UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 10, 2024

Morphic Holding, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-38940**	**47-3878772**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

35 Gatehouse Drive, A2 **Waltham, Massachusetts** **(Address of principal executive offices)**	**02451** **(Zip Code)**

Registrant's telephone number, including area code: (781) 996-0955

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	MORF	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On January 10, 2024, Morphic Holding, Inc. (the "Company") announced in a Q&A session during a public presentation that as of December 31, 2023, it had preliminary cash, cash equivalents and marketable securities totaling approximately $700 million. A copy of the portion of the transcript of the public presentation is attached hereto as Exhibit 99.1.

The Company's audited financial statements as of and for the quarter and year ended December 31, 2023 are not yet available. Accordingly, the information presented reflects the Company's preliminary financial data subject to the completion of the Company's financial closing procedures and any adjustments that may result from the completion of the audit of the Company's financial statements. Actual financial results that will be reflected in the Company's Annual Report on Form 10-K as of and for the quarter and year ended December 31, 2023 when they are completed and publicly disclosed may differ from the preliminary results presented here.

Item 7.01 Regulation FD Disclosure.

On January 10, 2024, the Company updated its corporate presentation. A copy of the updated corporate presentation is attached hereto as Exhibit 99.2 and is incorporated herein by reference.

The information in this Current Report on Form 8-K including Exhibits 99.1 and 99.2 to this report, shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"). The information contained in this Current Report on Form 8-K and in the accompanying Exhibits 99.1 and 99.2 shall not be incorporated by reference into any other filing under the Exchange Act or under the Securities Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Excerpt from Q&A session
99.2	Corporate Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

MORPHIC HOLDING, INC.

Date: January 11, 2024

By: /s/ Marc Schegerin

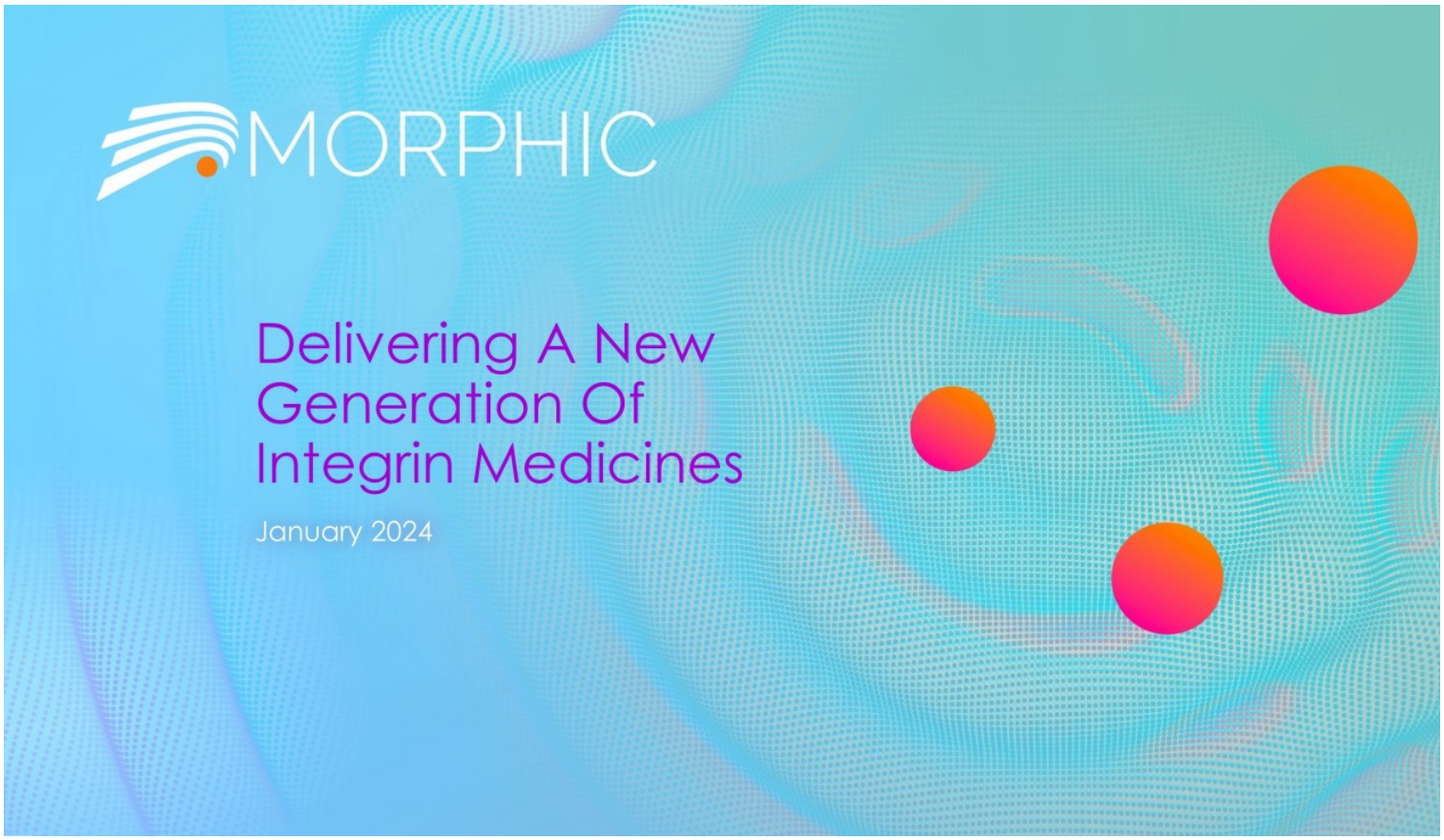
Marc Schegerin, M.D.

