MEK1/2 Inhibitor

REC-4881

August 2026

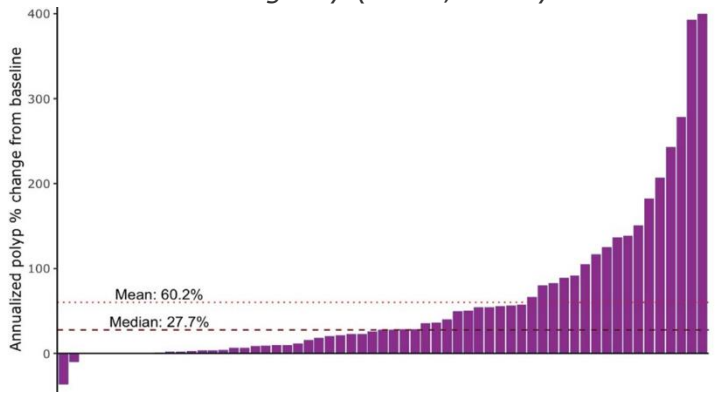
FAP: A serious, lifelong chronic disease with zero approved therapies

A surgically managed disease lacking effective treatment options

- **Most penetrant driver of GI cancer[1],** with a genetically defined patient pop., analogous to BRCA1/2
- **Lifelong chronic disease;** multiple major surgeries and a lifetime of surveillance[2]
- Patients develop **anxiety and/or PTSD** from **constant threat of cancer, life-altering interventions** and complications[3]

In the real world, polyps continue to grow

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



87%

of evaluated patients had annual polyp-burden increase

>50k

Diagnosed post-colectomy patients (US + EU5)[5]

0

Approved therapies

>$10B

Total addressable market(US + EU5)[6]

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. EMA/NORD and Orphanet, adjusted for colectomy rate (Syngal S, et al. Am J Gastroenterol 2015;110(2):223–62. DOI 10.1038/ajg.2014.435). 20-30% of patients are diagnosed late or misdiagnosed 6. Modeled total addressable market (not realized or forecasted sales): diagnosed prevalence (~50k) × rare-disease oral net price (benchmark GOMEKLI ~$22–30k/mo ≈ $260–360k/yr; ATTR/PAH orals); sensitive to price treated fraction

FAP patient journey: A lifetime of surveillance and surgeries

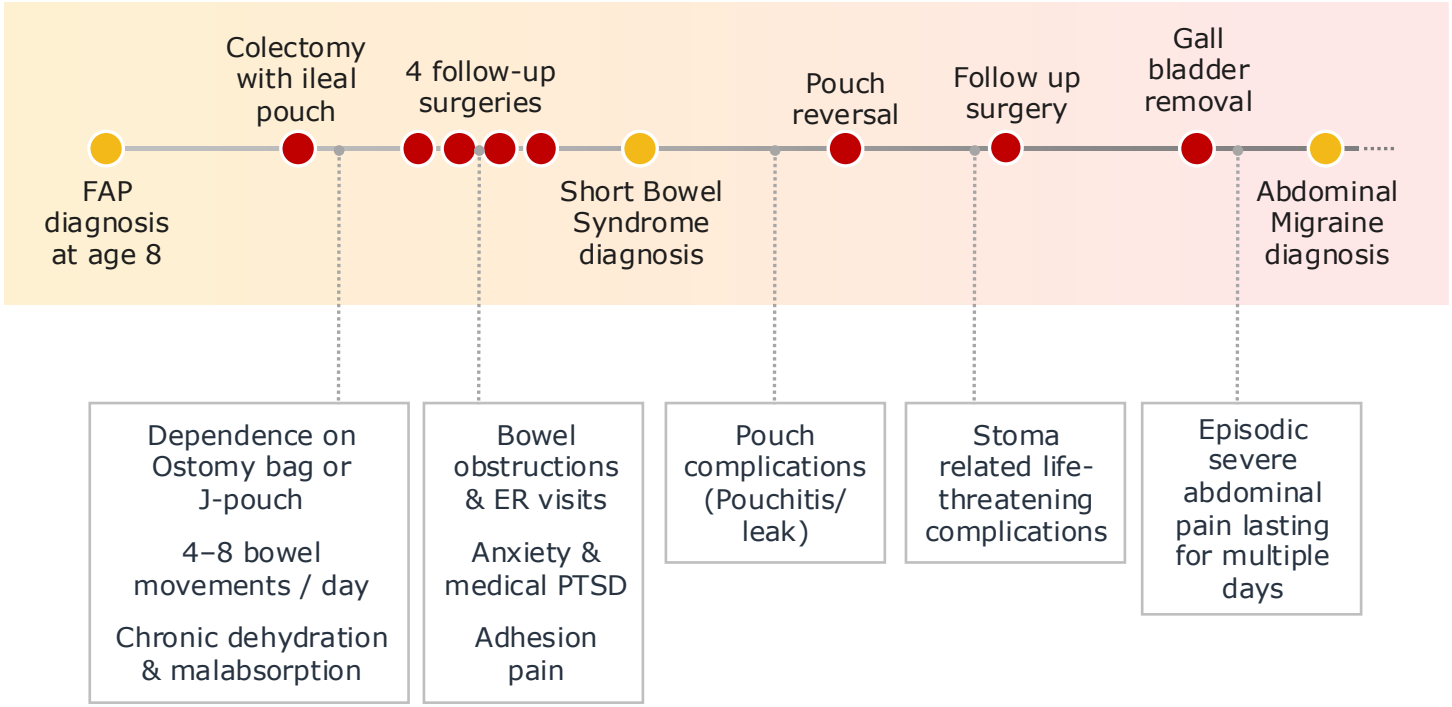
Jenny J.

