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Safety and Efficacy of OD-001, a First-in-Class Oral RIPK2 Scaffolding Inhibitor, in Patients With Moderately to Severely Active Ulcerative Colitis: Results From a Phase 2a Trial

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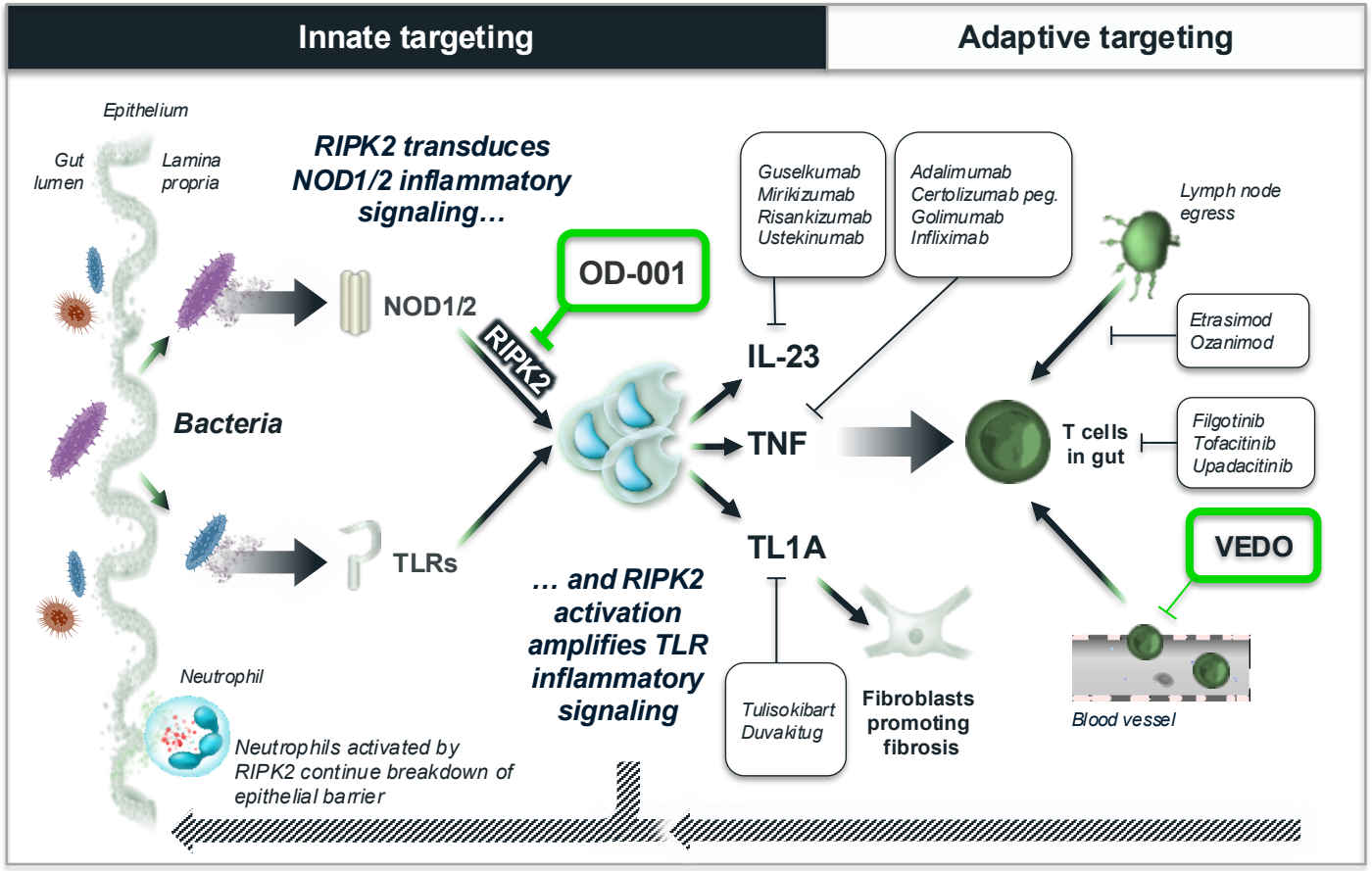
Disclosure of Conflicts of Interest

I herewith declare the following paid or unpaid consultancies, business interests, or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

BES reports honoraria for consulting from Aclaris Therapeutics, Adaxion Therapeutics, Adiso Therapeutics, Agomab Therapeutics, Alfasigma, Alimentiv, Amgen, AnaptysBio, AstraZeneca, Attovia Therapeutics, Biolojic Design, BiomeBank, Biora Therapeutics, Boehringer Ingelheim, Caldera Therapeutics, Cellarity, Cytoki Pharma, Disc Medicine, Eli Lilly and Company, Ensho Therapeutics, Enthera, Enveda Biosciences, Equilium, Evommune, Ferring, Fzata, Galapagos, Genentech (Roche), Genesis Therapeutics, Gilead Sciences, GlaxoSmithKline, Globalport, Ignite Biomedical, Imedex, Imhotex, Immunitas Therapeutics, Immunyx Pharma, Kallyope, Kyowa Kirin, LifeMine Therapeutics, Merck & Company, Merck Sharp & Dohme, Microba, Microbiotica, Mirador Therapeutics, Mitsubishi Tanabe Pharma, Mobius Care, Morphic Therapeutic, MRM Health, Nexus Therapeutics, Nimbus Discovery, Novartis, Numab Therapeutics, Odyssey Therapeutics, ONO Pharmaceutical, OSE Immunotherapeutics, Palisade Bio, Pioneering Medicines Explorations, Prometheus Biosciences, Protagonist Therapeutics, Q32 Bio, Quotient Therapeutics, Rasayana Therapeutics, Recludix Pharma, Reistone Biopharma, Sanofi, Slate Bio, Sorriso Pharmaceuticals, Spyre Therapeutics, Synlogic, Target RWE, Televant, Teva, Thetis Pharmaceuticals, SRT Therapeutics, TR1X, Trex Bio, Union Therapeutics, VectivBio, Vedanta Biosciences, Vividion Therapeutics, Xencor; honoraria for consulting and speaking and other support from AbbVie, Abivax, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Genentech (Roche), J&J Innovative Medicine/Janssen, Merck & Company, Pfizer, Takeda, Teva; honoraria for consulting and stock options from Caldera Therapeutics, Mirador Therapeutics, and SRT Therapeutics; and stock from Doximity.