Chief Financial Officer and Chief Operating Officer

Exhibit 99.1

Excerpt of Transcript from the Question and Answer Session of a
Morphic Holding, Inc. Public Presentation Held on January 10, 2024

Marc Schegerin: So, you know we have a [Form 10-]K in a few weeks, but I think it's no surprise given our last [Form 10-]Q that we have approximately $700 million in the bank at the end of '23 and that our guidance has been very consistent for the last year or so, which should take us into the second half of 2027.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Delivering A New Generation Of Integrin Medicines
January 2024

Forward-Looking Statements

This presentation contains "forward-looking" statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to statements regarding the timing and success of Morphic's ongoing clinical trials and related data, updates and results from Morphic's clinical trials and the potential therapeutic benefits of MORF-057.

Certain data in this presentation are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

Statements including words such as "believe," "plan," "continue," "expect," "will," "develop," "signal," "potential," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements.

Forward-looking statements are subject to risks and uncertainties that may cause Morphic's actual activities or results to differ significantly from those expressed in or implied by any forward-looking statement, including risks and uncertainties related to the forward-looking statements in this presentation and other risks set forth in our filings with the Securities and Exchange Commission (SEC), including the Annual Report on Form 10-K for the fiscal year ended December 31, 2022 filed with the SEC on February 23, 2023, and the Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2023 filed with the SEC on November 3, 2023. These forward-looking statements speak only as of the date hereof and Morphic specifically disclaims any obligation to update these forward-looking statements or reasons why actual results might differ, whether as a result of new information, future events or otherwise, except as required by law.

Note regarding trademarks: all third-party trademarks, including names, logos and brands, referenced by in this presentation are the property of their respective owners. All references to third-party trademarks are for identification purposes only and shall be considered nominative fair use under trademark law.

Unique Receptors: Unique Therapeutic Potential

What are integrins?

- Only receptor to signal bidirectionally, giving them central biologic roles in complex diseases: autoimmune, fibrotic, cardio-metabolic and oncologic
- Expensive, complex biologics have shown clinically meaningful efficacy by targeting integrins

