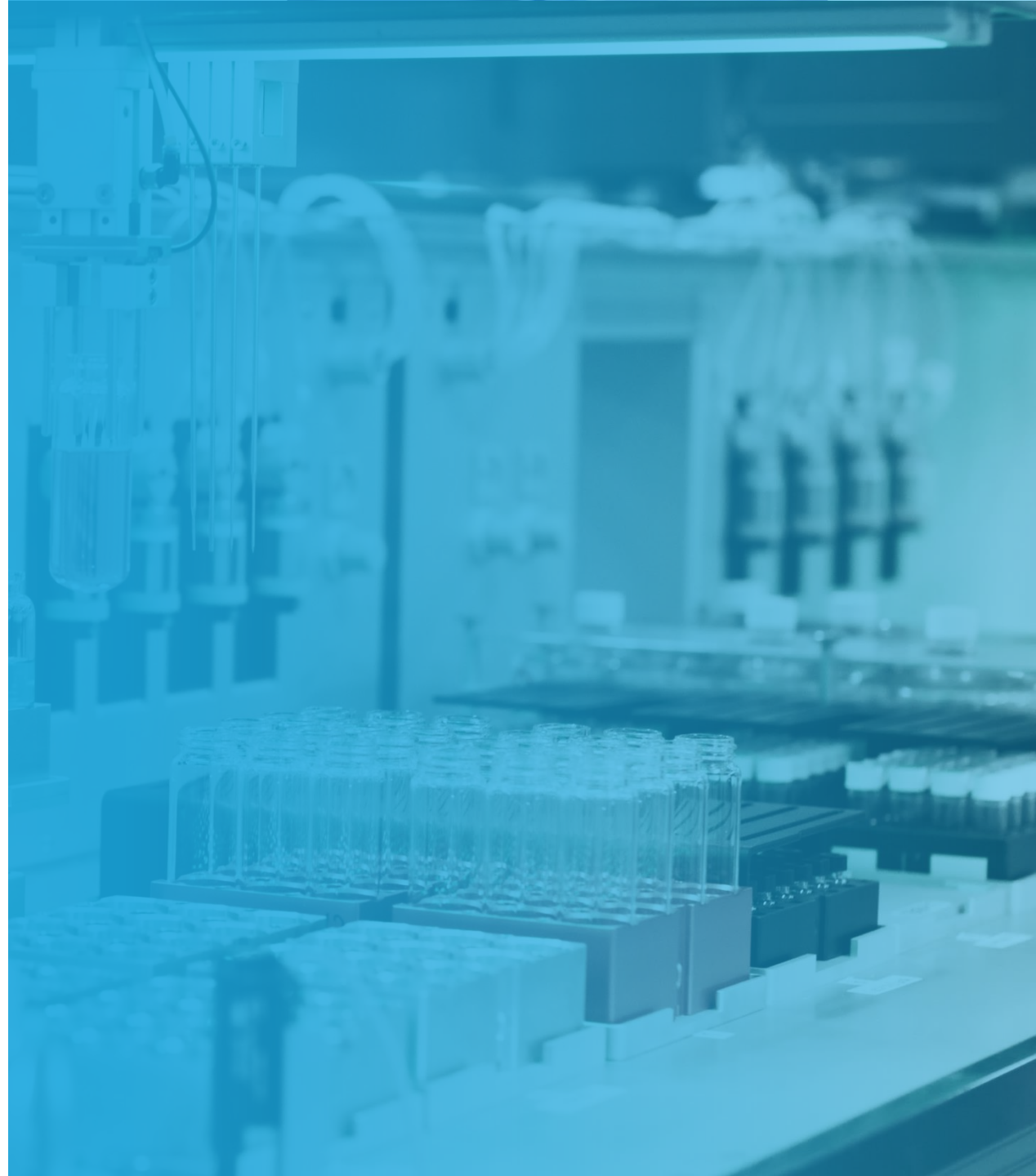




Translating proof to products

REC-4881

MEK1/2



REC-4881: Potential to transform FAP care

Deep upper GI reductions and durability off treatment support a potential new oral treatment approach