Inflammatory Bowel Disease Is Driven by Inappropriate Activation of Innate and Adaptive Immune Responses

Innate immune response to gut microbes is the root cause of both UC and CD



STEP 1: Loss of epithelial integrity; microbes breach gut barrier

STEP 2: Innate immune cell activation *(e.g., monocytes, neutrophils, and macrophages)*

STEP 3: Recruitment and activation of adaptive immune cells *(e.g., T cells and fibroblasts)*

RIPK2, or receptor-interacting protein kinase 2, plays a central role in the pathogenesis of ulcerative colitis (UC) and Crohn's disease (CD) [1]

- RIPK2 is a key signaling node that connects bacterial sensing from NOD1/2 in the innate immune response to activation of the adaptive immune response through production of multiple inflammatory cytokines that are validated targets in inflammatory bowel disease (IBD) (e.g., TNF, IL-23, and TL1A) [1–3]
- Inhibition of RIPK2 scaffold function is a therapeutic strategy being investigated for IBD
- Activation is confirmed in UC and CD patient biopsies [1,4]
- Genetic polymorphisms in the pathway that increase RIPK2 activity predispose to IBD development [1,4]
- RIPK2 knockout mice are phenotypically normal, but knockout or inhibition is effective in animal models of IBD [5,6]

Note: IBD = inflammatory bowel disease.

Sources: (1) Am J Physiol Gastrointest Liver Physiol 2021;321(5):G500; (2) J Med Chem 2019;62(14):6482; (3) Proc Natl Acad Sci U S A 2014;111(25):E2559; (4) Front Immunol 2019;10:419; (5) Cell Rep 2018;22(6):1496; (6) Int Immunol 2019;31(10):669.

Overview of RIPK2 Program

OD-001 is a first-in-class RIPK2 scaffolding inhibitor that achieved clinical proof of concept (PoC) in patients with moderately to severely active ulcerative colitis

Initial phase 2a PoC data reported in May 2026 (1)

1. Absolute clinical remission rate of 27% in 49 evaluable patients
2. Similar efficacy observed in advanced therapy (AT)-naïve and AT-experienced patients
3. OD-001 was safe and well tolerated

Present analysis:

Phase 2a monotherapy with data on seven additional evaluable patients from the induction phase; additional subgroup analyses by baseline Mayo endoscopic subscore (MES), and exploratory and biomarker analyses

Source: (1) Odyssey Therapeutics Form S-1.

Phase 2a Monotherapy Trial Overview

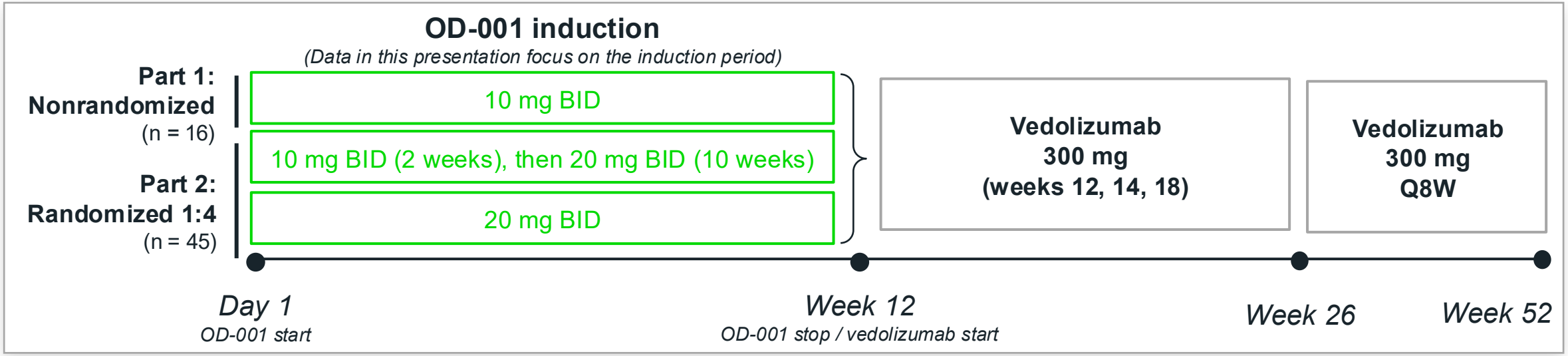
Overall trial design

Enrollment criteria

- Moderate-to-severe UC, modified Mayo Clinic score (mMS) of 5–9 with required endoscopic subscore (MES) ≥ 2 and rectal bleeding subscore of ≥ 1
- ≤ 3 prior advanced therapies
- ≤ 20 mg concomitant prednisone