Founder of Life's a Polyp, rare disease advocate, and patient living with FAP

"My biggest hope, for now and for the future, is just to make lives easier for FAP patients and families… ***to find new treatment modalities rather than just surgery****."*

"Adhesions cause pain from my surgeries. It causes obstructions. *I have to be careful with what I eat. When I do get an intestinal obstruction, I try to manage that at home. I [have] something always on the mind.* ***Mentally, it affects me every day because I have medical PTSD from my surgeries."***

8
Major Surgeries to Date

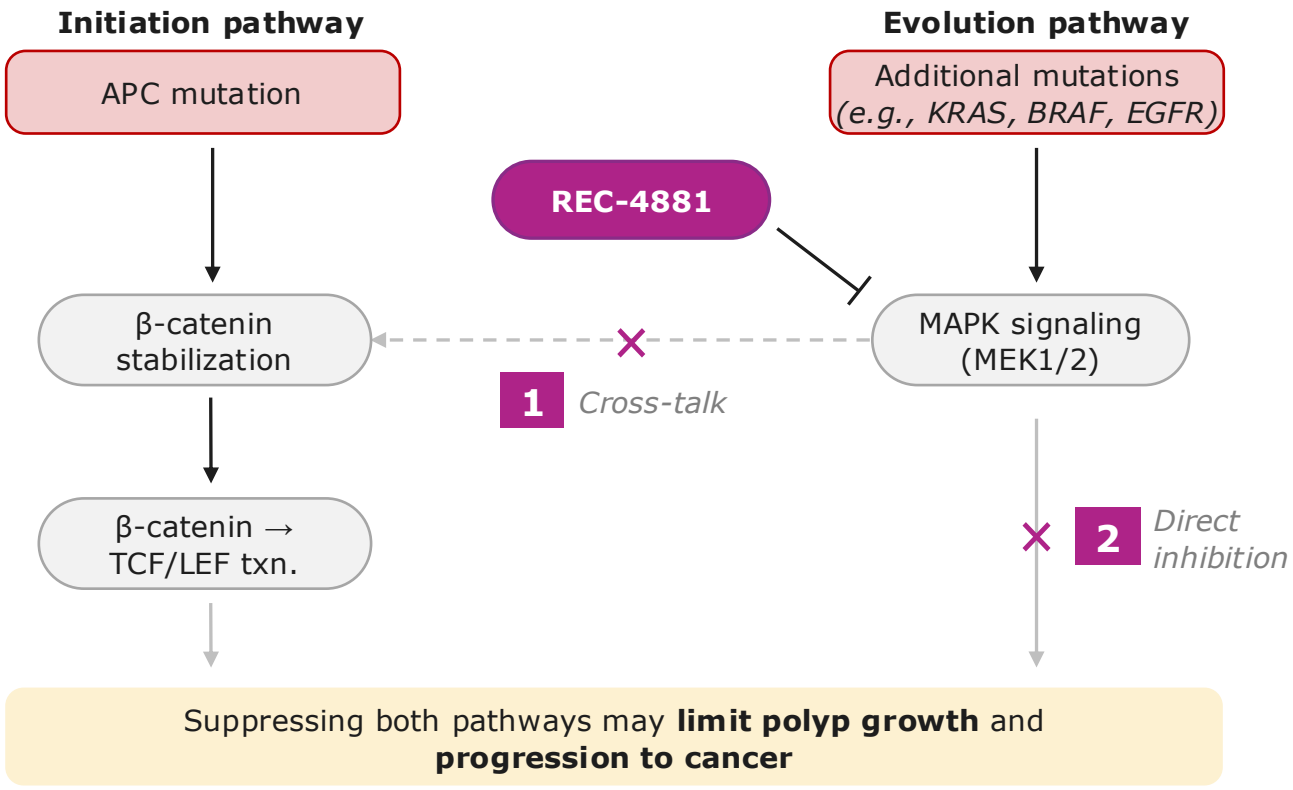


Note: Jenny's treatment journey may not be typical of all FAP patients

Recursion

REC-4881 addresses both drivers of FAP polyp growth with a single target

Overview of REC-4881 mechanism of action



Recursion's AI engine uncovered a **non-obvious insight: REC-4881 addresses both drivers of FAP polyp growth with a single target**

FAP is a complex disease driven by multiple pathways

- APC-deficient cells start as being highly Wnt/β-catenin dependent
- Over time, they typically acquire additional mutations (e.g., KRAS/BRAF, TP53) that reduce reliance on β-catenin

REC-4881 inhibits MEK1/2 to block:

1. The MAPK/ERK evolution pathway
2. The Wnt initiation pathway, via β-catenin crosstalk

By hitting drivers of **both initiation and evolution**, REC-4881 may offer significant, **durable suppression**