Rapid reductions that persist off treatment

- **87%¹** with reductions in total polyp burden²
- **1 in 3** achieved $\geq 65\%$ reduction after 12 weeks of treatment (**47%** median reduction)
- **85%** (11 of 13) maintained reductions below baseline after 12 weeks off-treatment

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



Deep reductions in upper GI polyp burden

- **92%** had reductions in upper GI polyp burden³
- **~1 in 2** achieved $\geq 65\%$ reduction in upper GI polyp burden
- **92%** (11 of 12) maintained reductions below baseline 12 weeks off treatment

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



Oral therapy with a favorable safety profile

- **Favorable safety profile⁴** with 15.4% Gr 3 TRAEs and no TRAEs above Gr3
- **Durable benefit** off therapy may allow for flexible dosing potential

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 missed Week 13 screening. At Week 25, n=13 efficacy evaluable patients, as 2 patients did not have Week 25 results at the data cutoff, and 1 patient was lost to follow-up

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. Upper GI: n=13 2 patients had no upper GI disease.

4. Safety evaluable (n=26; 5 Ph 1/ and 21 Ph 2. Of the 21 Ph 2, 16 are efficacy evaluable per the definition noted above

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

~\$15B

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

EPIDEMIOLOGY

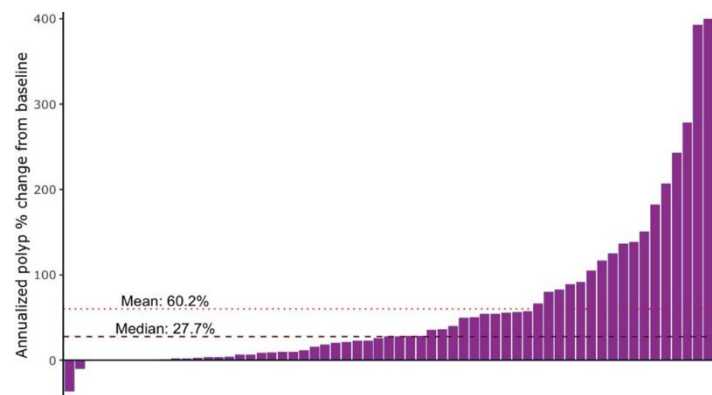
>50K Diagnosed FAP patients
US + EU5⁵

Inherited APC-driven disease

Characterized by precancerous polyps

Real world data show persistent polyp growth over time

Amsterdam UMC registry (n=55, ~20-year follow-up)⁴



87%

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 cancer¹

Multiple major surgeries and a lifetime of surveillance²

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 interventions³

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; analysis shown represents a subset of patients who satisfy key inclusion criteria of TUPELO. Study is intended to contextualize the TUPELO single arm data, better understand background natural history of FAP disease progression. Study 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; 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

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 removal¹



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

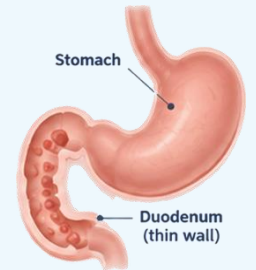
Polyp shape and thin duodenal walls complicate upper GI polyp removal



Sessile polyp in upper GI²



Peduncular polyp in lower GI³



“ [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

Recursion's platform uncovered a novel therapeutic opportunity in FAP

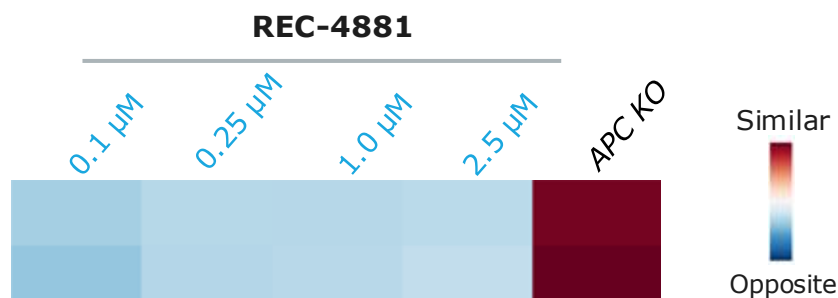
Novel insight uncovered by platform

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

Initiation pathway

APC mutation

β -catenin
stabilization

β -catenin $\rightarrow$
TCF/LEF txn.