Efficacy endpoints and powering

- Primary: Change from baseline in 3-component mMS at week 12
  - 90% power to detect 2-point change in mMS at the two-sided 5% significance level
- Secondary: ≥ 15% placebo-adjusted clinical remission rate at week 12 (comparison to historical placebo data of 10%)
  - 82% power at the two-sided 10% significance level



- 10 mg and 20 mg doses expected to be active based on phase 1 ex vivo TNF release assay with 70% and 90% inhibition, respectively
- Part 2 enrollment initiated following DSMB review of Part 1 safety data
- Centralized and blinded endoscopy reads
- For the analyses presented, data from the two 20 mg BID groups (20 mg BID throughout and 10 mg BID followed by 20 mg BID) were pooled

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Notes: BID = twice daily; DSMB = data and safety monitoring board; Q8W = every 8 weeks.

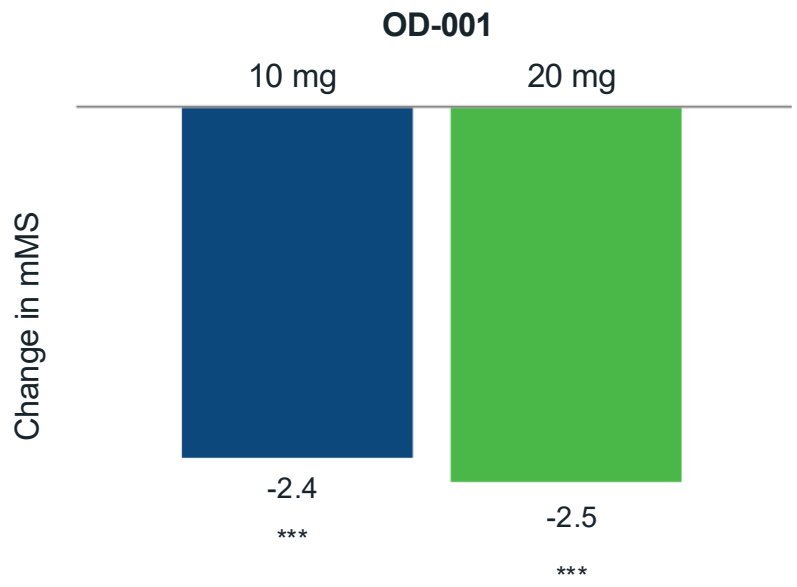
Phase 2a Monotherapy Baseline Characteristics

		Part 1 [1]	Part 2 [2]		Overall
		10 mg BID (n = 16)	Group 1: 10/20 mg BID (n = 9)	Group 2: 20 mg BID (n = 36)	(n = 61)
Age, mean, years		39.3	39.9	40.6	40.0
Sex, male		9 (56%)	1 (11%)	20 (56%)	30 (49%)
Duration of disease, mean (SD), years		4.8 (4.4)	8.2 (5.6)	7.8 (6.2)	7.1 (5.8)
Disease extent	Proctosigmoiditis	0 (0%)	2 (22%)	6 (17%)	8 (13%)
	Left-sided colitis	9 (56%)	4 (44%)	18 (50%)	31 (51%)
	Pancolitis	7 (44%)	3 (33%)	12 (33%)	22 (36%)
Baseline mMS, mean (SD)		6.8 (1.2)	6.6 (1.1)	6.4 (1.2)	6.5 (1.2)
MES = 3		9 (56%)	4 (44%)	18 (50%)	31 (51%)
Fecal calprotectin, mean (SD), µg/g		2,326.7 (3,312.7)	1,846.9 (1,604.4)	3,218.7 (4,552.2)	2,782.3 (3,933.9)
Advanced therapy-experienced		4 (25%)	5 (56%)	9 (25%)	18 (30%)
1 advanced therapy		3 (19%)	3 (33%)	6 (17%)	12 (20%)
≥ 2 advanced therapies		1 (6%)	2 (22%)	3 (8%)	6 (10%)
Concomitant corticosteroid use		3 (19%)	3 (33%)	8 (22%)	14 (23%)
Concomitant immunomodulator use		0 (0%)	2 (22%)	1 (3%)	3 (5%)

Notes: Percentages may not sum to 100% due to rounding. (1) 16 participants treated and 15 evaluable for efficacy; (2) 45 participants treated and 41 evaluable for efficacy.
Source: Odyssey Therapeutics, Inc., data on file, 2026.