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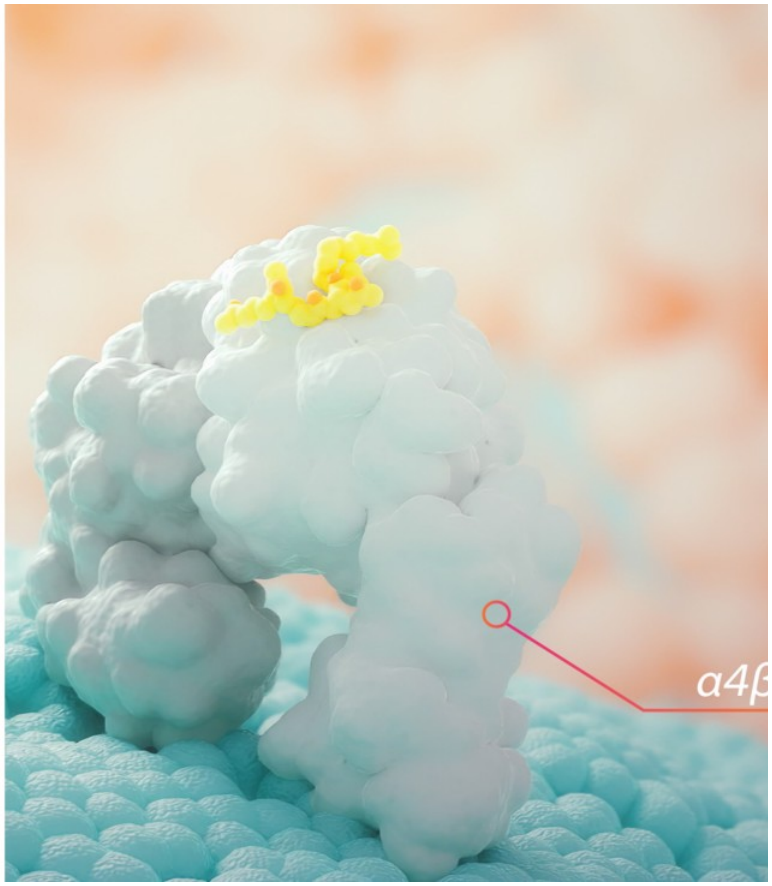
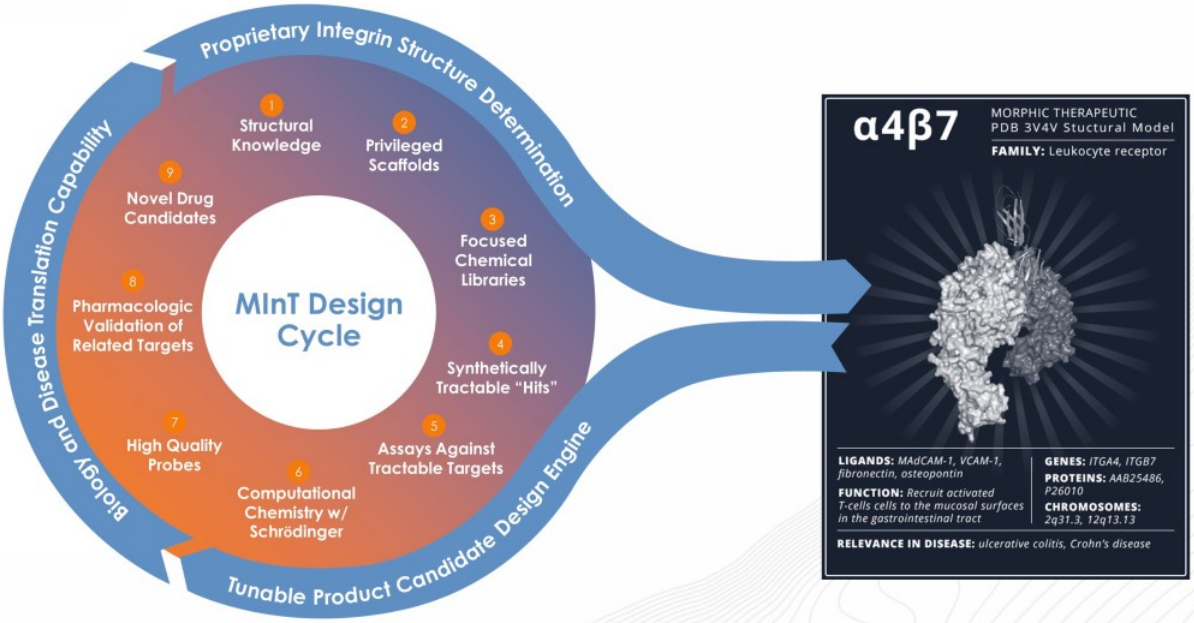


MInT Platform: Morphic's Solution to the Oral Integrin Challenge



Proprietary Pipeline

Candidate	Target (Program)	Indication	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3
MORF-057	$\alpha_4\beta_7$	Ulcerative Colitis					
		Crohn's disease					
Next-generation	$\alpha_4\beta_7$	GI Disorders					
MORF SMI[1]	Non-integrin targets	GI Disorders					
MORF SMI	$\alpha_5\beta_1$	Pulmonary Hypertensive Diseases					
MORF-088	$\alpha_v\beta_8$	Myelofibrosis Solid Tumors					
MORF SMI/mAbs	Undisclosed	Multiple Indications					

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[1] SMI: oral small molecule inhibitor

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MORF-057

Small molecule inhibitor of $\alpha_4\beta_7$: a well-validated mechanism to treat IBD