Evolution pathway

Additional mutations
(e.g., KRAS, BRAF, EGFR)

MAPK signaling
(MEK1/2)

REC-4881

1 Cross-talk

2 Direct inhibition

Suppressing both pathways leads to polyp burden reduction

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

87%

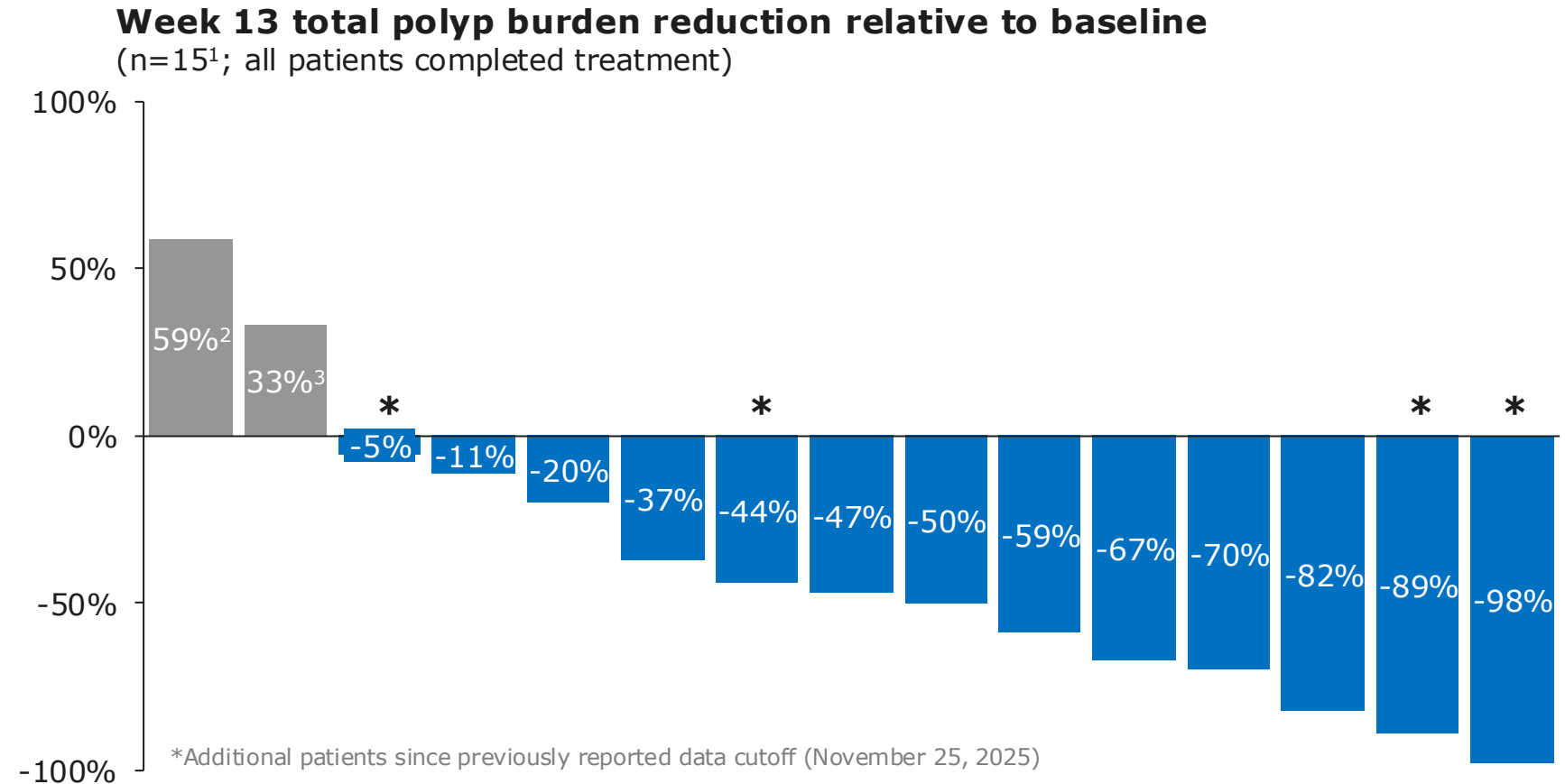
Had a reduction in total polyp burden

≥ 65%