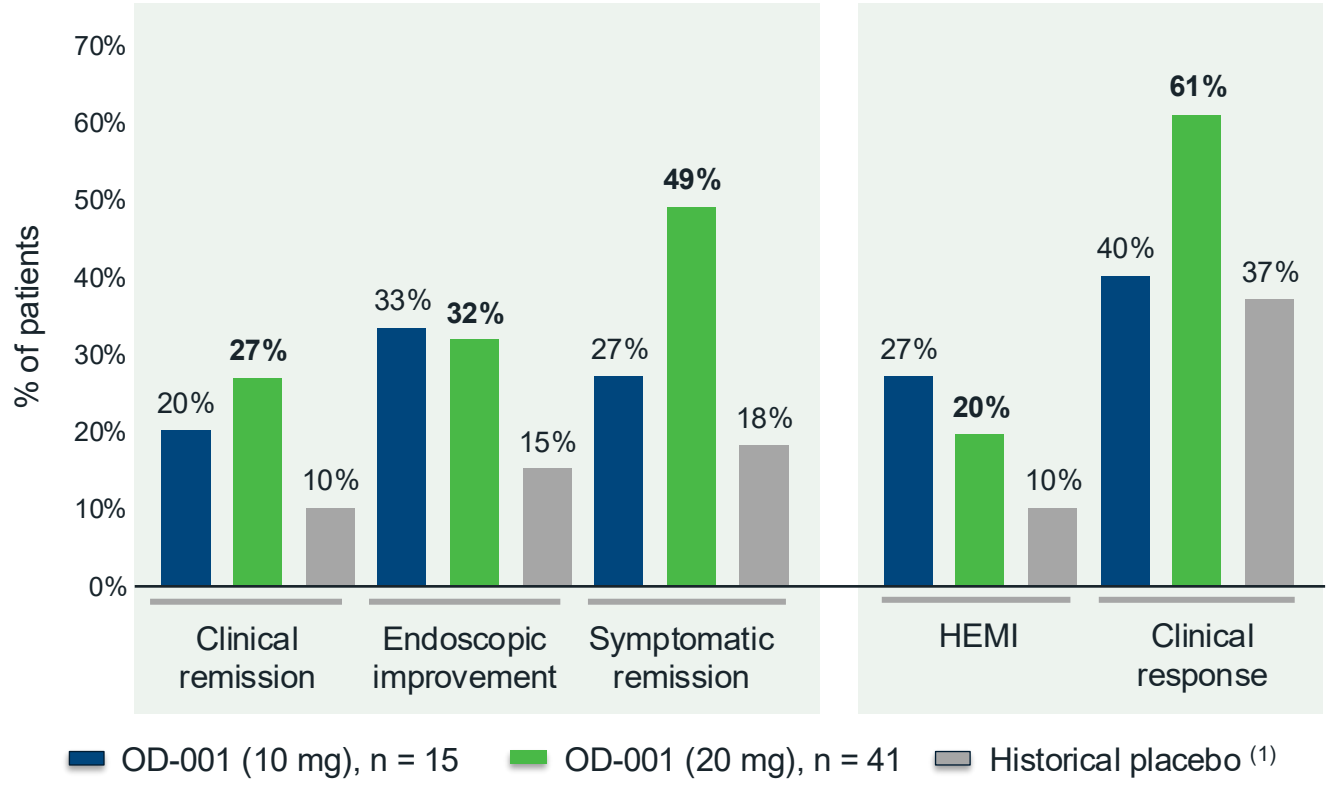
OD-001 Demonstrated Efficacy Across Key Week 12 Outcomes

Met primary endpoint of change in mMS from baseline in both parts and on a combined basis (-2.4, p < 0.001)



*** p < 0.001

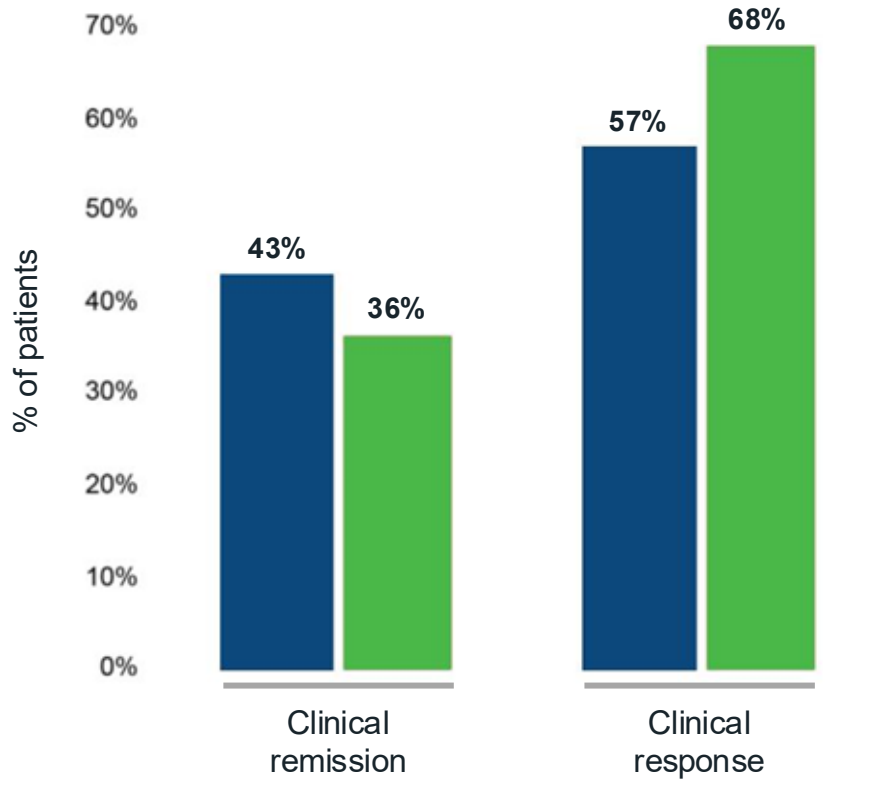
Greater efficacy observed at 20 mg BID across week 12 secondary endpoints