EMERALD-2 Phase 2b study ongoing

IBD: Ideal Future Treatment Paradigm

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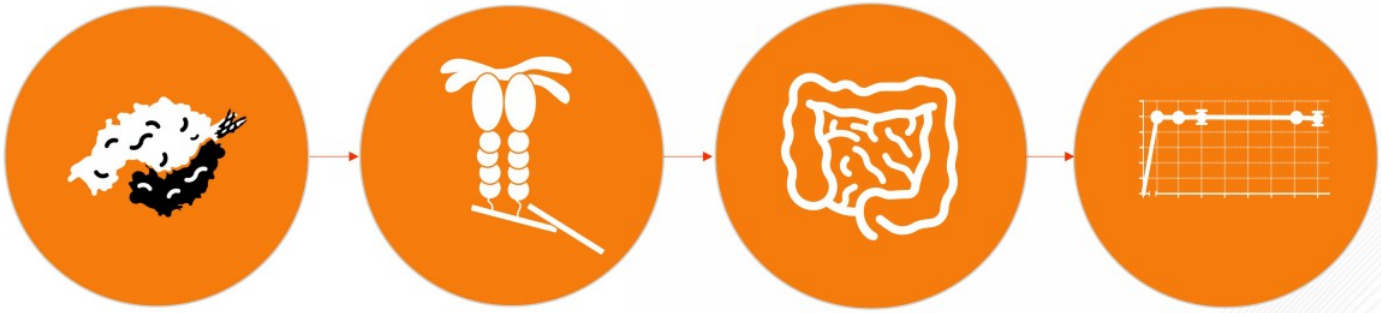
MORF-057: First-In-Class Oral Integrin Drug for IBD



MORF-057

Highly selective orally available small molecule inhibitor of $\alpha_4\beta_7$, well validated mechanism for the treatment of IBD through approved monoclonal antibody vedolizumab

Mechanism

Occluding $\alpha_4\beta_7$ blocks intestinal homing of lymphocytes, which in turn reduces pathologic inflammation in IBD

Indications

Inflammatory bowel disease with initial focus on ulcerative colitis

Approximately 1.6 million Americans currently have irritable bowel disease [1]

Clinical Data

Clinically meaningful and consistent activity data across multiple validated efficacy measures in Phase 2a study

Well tolerated to date across multiple clinical trials

Phase 2b ongoing in UC, Crohn's disease to begin 1H24

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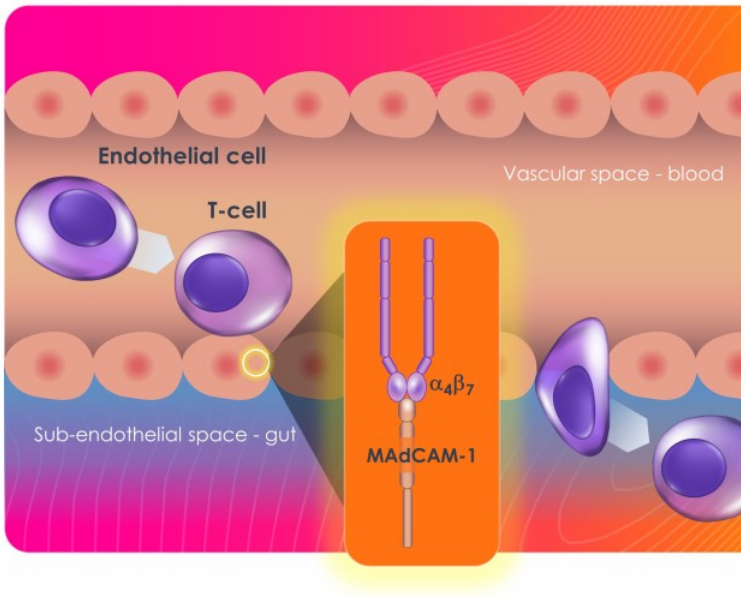
[1] Chrohn's and Colitis Foundation of America

$\alpha_4\beta_7$ Inhibition is a Proven Mechanism to Treat IBD

- **Approved antibody Entyvio® (vedolizumab)**
- Vedolizumab, an anti-$\alpha_4\beta_7$ antibody, inhibits T-cell trafficking via well validated mechanism to treat UC and Crohn's disease
- Since approval, over 265,000 patients have received vedolizumab
- Vedolizumab generated $5.2B sales in FY2022



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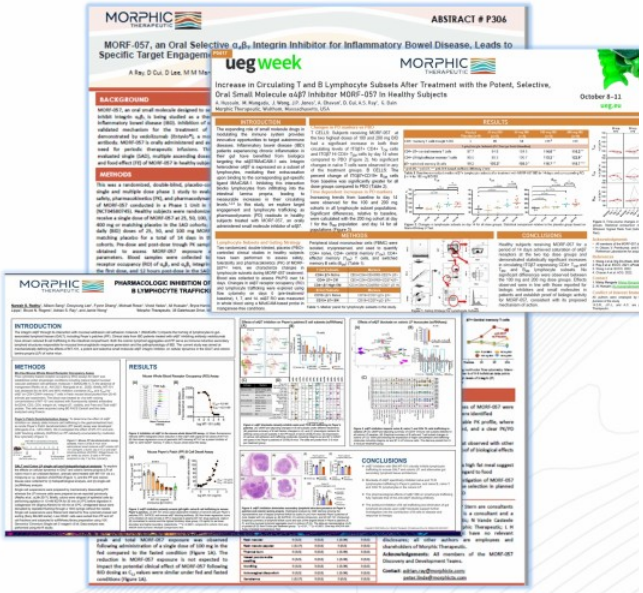
[1]Takeda press release
[2]Global Data
ENTYVIO® is a registered trademark of Millennium Pharmaceuticals, Inc.