Reduction in 1 in 3 patients

47%

Median total polyp burden reduction



1. 15 of 16 efficacy evaluable patients are shown, as 1 patient was not screened at Week 13

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%

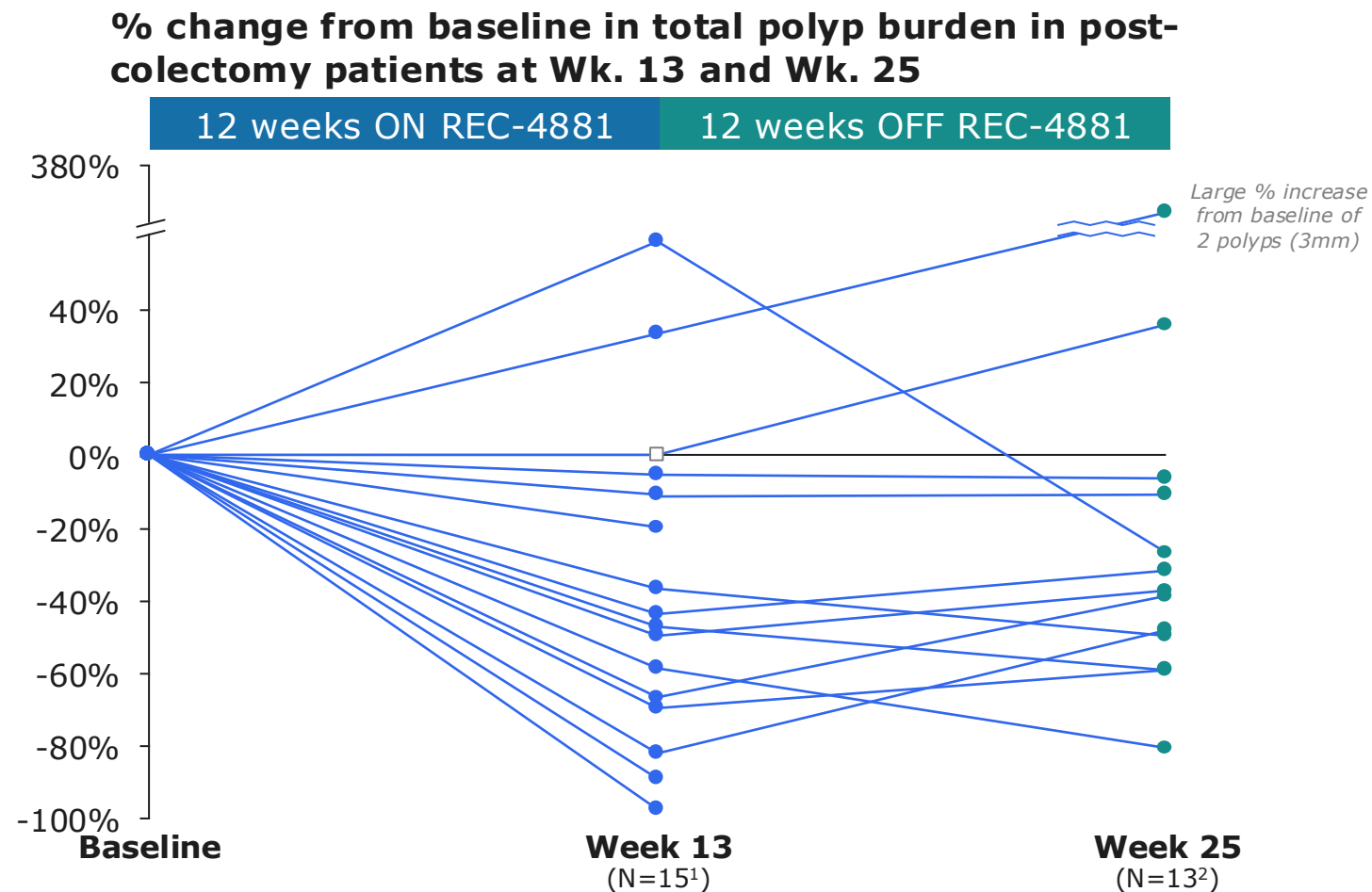
3. Baseline polyp burden of 3 mm (2 polyps), increasing to 4 mm (1 polyp) at Week 13, all in the lower GI