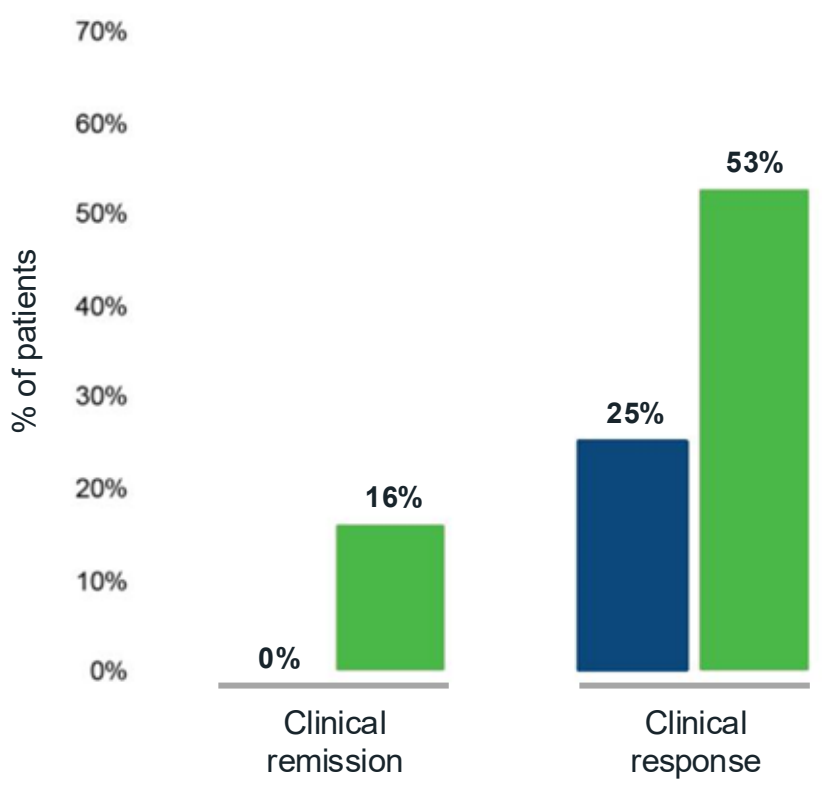
Disclaimer: Data presented are from ongoing studies, which will not be finalized until database lock; thus, these data are subject to change prior to release of the CSR. Future results may differ from those shown here.
Notes: Odyssey Therapeutics, Inc., data on file, 2026. OD-001 results represent all patients who completed 12 weeks of treatment per protocol (n = 56); one participant in Part 1 and three participants in Part 2 discontinued treatment for reasons unrelated to the trial drug and one participant in Part 2 was not evaluable for efficacy. HEMI = histologic-endoscopic mucosal improvement, defined as MES of 0 or 1 and Geboes index score ≤ 3.1. (1) Historical placebo benchmarks are derived from contemporary post-PoC UC studies (2020–2025); benchmark rates and supporting datasets are as follows: clinical remission 10% (average from 11 trials; n = 3,012 total; 820 placebo-treated patients); endoscopic improvement 15% (average from 10 trials; n = 2,920 total; 789 placebo-treated patients); symptomatic remission 18% (average from 5 trials; n = 1,872 total; 517 placebo-treated patients); HEMI 10% (average from 8 trials; n = 2,565 total; 676 placebo-treated patients); clinical response 37% (average from 9 trials; n = 2,633 total; 726 placebo-treated patients). Internal assessment of historical placebo rate is supported by third-party publications assessing placebo rates using individual patient data (J Crohns Colitis 2025;19(10):jjaf191). CSR = clinical study report.

Dose-Response Improvement in Participants With Moderate and Severe Endoscopic Disease

Similar activity observed at both doses in patients with moderate disease (MES = 2)



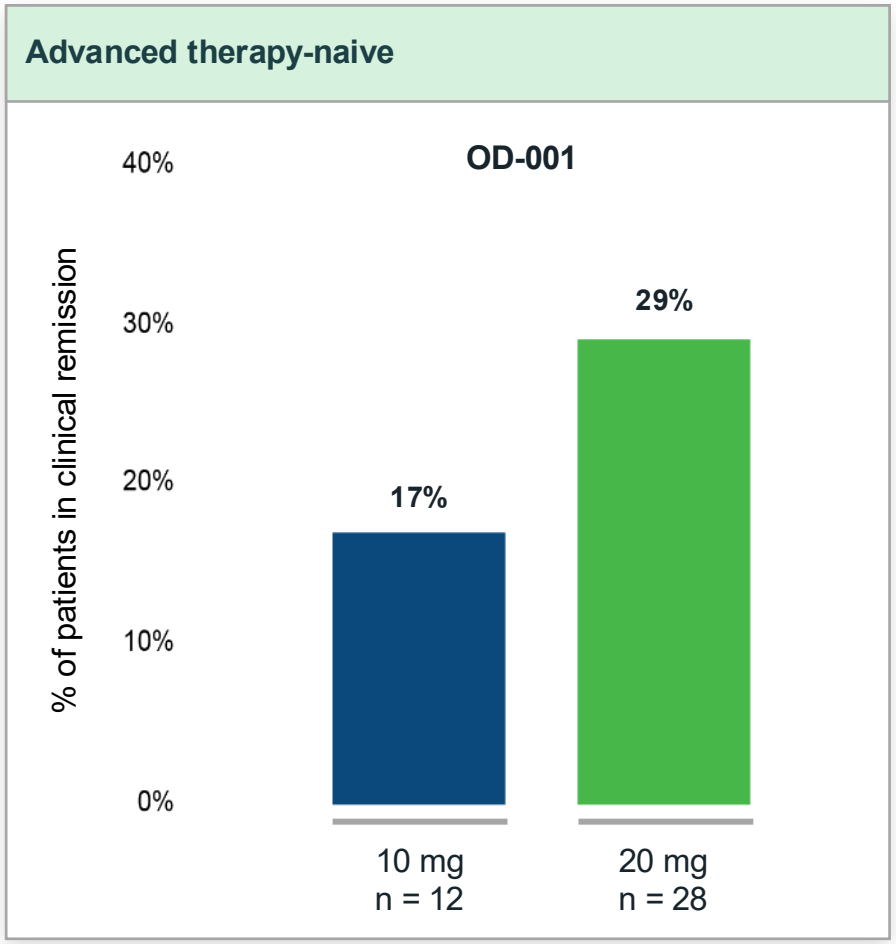
In patients with severe endoscopic disease (MES = 3), the high dose outperformed numerically on clinical remission and response

