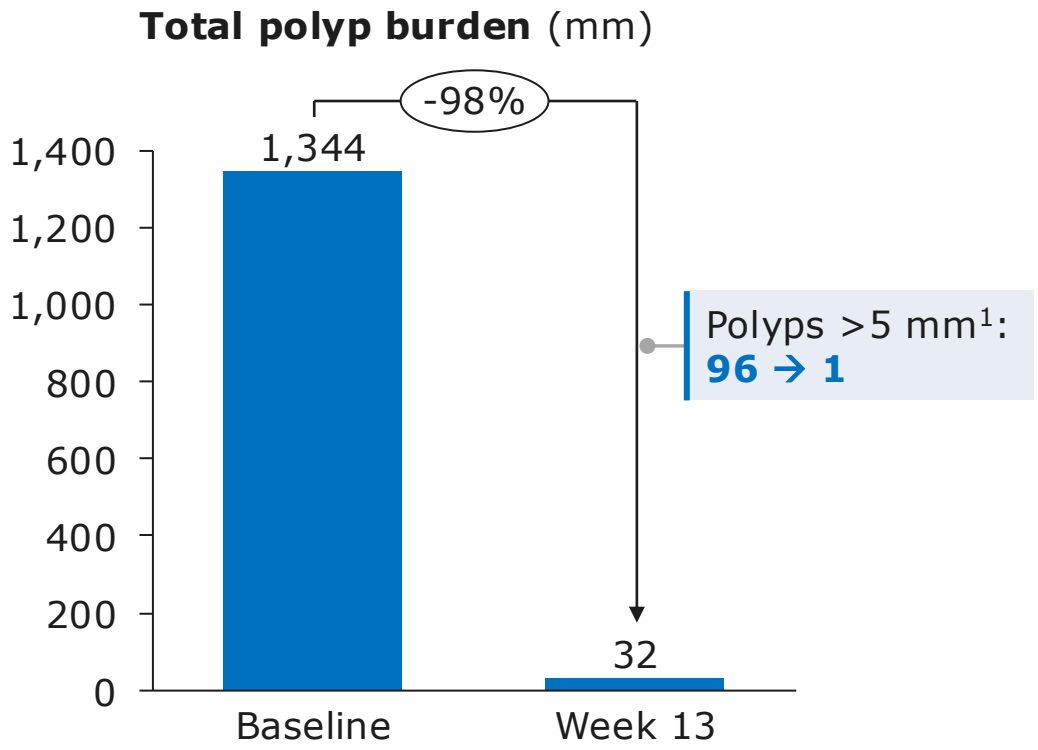
1. Upper GI evaluable at week 13: n=13 of 16 efficacy evaluable patients; 2 patients had no upper GI anatomy and 1 did not have a Week 13 endoscopy (shown at Wk. 13 as an open square)
2. Upper GI evaluable at week 25: n=12 of 16 efficacy evaluable patients; 2 patients had no upper GI anatomy and 2 did not have Week 25 results at the data cutoff
3. Of the 11 patients with both Week 13 and Week 25 upper GI assessments

Note: For any excisions at the week 13 endoscopy, the excised polyp burden was added back to the week 25 polyp burden before calculating the change from baseline.

Recursion

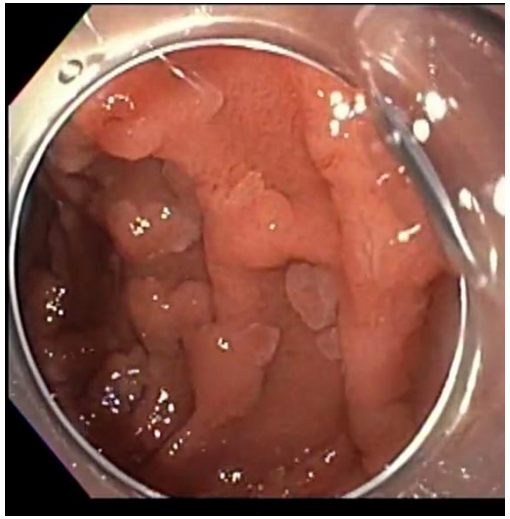
Additional detail on highest Week 13 responder

The result presented here is only for one out of the 16 total efficacy evaluable patient population; this result is not representative of the overall efficacy of the evaluable patient population to date