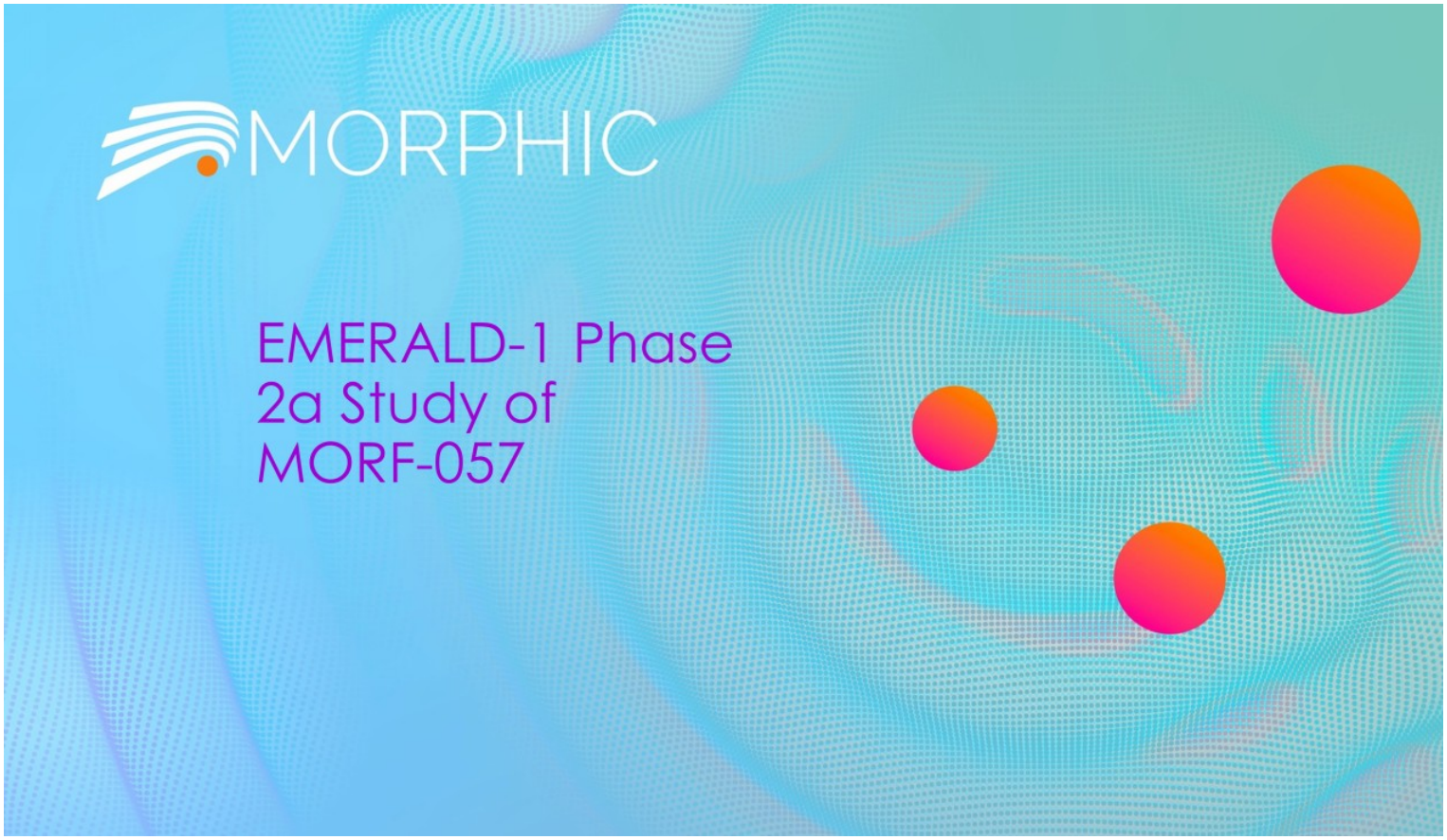
MORF-057 has Consistently Delivered on Expectations for an Oral $\alpha_4\beta_7$ Inhibitor in IBD

	MORF-057		
	PRECLINICAL	PHASE 1	PHASE 2a
Meaningful Clinical Effects			✓
30-50% ↑ in Key Lymphocytes		✓	✓
α4β7 Saturation (serum)	✓	✓	✓
Favorable Tolerability Profile	✓	✓	✓
Oral Route of Administration	✓	✓	✓