Sources: Fujishita et al. Cancer Sci. 2015 Jun;106(6):692-699. doi: 10.1111/cas.12670; Blaj et al. Cancer Res. 2017 Apr 1;77(7):1763-1774. doi: 10.1158/00085472.CAN-16-2821.; Daniele Guardavaccaro and Clevers, *Sci. Signal.***5**,pe15-pe15(2012).DOI:10.1126/scisignal.2002921; Cheng et al. Part Fibre Toxicol. 2026 Jan 16;23(1):4. doi: 10.1186/s12989-025-00656-3. Georgopoulos et al. J Cell Sci. 2014 Jul 1;127(Pt 13):2967-82. doi: 10.1242/jcs.150888

Recursion

REC-4881: A potential paradigm shift for FAP — echoed by physicians treating these patients today

Rapid, durable efficacy

- **43%** median polyp burden reduction in 3 months
- **Reduction sustained off treatment** for 3 months

*"The **most compelling piece of data is the durability of REC-4881 from week 13 to 25**. The fact that the biological effect persists after the dosing ends."*
- Practicing Gastroenterologist, US academic medical center

Efficacy across the entire GI tract

- **Strong upper & lower GI efficacy**
  Upper GI is area of highest unmet need

*"A drug that impacts **both the retained rectum or the pouch, and the duodenum..** the combination of effectiveness **at both locations** is absolutely a critical observation"*
- Former Head of Colorectal Surgery, MSKCC

Tolerable safety, with oral, chronic dosing potential

- **1st-in-class potential**
  oral, chronically dosed therapy
- Safety consistent with MEK1/2 inhibition[1]: **No Grade ≥4 TRAEs**; Grade 3 in 15.8% of patients

*"This initial trial data could position [REC-4881] as something **that's taken daily, or perhaps we'll find it's effective in a cyclic fashion**, which might be a really **alluring option for patients** "*
- Practicing Gastroenterologist, US academic medical center

Dual**-mechanism MoA: **Targets 2 drivers of FAP
Wnt/APC initiation pathway and MEK1/2-driven evolution pathway