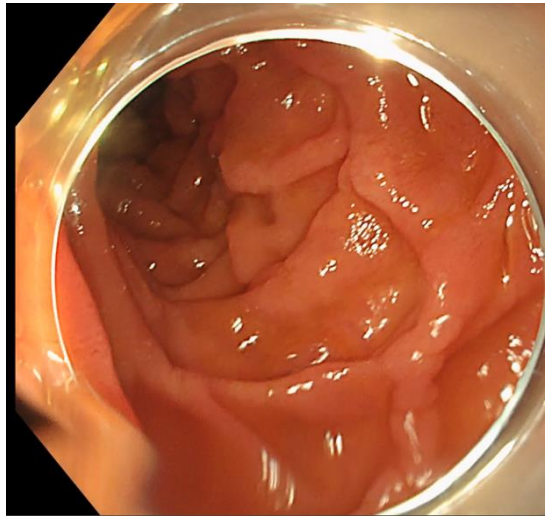


Images taken from the 2nd portion of the duodenum of highest responder

Baseline



Week 13



1. Patient had 96 polyps >5 mm at baseline which were reduced to 1 polyp >5 mm at Week 13

Recursion

Spigelman staging is used by clinicians to classify disease severity and inform need for interventions, including surgery

Spigelman stage grades duodenal & ampullary disease; clinically, it drives how often patients are scoped and when surgery is needed

Stage 0	Stage I	Stage II	Stage III	Stage IV
No polyps No Dysplasia	**<5mm sized polyp only** <5 polyps Low Grade Dysplasia, limited risk of HGD	**<5mm sized polyp only** 5-20 polyps Low Grade Dysplasia, limited risk of HGD	**5-10mm sized polyp present** >20 polyps Low Grade Dysplasia, at risk of HGD	**>10mm sized polyp present** >20 polyps High Grade Dysplasia (HGD)

Note: Stage is a points total across number, size, histology and dysplasia; boxes show typical findings

"Really what you're looking for is a drug … that can manage duodenal adenomas to the point where it decreases the need for surgical intervention—that's ideal."
- Practicing Gastroenterologist, US AMC

Yen T, Stanich PP, Axell L, et al. APC-Associated Polyposis Conditions. 1998 Dec 18 [Updated 2022 May 12] GeneReviews

Week 13 Spigelman stage: 50% achieved Spigelman downstaging at Week 13, reflecting upper GI disease improvement

Baseline	Week 13	Week 25
III	III	III
I	N/A[1]	II
III	II	II
II	II	II
III	II	II
III	II	II
III	II	N/A[1]
II	0	N/A[1]
IV	IV	IV
III	III	III
III	III	III
III	III	N/A[1]
III	N/A[1]	I
IV	II	III

Patient had a 2-stage change at Week 25

Week 13 | ON TREATMENT

50% 6 of 12 patients achieved ≥1-stage Spigelman downstaging

Week 25 | 12 weeks OFF TREATMENT

4 of 6 Patients down-staged at Week 13 maintained ≥1-stage improvement compared baseline, the other 2 were not assessed

One additional patient was not assessed at Week 13 but showed a 2-stage decrease at Week 25

Natural history context

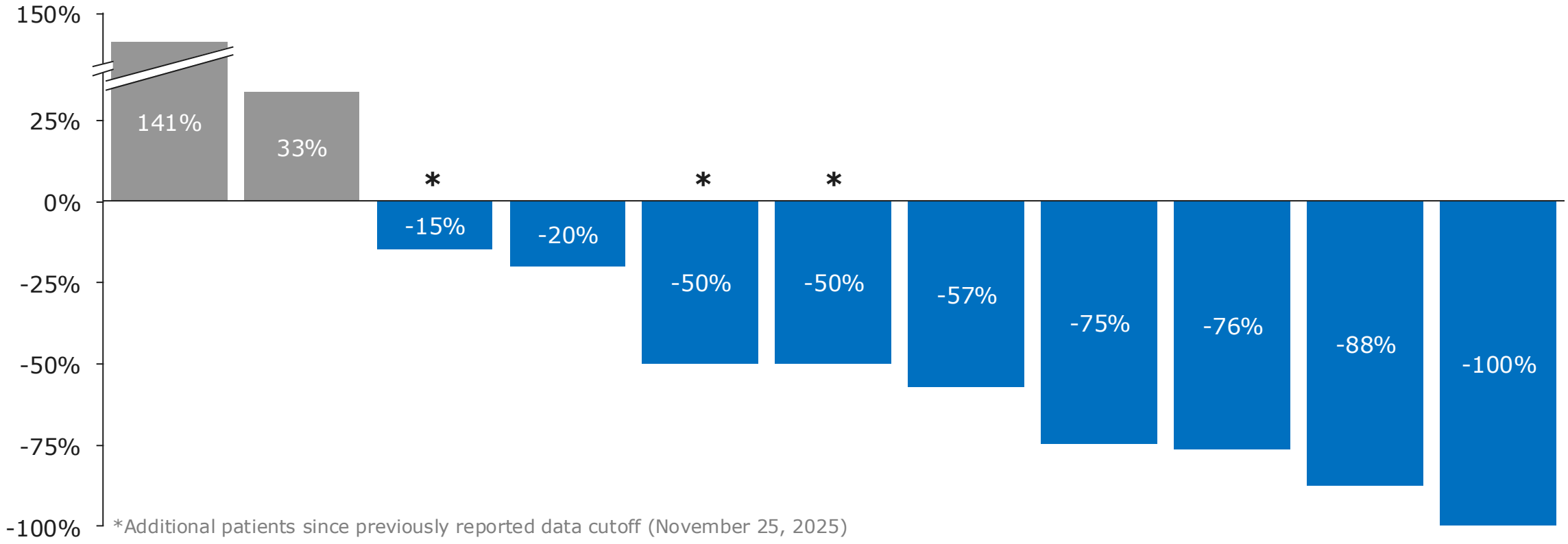
20% Experienced stage progression between annual endoscopies; no downstaging observed[2]