Please click on links in row headings above for underlying data



All scientific posters and presentations available at https://investor.morphictx.com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EMERALD-1 Phase 2a Study of MORF-057

MORF-057 Phase 2a: EMERALD-1Study in Moderate to Severe UC

EMERALD

Phase 2a open-label single-arm study of MORF-057 (100mg BID) in patients with moderately to severely active ulcerative colitis (n=35 main cohort)

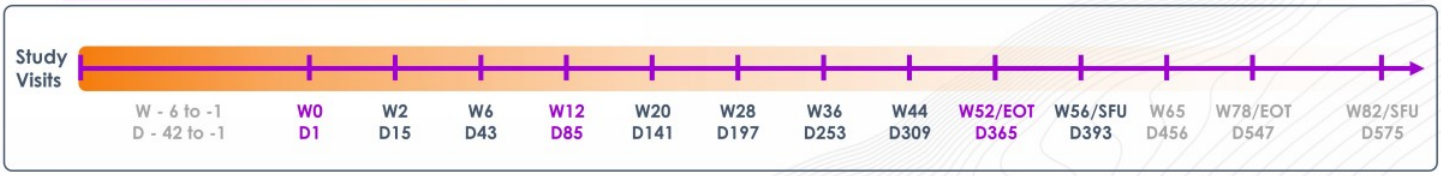
Phase 2a

- Primary endpoint: Change in RHI measured at 12 weeks
- Secondary endpoints: mMCS change from baseline, safety
- Pre-specified exploratory endpoints:
  - RHI remission
  - mMCS remission
  - mMCS response
  - Multiple PK/PD parameters
  - Relevant biomarkers

Open-Label Treatment Period
MORF-057 (100mg B.I.D. P.O.)
for 52 weeks
Primary endpoint at week 12

Long-Term Extension
Direct rollover to extension
MORF-057 (100mg B.I.D. P.O.)
for 26 weeks

Safety Follow-Up Period
Safety Follow-up Visit
to occur 4 weeks
after last dose of study drug



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Baseline Patient Demographics: a Moderately-to-Severely Active UC population with High Disease Burden

Category		Patients, N=35
Age, mean ± SD	Years	39.2 ± 14.1
Sex, n (%)	Female	16 (45.7)
Geography, n (%)	Poland United States	28 (80.0) 7 (20.0)
Duration of disease, mean ± SD	Years	7.5 ± 8.0
Extent of disease, n (%)	Proctosigmoiditis L-sided colitis Pancolitis	12 (34.3) 10 (28.6) 10 (28.6)
RHI Score, mean ± SD	Points	22.7 ± 7.3
mMCS, mean ± SD	Points	6.7 ± 1.1
MES, n (%)	2 3	18 (51.4) 17 (48.6)
Corticosteroid use, n (%)	No Yes	26 (74.3) 9 (25.7)
Previous use of AT*, n (%)	Naïve Experienced	21 (60.0) 14 (40.0)

AT, advanced therapy; MES, Mayo endoscopic score; mMCS, modified Mayo Clinic score; RHI, Robarts histopathology index; SD, standard deviation
*The number of AT-experienced patients was updated from n=13/35 to n=14/35 during re-review of data for presentation at a medical conference. During this re-review, It was determined that one patient had received an investigational agent deemed to be an advanced therapy before the MORF-057-201 trial. This change does not impact any of the clinical efficacy data presented from the EMERALD-1 study.

MORF-057: Generally Well-Tolerated in EMERALD-1 No Safety Signal Observed

Adverse Event (AE) profile consistent with underlying disease state

Patients with at least one AE	**12 (34.3%)**
Patients with any serious AE	**0**
Patients with AE leading to death	**0**
Patients with any grade 3 AE	**2 (5.7%)[1]**
Patients with treatment-related AE	**2 (5.7%)**
Common (>5%) AEs Exacerbation of UC Anemia	 **4 (11.4%)** **3 (8.6%)[2]**

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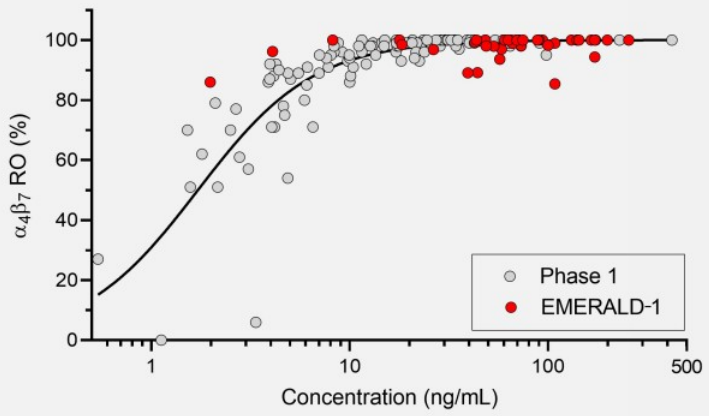
1. Both UC exacerbations, one led to early discontinuation
2. All anemic at baseline and continued on study with iron supplements

*As of 4/25/23 patients have been on EMERALD-1 study beyond the 12-week induction period and no other safety signals or SAEs have been reported.