1. In approved oncology and non-oncology indications

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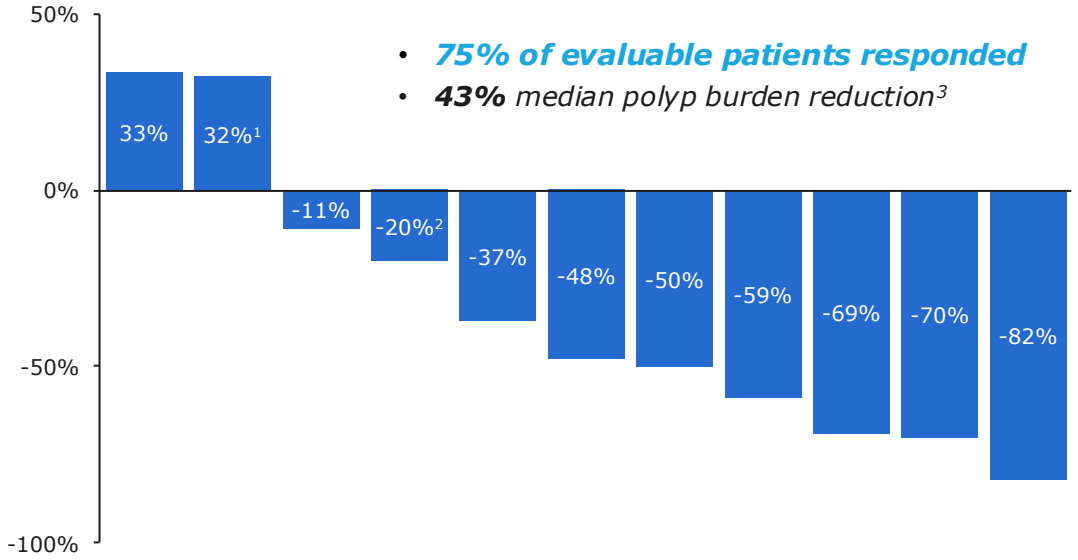
Rapid reductions in polyp burden across the GI tract persist 12 weeks after stopping drug

Phase 2 TUPELO study design *(N=12)*

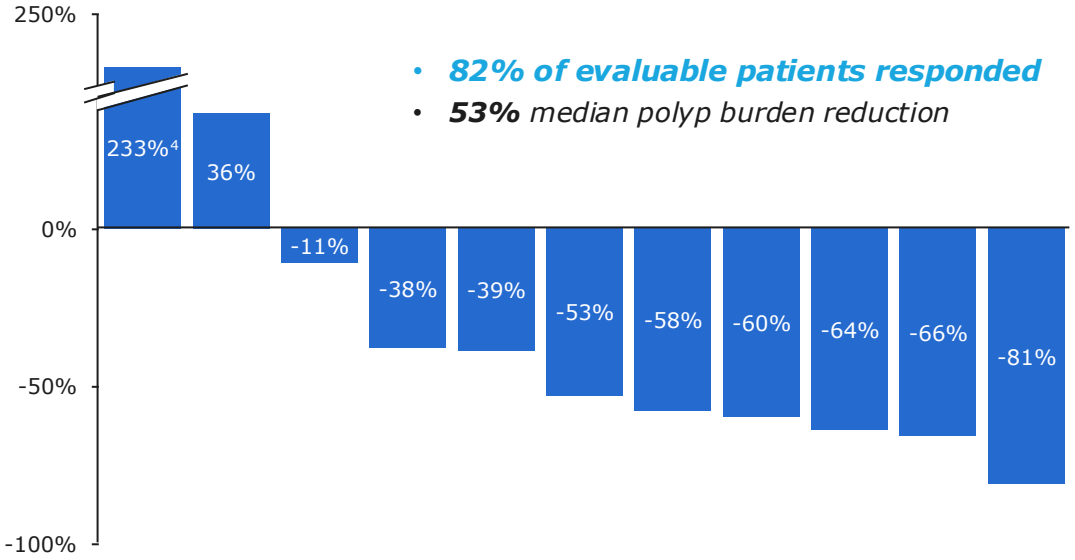
Baseline endoscopy — Week 13 endoscopy — Week 25 endoscopy

12 weeks **ON drug** (4mg QD) | 12 weeks **OFF drug** (4mg QD)

% change from baseline in total polyp burden at wk. 13



% change from baseline in total polyp burden at wk. 25



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.
4. Non-responder with 233% increase – polyp burden increased from 3mm to 10mm due to one polyp growth at Week 25

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REC-4881 reduces polyp burden across entire GI tract, potentially addressing a major unmet need in upper GI