1. Spigelman assessment not provided 2. Natural History Analysis evaluated data from ~200 FAP patients
Note: N=14 efficacy evaluable for Spigelman staging; two patients did not have upper GI anatomy

Lower GI | 82% of patients had reductions in polyp burden from baseline after 12 weeks of treatment

~1 in 3 patients with ≥65% polyp burden reduction from baseline[1]

Week 13 lower GI polyp burden reduction (n=11[2])



*Additional patients since previously reported data cutoff (November 25, 2025)

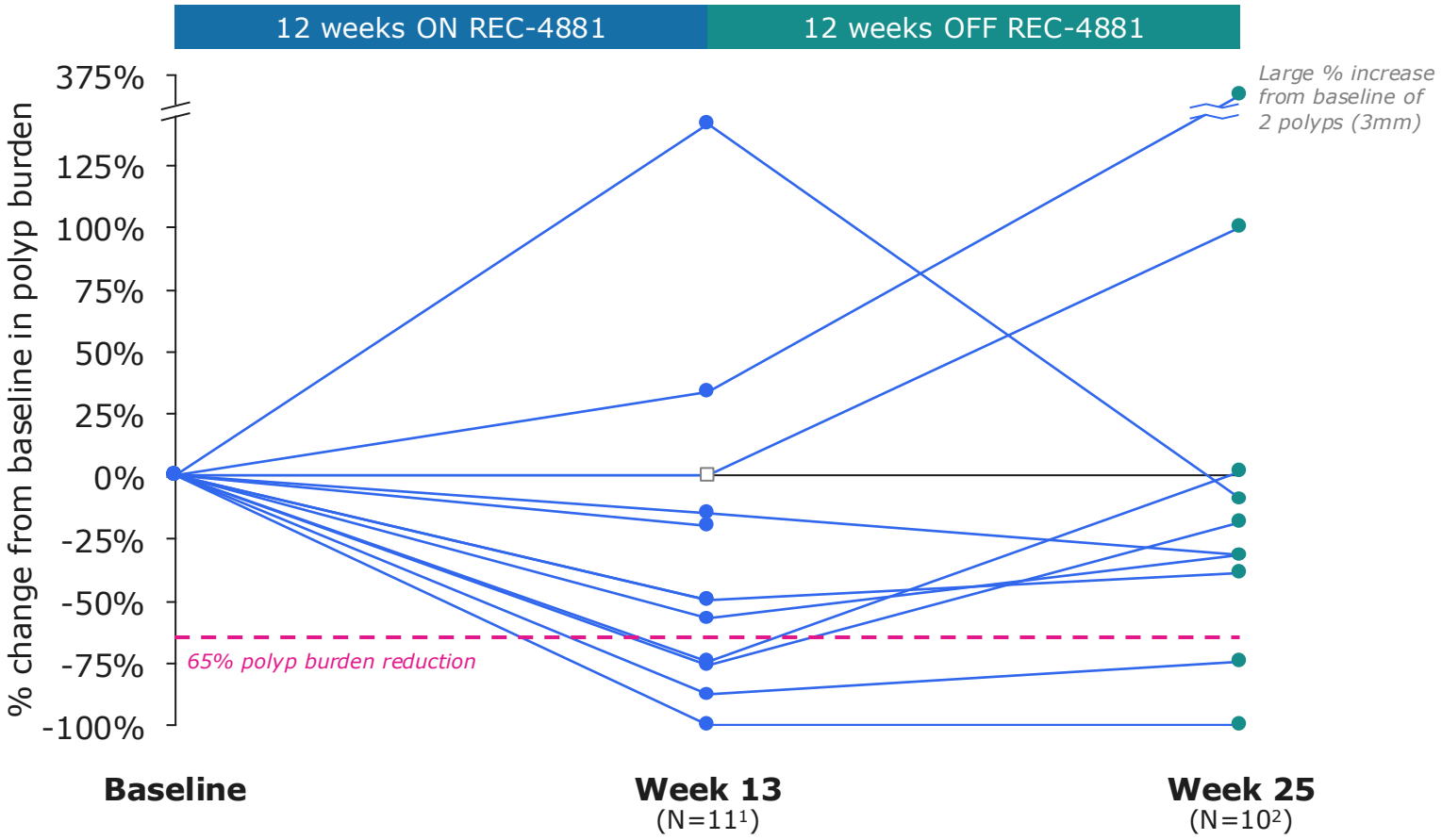
Not shown: Two patients with no lower GI polyp burden at baseline but non-zero lower GI polyp burden at Week 13 so % change cannot be calculated[3]