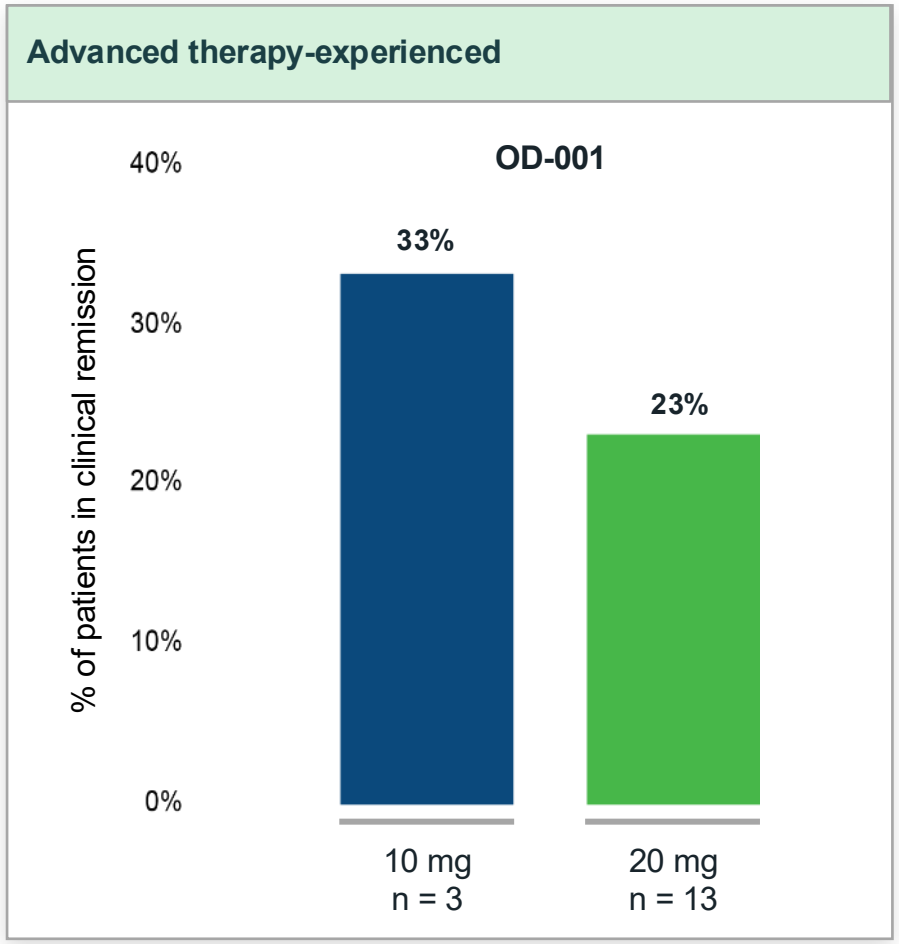


Source: Odyssey Therapeutics, Inc., data on file, 2026.

Subgroup analyses are descriptive and should be interpreted with caution given the small sample sizes

Efficacy in Advanced Therapy-Naïve Versus Advanced Therapy-Experienced Participants