Note: Efficacy Evaluable (n=16); Efficacy-evaluable population: 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%

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

11 of 13 patients remained below baseline at Week 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 discontinued treatment 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 before calculating the change from baseline

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

92%

Had a reduction in upper GI polyp burden

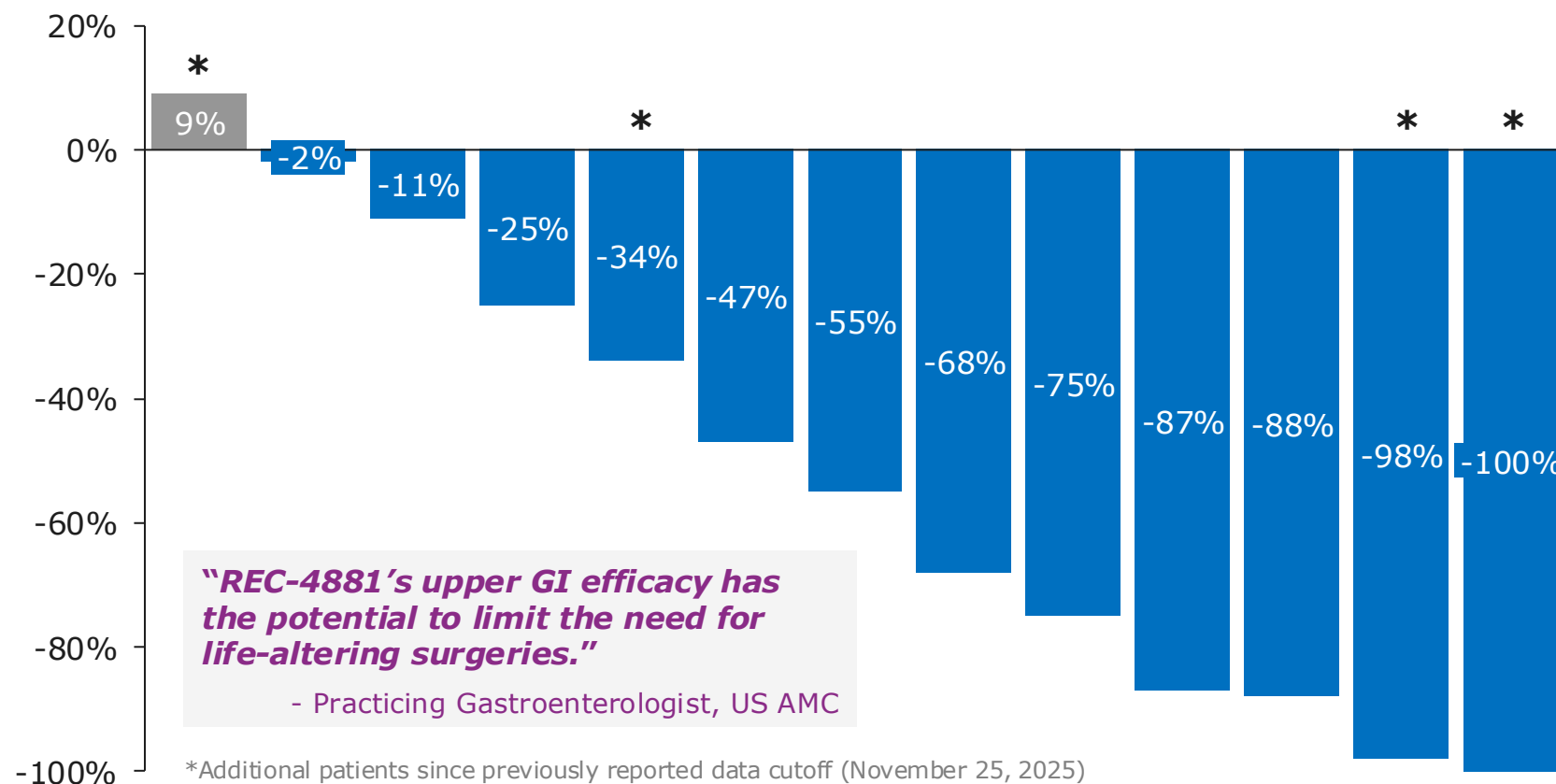
$\geq 65\%$

Reduction in ~1 in 2 patients

2 pts

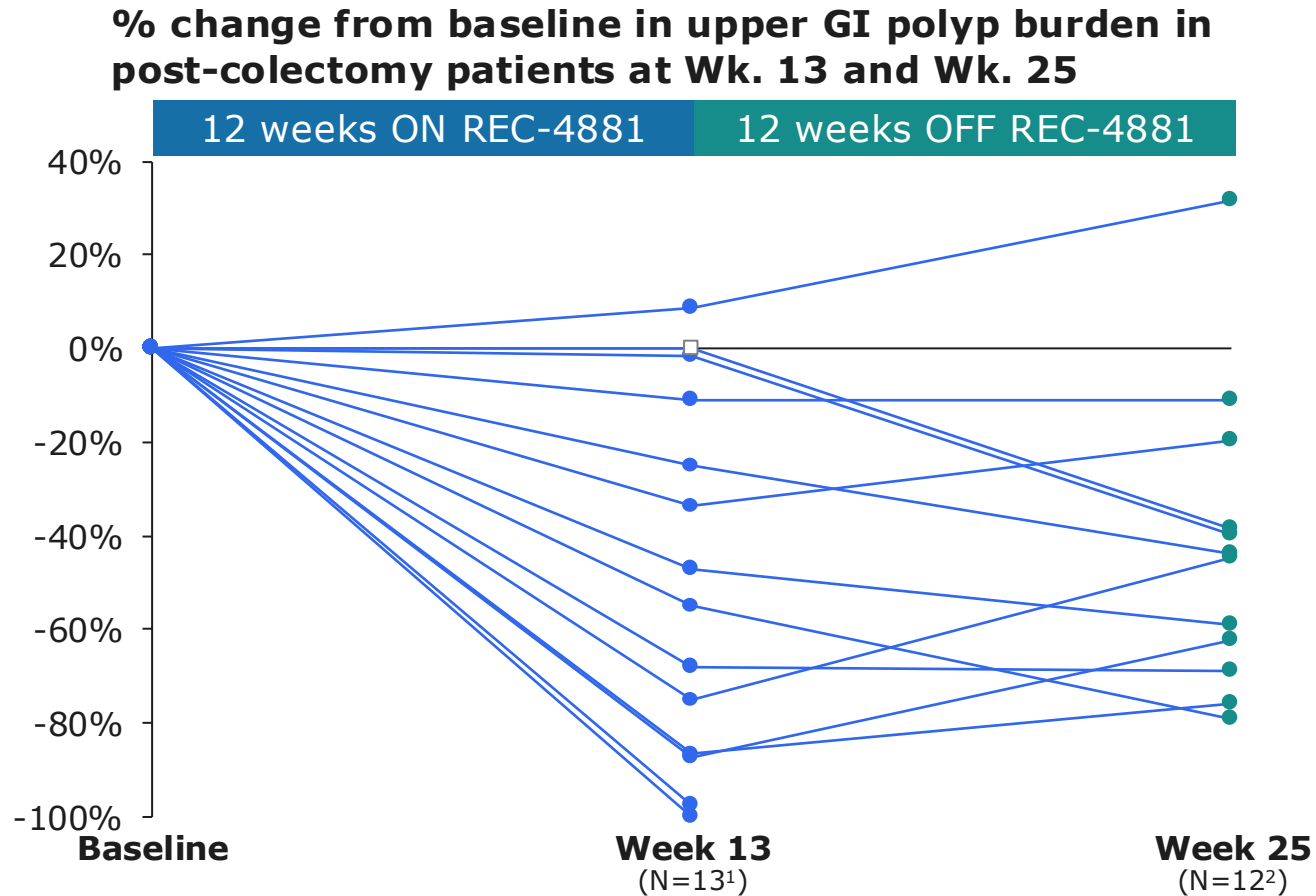
Achieved $\geq 98\%$ reductions

Week 13 upper GI polyp burden reduction (n=13¹)



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

11 of 12 patients remained below baseline at Week 25



92%

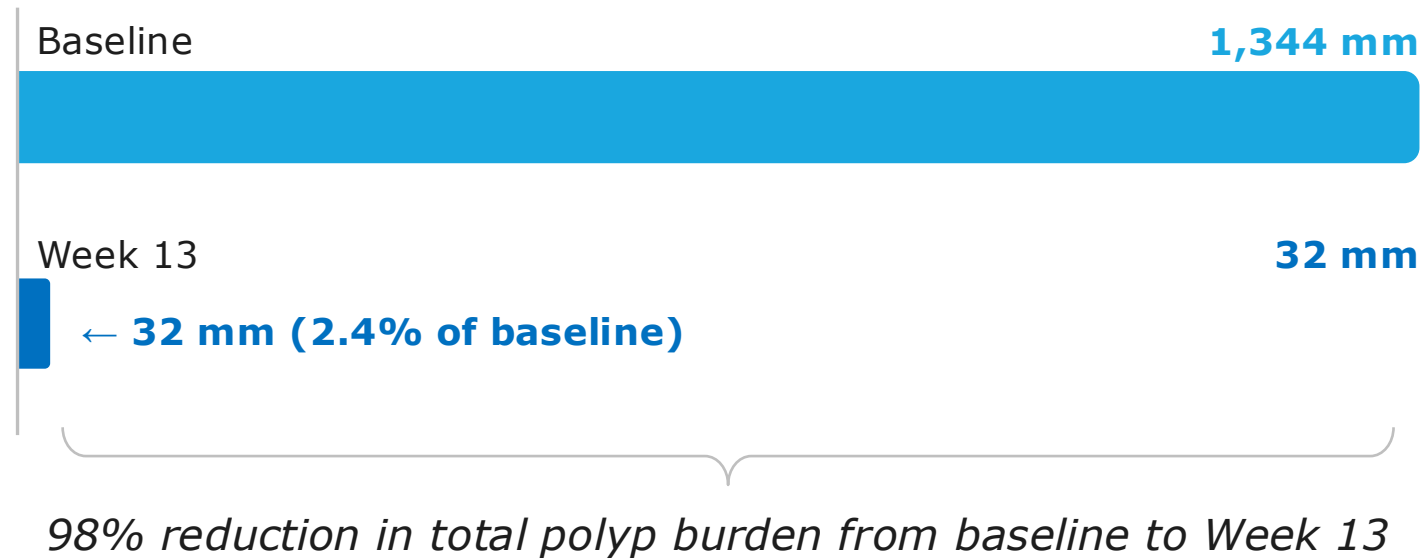
11 of 12 patients remained below baseline after 12 weeks off treatment

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

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

Total polyp burden (mm)



Upper GI polyps > 5 mm

96
at baseline

↓

1
at Week 13

95 fewer polyps

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

Week 13 Spigelman stage: 50% achieved Spigelman downstaging at Week 13, reflecting UGI 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