1. 4 of 11 (36%) patients had ≥65% polyp burden reduction from baseline
2. Of the full set of 16 efficacy evaluable patients, 11 patients are shown: 1 patient had no lower GI anatomy, 1 patient missed their Week 13 visit, and 3 patients had no polyp burden at baseline
3. One patient had an increase in polyp burden of 0 mm to 1 mm (new patient since last data cut); the second patient had an increase in polyp burden of 0 mm to 6 mm

Lower GI | Polyp burden in the lower GI remained below baseline in 70% of patients 12 weeks after stopping REC-4881

Lower GI polyp burden reduction

Week 13 & Week 25



Key findings

- **4 of 11 patients** at Week 13 with lower GI polyp burden **reduction ≥65%**
- **7 of 10 patients** with lower GI polyp burden below baseline at Week 25, after 12 weeks off drug

1. Lower GI evaluable at Week 13: n=11 of 16 efficacy-evaluable pts; 3 had no lower GI polyps at baseline, 1 had no Lower GI anatomy, and 1 did not have a Week 13 endoscopy (shown at Wk. 13 as an open square)
2. Lower GI evaluable at Week 25: n=10; 3 had no lower GI polyps at baseline, 1 had no Lower GI anatomy, 1 patient discontinued the study after Week 13, and 1 did not have Week 25 results at the data cutoff

Note: For any excisions at the week 13 endoscopy, the excised polyp burden was added back to the week 25 polyp burden before calculating the change from baseline

Recursion

Favorable safety profile supports potential for chronic dosing

Event, n (%)	REC-4881 4 mg QD (N=26 safety evaluable)[1]
Any TEAE related to study drug (TRAE)	**25** (96.2)
Grade 1/2 TRAE	**21** (80.8)
Grade 3 TRAE	**4** (15.4)
Grade 4/5 TRAE	**0** (0)
Discontinuation due to TRAE	**4** (15.4)
Dose interruption due to TRAE	**2** (7.7)

80.8% patients had TRAEs ≤ Grade 2 consistent with mechanism of MEK1/2 inhibition

Most common TRAEs Grade 1/2

- Dermatitis acneiform (57.7%)
- Blood CPK increase (26.9%)
- Rash (23.1%)
- Diarrhea (19.2%)
- LVEF decrease (11.5%)[2]

Low rates of Grade 3 TRAEs, no TRAEs >Grade 3:

- Blood CPK increase (7.7%, n=2)
- Dermatitis acneiform (3.8%, n=1)
- Rash (3.8%, n=1)

Discontinuations (n=4) due to:

- Grade 1 (n=2): 1 diarrhea, 1 left atrial enlargement (pre-existing)[3]
- Grade 2 (n=2): 1 retinopathy (pre-existing ocular condition)[4], 1 rash

AEs were manageable and most resolved within 12 weeks off treatment

1. For 4 mg, N=5 patients in Phase 1b and N=21 patients in the 12 weeks on/12 weeks off QD arm of the Phase 2 were dosed; safety data cutoff date of 2026-09-10
2. Occurred in N=3 patients. Patients were asymptomatic and 2 returned to >50% (the 3rd patient was 49% at the end of follow-up). Based on absolute percent change in LVEF and CTCAE v5.0, the approach widely used to measure LVEF changes in trials, including for MEK inhibitors.
3. Patient had pre-existing left atrial enlargement. Protocol was subsequently amended to exclude this condition
4. Patient had pre-existing ocular condition which worsened during treatment

Conclusions

Natural history analysis demonstrates consistent progression in polyp burden over time, contextualizing polyp burden reductions driven by REC-4881

REC-4881 safety

- Favorable safety profile; AEs consistent with the MEK1/2 inhibitor class
- Treatment-related AEs mostly Grade 1/2; Grade 3 (15%) and no Grade 4/5

REC-4881 polyp burden reduction

- Polyp burden reduction observed across both upper and lower GI, in 92% and 82% of evaluable patients, respectively
- Durability demonstrated in both upper and lower GI, with 92% and 70% of evaluable patients, respectively, remaining below baseline at Week 25
- 75% of patients evaluated with polyps >5 mm had reductions, which is important for endoscopic excisional management

Results to be further investigated in a registrational study anticipated to begin 2H 2027[1]

1. Pending outcome of ongoing FDA discussions