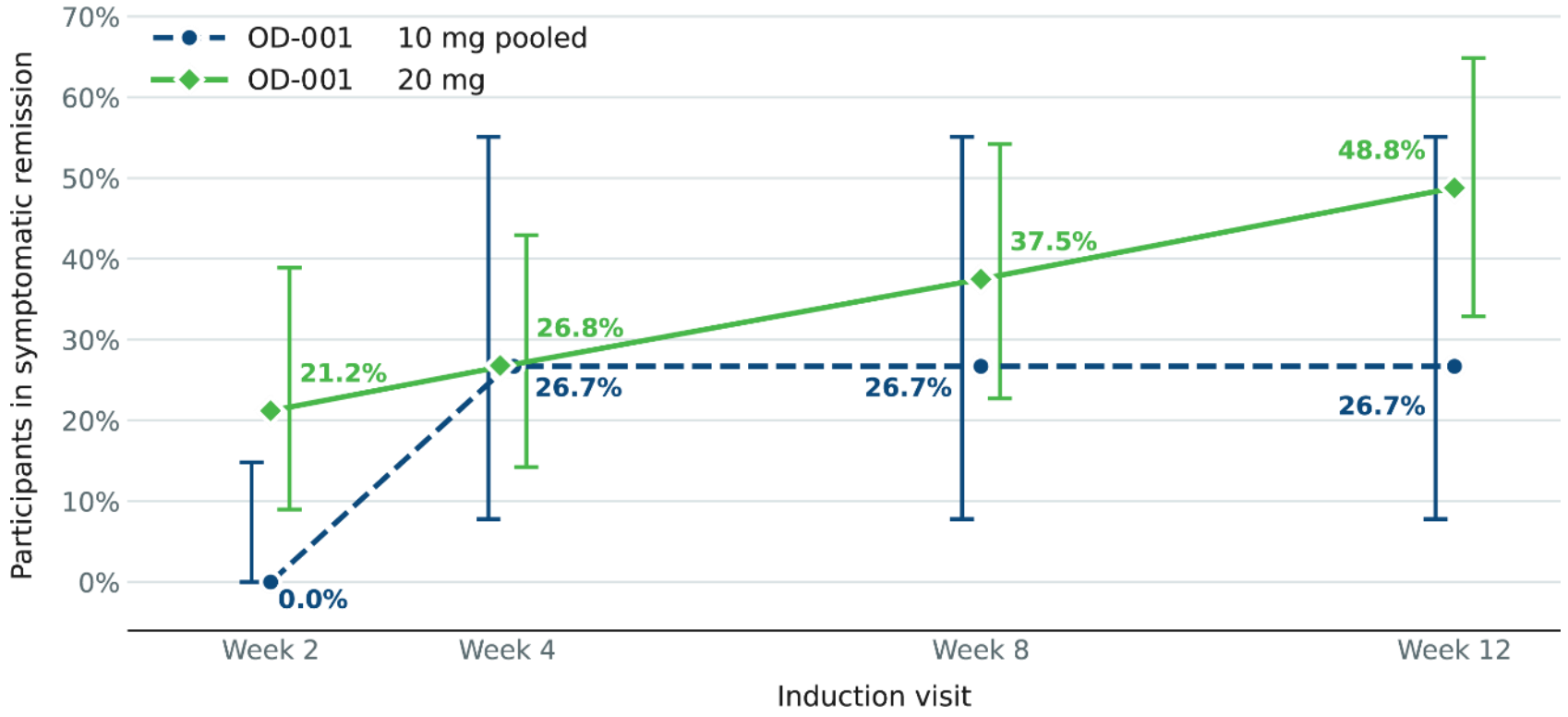




Source: Odyssey Therapeutics, Inc., data on file, 2026.

Note: Subgroup analyses are descriptive and should be interpreted with caution given the small sample sizes.

Dose-Dependent Symptomatic Remission Improved Through Week 12; 20 mg BID Selected as the Optimal Dose



OD-001	Week 2	Week 4	Week 8	Week 12
10 mg pooled (n)	23	15	15	15
20 mg (n)	33	41	40	41
p value (nominal)	0.03	> 0.99	0.54	0.22

Symptomatic remission: SFS ≤ 1 and RBS = 0

Notes: Error bars show 95% confidence intervals (exact methods); observed cases, no imputation; p values from exact methods are for the between-dose difference. Participants were assessed at each visit. RBS = rectal bleeding subscore; SFS = stool frequency subscore.
Source: Odyssey Therapeutics, Inc., data on file, 2026.

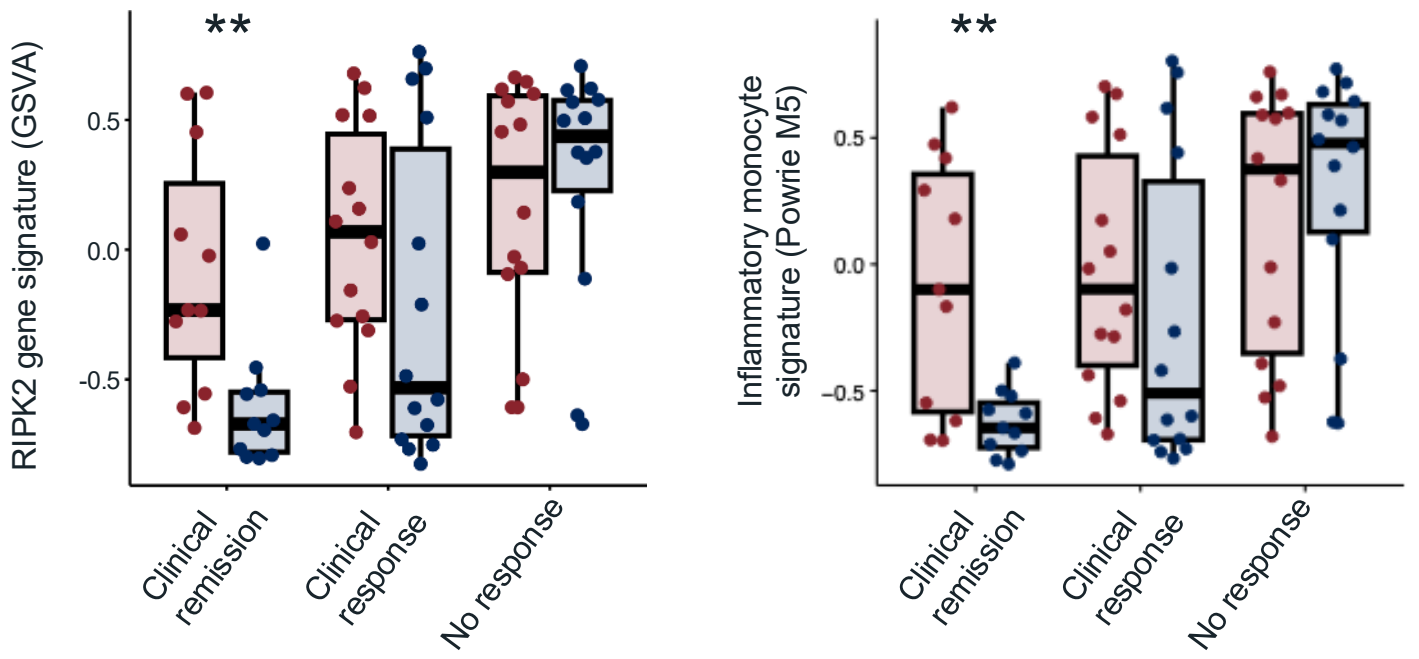
OD-001 Is Safe and Well Tolerated at 10 and 20 mg BID