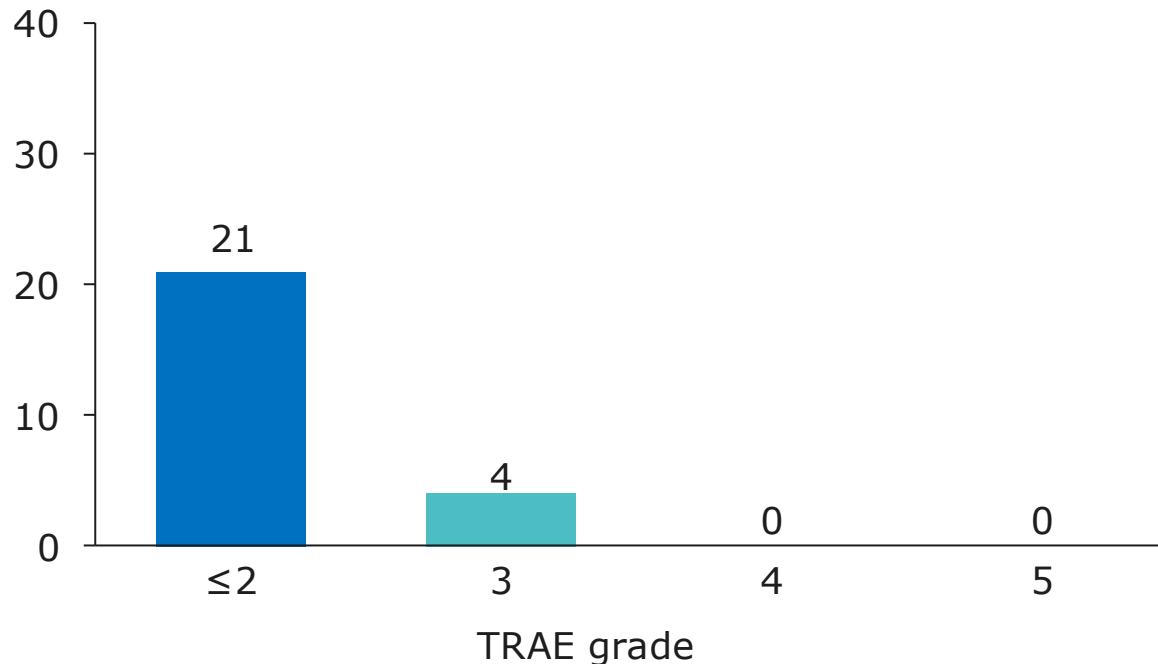
20%

Experienced stage progression between annual endoscopies; no downstaging observed²

Favorable safety profile supports potential for chronic dosing

Summary of treatment-related AEs (n=26 safety evaluable)¹

Patients with events



- **21 of 26 (80.8%) patients had TRAEs ≤ Grade 2 consistent with mechanism of MEK1/2 inhibition:**
 - E.g., Dermatitis acneiform, CPK increases, rash, diarrhea, LVEF decrease²
- **Low rates** of Grade 3 TRAEs (n=4)³
- **No TRAEs >Grade 3**
- **AEs were manageable** and most resolved within 12 weeks off treatment
- Discontinuations due to AE (n=4)⁴

1. For 4 mg, N=5 patients in Phase 1b and N=21 patients in Phase 2 were dosed; safety data cutoff date of 2026-09-10

2. Patients were asymptomatic and decrease was reversible, 1 patient was lost to follow-up

3. Dermatitis acneiform/rash (n=1 each), blood CPK increase (n=2)

4. Discontinuations: Grade 1 (n=2): 1 diarrhea, 1 left atrial enlargement (present in medical history at baseline); Grade 2 (n=2): 1 retinopathy (present in medical history at baseline), 1 perineal rash

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

US + EU5 FAP ADDRESSABLE MARKET¹

Estimated prevalence ~67,100

Diagnosed prevalence² ~55,700

POST-COLECTOMY³

~37,200

67% | Immediate focus



PRE-COLECTOMY³

~18,500

33% | Future expansion

~\$10B⁴

Post-colectomy
opportunity



~\$5B⁴

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