Patient α4β7 Receptor Occupancy (RO) Consistent with Healthy Volunteer RO



α4β7 selectivity over α4β1 consistent with Phase 1 results

RO at 12 weeks		
	α4β7	α4β1
Mean	**>98%**	BLQ
Median	**>99%**	BLQ

- α4β7 RO achieved early and sustained saturating levels
- α4β1 RO remained at low levels
- No lymphocytosis or changes to circulating naïve T-cells were observed
- α4β1 projected RO was below the limit of quantitation with mean trough value estimated to be <15%

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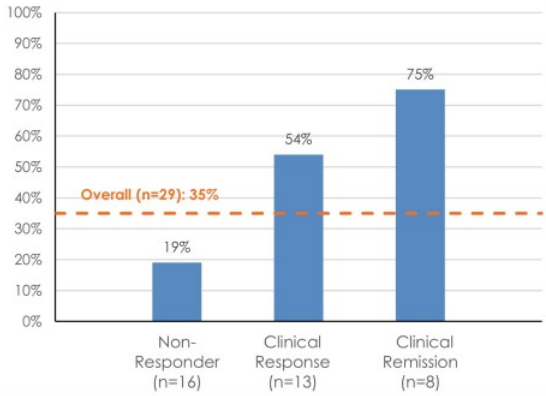
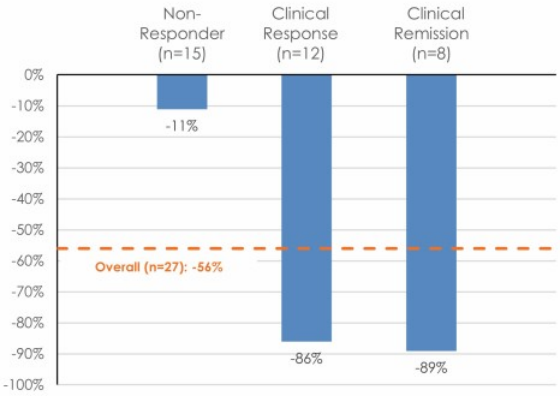
Fecal Calprotectin Decreases Correlated with Disease Improvement

Proportion of Patients with Fecal Cal < 250 mg/kg at Week 12 (Baseline > 250 mg/kg), n=29



Percentage Reduction From Baseline in Fecal Cal at Week 12 (Baseline > 250 mg/kg & Week 12 data available), n=27[a]



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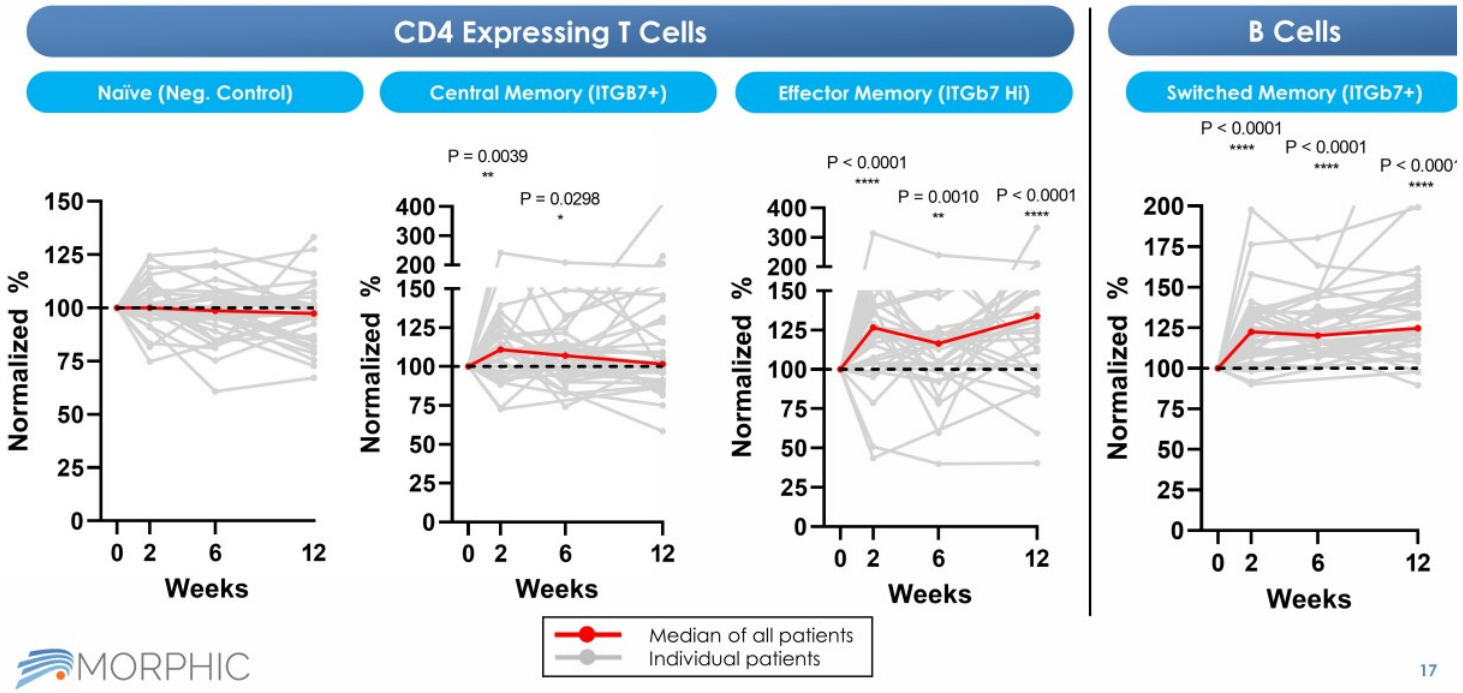
n = Patients with baseline FC > 250 mg/kg. No inclusion/exclusion criteria for FC levels
Patients experiencing clinical remission also included in clinical response
a. Data unavailable for 2 patients at week 12