Upper GI is area of major unmet need

- **Highest risk interventions –** thin-walled upper GI makes endoscopy resection risky (perforation & bleeding); severe cases need duodenectomy / Whipple, among the most morbid GI surgeries
- **Highest cancer risk post-colectomy** – duodenal/ampullary cancer a leading cause of death; gastric cancer emerging as a major risk
- **No effective options** – no therapies to date with efficacy in the upper GI tract

"These [upper GI] ***surgeries have a lot of complications****, way more than the colon…* ***This is really surgery you want to prevent****." - KOL*

REC-4881 has efficacy in upper & lower GI

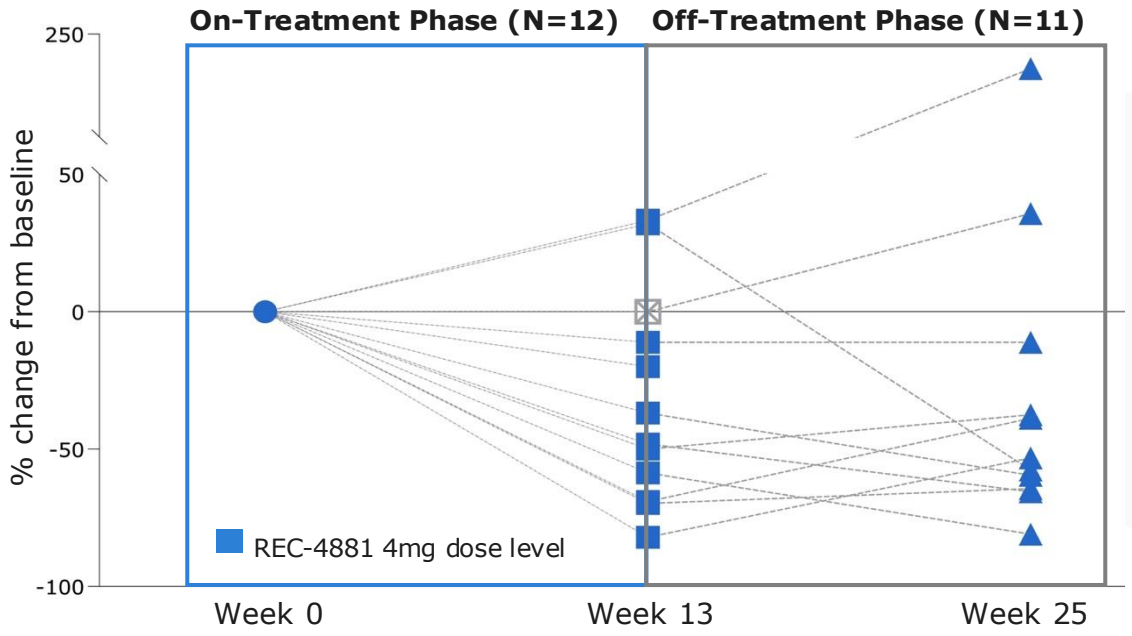
Upper GI	Lower GI
52%	**57%**
Median reduction in polyp burden (N=10)	*Median reduction in polyp burden (N=9)*

"If we go to the upper GI, I think ***there's really an unmet need regarding duodenal cancer and especially gastric cancer****... In the past, all chemopreventive agents have* ***failed to show any effect on the duodenum****... That's really an issue" – KOL*

Additional data to be presented at plenary session at CGA-IGC on November 2, 2026

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

% change from baseline in total polyp burden in post-colectomy patients at Wk. 13 and Wk. 25[1]



	Week 13 *12 weeks **ON** drug (N=12)*	**Week 25** *12 weeks **OFF** drug (N=11)*
% of patients with reduced polyp burden	75%	**82%**
Median polyp burden reduction	43%	**53%**

1. Efficacy-evaluable population: N=12 at Week 13 and N=11 at Week 25. One patient reached Week 25 but did not undergo the Week 25 endoscopic assessment and is excluded from the Week 25 analysis. A separate patient without a Week 13 assessment had baseline carried forward per the statistical analysis plan (shown as the "X" at Week 13).
Note: 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. Note: Polyp burden defined as the sum of all polyp diameters; percent change from baseline is measured at the Week 13 and Week 25 endoscopies. Note: 5 of 11 evaluable patients maintained or improved polyp-burden reduction between Week 13 and Week 25, during the off-treatment period.