	Part 1 + Expansion	Part 2		
	10 mg BID, n = 16	Group 1 10 then 20 mg BID, n = 9	Group 2 20 mg BID, n = 36	Total n = 45
Total number of TEAEs	**11**	**20**	**20**	**40**
Severe (grade ≥ 3) TEAE	1 (anemia)	0	0	0
Drug-related TEAE	0	0	3	3
Liver function abnormality identified as a TEAE	0	0	0	0
Drug-related TEAEs leading to trial drug discontinuation	0	0	0	0
SAE	0	0	0	0
TEAEs of special interest				
Temperature > 39.4 ºC on two consecutive readings ≥ 30 minutes apart or > 38.0 ºC on four consecutive readings separated by ≥ 12 hours	0	0	0	0
CRP > 3× the highest baseline value for at least 72 hours AND ≥ 45 mg/L OR > 5× the highest baseline value AND > 100 mg/L	0	0	0	0
Serious infection	0	0	0	0
Drug-related TEAEs				
Fever	0	0	2	2
Headache	0	0	1	1

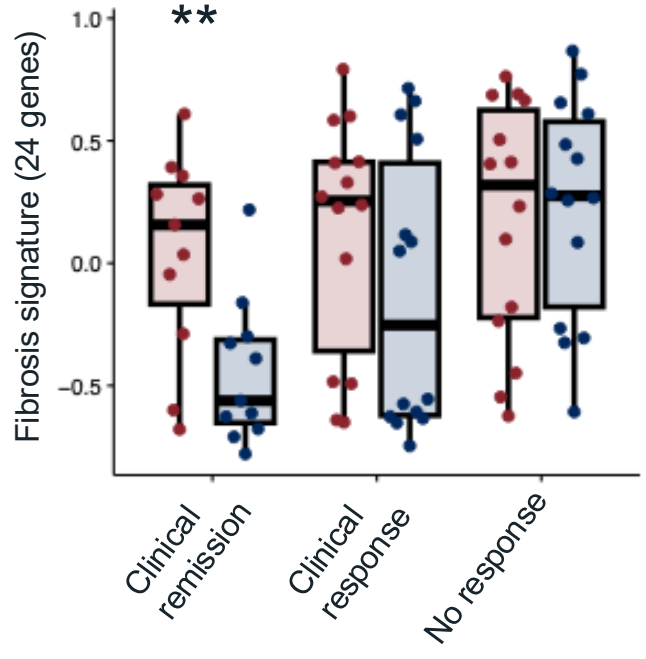
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Notes: Odyssey Therapeutics, Inc., data on file, 2026. One participant in Part 1 expansion and three participants in Part 2 discontinued treatment for reasons unrelated to the trial drug. One participant in Part 2 was not evaluable for efficacy. A total of 56 patients between Part 1 expansion and Part 2 completed 12 weeks of induction treatment per protocol. BID = twice daily; CRP = C-reactive protein; SAE = serious adverse event; TEAE = treatment-emergent adverse event.

Colonic Biopsies Demonstrate Target Engagement and Reduced Inflammatory and Fibrotic Gene Signatures

Reductions in RIPK2 and inflammatory monocyte gene signatures are observed in patients with clinical remission or response treated with 20 mg BID…



… along with reductions in a fibrosis gene signature



Baseline Week 12 ** p < 0.01

Notes: Nominal, unadjusted p values are from paired Wilcoxon signed-rank tests. Analysis includes n = 39 paired baseline/week 12 samples from the 20 mg cohort; one patient was not efficacy-evaluable and two non-responder samples failed RNA-seq QC. GSVA scores were calculated for a prespecified internal RIPK2 gene signature, the inflammatory monocyte signature (Powrie M5; Nat Med 2021;27(11):1970–1981), and the penetrating fibrosis signature (Gut 2022;71(7):1289–1301); clinical remission: mMS ≤ 2, SFS ≤ 1, RBS = 0, and MES ≤ 1 at week 12; clinical response: ≥ 2-point and > 30% decrease in mMS, with either ≥ 1-point decrease in RBS or absolute RBS 0 or 1. GSVA = gene set variation analysis.

Summary of Key Findings and Upcoming Trial Information

- Clinical proof of concept for a first-in-class oral therapy targeting RIPK2 to block innate immune activation in UC
  - 27% absolute clinical remission rate at week 12 with 20 mg BID
  - Similar efficacy observed in AT-experienced and AT-naïve patients
- 20 mg BID selected as the optimal dose based on superiority to 10 mg BID on multiple efficacy endpoints
- Symptomatic remission seen as early as week 2
- Significant reduction in gene expression associated with RIPK2 activation, inflammation, and fibrosis in patients with clinical remission
- Favorable safety and tolerability profile to date

OD-001 development continues with two new trials launching in the second half of 2026

1. Phase 2b randomized, double-blind, placebo-controlled monotherapy trial
2. Phase 2a randomized, double-blind, active-controlled combination trial (OD-001 and vedolizumab vs. vedolizumab and placebo)

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Thank you to **the patients, their families,**

the investigators, and **the study staff**

for their participation in the **OD-001 clinical trials**