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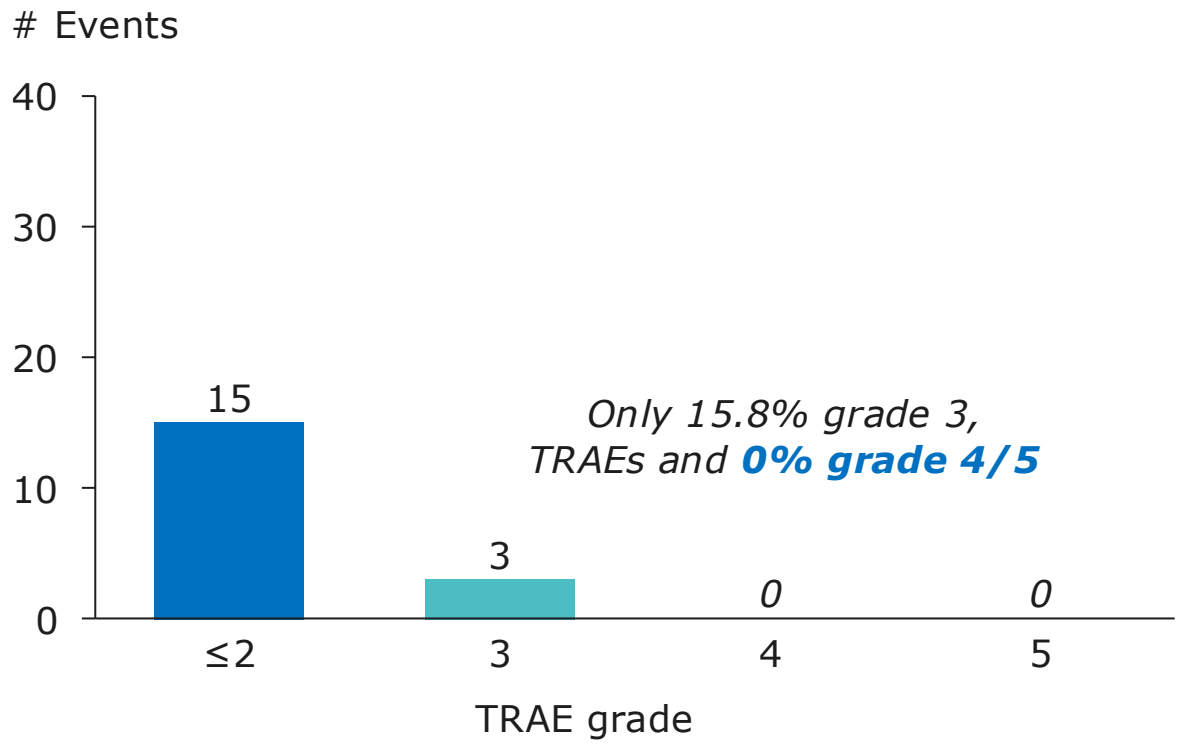
Manageable safety profile consistent with non-oncology MEK inhibitor profiles approved in rare disease

Summary of treatment-related AEs[1]



Safety profile **consistent with MEK1/2 inhibition:**

- **15 of 18 (84.2%) TRAEs were Grade 1/2**:
  - E.g., Dermatitis acneiform, CPK increases, rash, diarrhea, LVEF decrease[2]
- **Low rates** of Grade 3 TRAEs (n=3)[3]
- **No Grade 4/5 events**
- **AEs were manageable** and most resolved within 12 weeks
- Discontinuations (n=4)[4]

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. Dermatitis acneiform (n=1), blood CPK increase (n=2)
4. Discontinuations: Grade 1 (n=1): 1 diarrhea, Grade 2 (n=3): 1 retinopathy, 1 rash, 1 hypertension

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Near term value inflection across REC-4881: Regulatory update and key congress presentation

Key upcoming milestones

- **Ongoing**
  Enrollment of ≥18 cohort underway; dose optimization advancing
- **November 2026**
  Additional Phase 2 clinical data at CGA-IGC Annual Meeting
- **2H26**
  Update on FDA engagement to define potential registrational path
- **1H27**
  Additional Phase 2 clinical data

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

Session information

Presidential Plenary I
Mon. November 2, 2026 @ 13:30 - 15:00

Updated safety and efficacy data of REC-4881 monotherapy in familial adenomatous polyposis: Phase 1b/2 trial results contextualized with real-world registry data

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