Substantial Lymphocyte Subset Changes Observed, Consistent With Engagement Of α4β7



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Clinical Efficacy
Results

Primary Endpoint Met with Statistical Significance

Consistent Effects Observed Among All Exploratory Measures

Endpoint @ Week 12	Overall (N=35)
Change in RHI, Mean (SD)	**-6.4 (11.18)** *p=0.0019*
RHI remission, n (%)	8 (22.9%)
Clinical response (mMCS)[1], n (%)	16 (45.7%)
Clinical remission (mMCS)[2], n (%)	9 (25.7%)
Endoscopic Response/Improvement[3], n (%)	9 (25.7%)
Change from baseline to Week 12 in the Modified MCS, Mean (SD)	-2.3 (2.14)

1. Clinical response (mMCS): decrease from baseline in the mMCS ≥2 points and ≥30% from baseline, plus a decrease in rectal bleeding subscore ≥1 or an absolute rectal bleeding subscore ≤1
2. Clinical remission (mMCS): rectal bleeding subscore of 0; a stool frequency subscore of ≤1; and an MES of ≤1 without friability
3. Endoscopic response / improvement: MES ≤1

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EMERALD-1 Efficacy Results by AT Status and MES

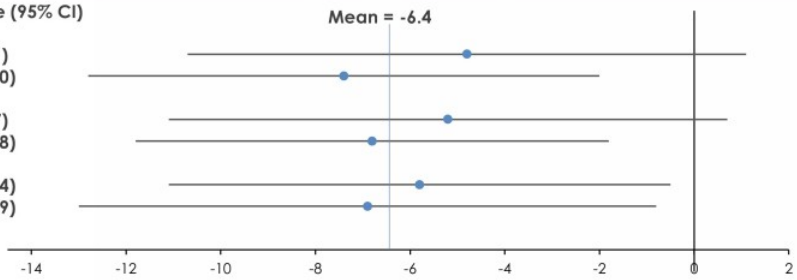
Endpoint @ Week 12	Overall N=35	AT-naïve n=21	AT-experienced n=14	MES =2 n=18	MES =3 n= 17
Change in RHI, mean ± SD	**-6.4 ± 11.2**	**-7.4 ± 11.9**	**-4.8 ± 10.3**	**-6.9 ± 12.1**	**-5.8 ± 10.4**
RHI change ≥ 7 points, n (%)	17 (48.6)	12 (57.1)	5 (35.7)	10 (55.6)	7 (41.2)
RHI remission[1], n (%)	8 (22.9)	6 (28.6)	2 (14.3)	6 (33.3)	2 (11.8)
RHI reduction ≥ 50%, n (%)	12 (34.3)	9 (42.9)	3 (21.4)	9 (50.0)	3 (17.6)
Change in mMCS, mean ± SD	-2.3 ± 2.1	-2.9 ± 2.4	-1.6 ± 1.5	-2.7 ± 2.3	-1.9 ± 1.9
Clinical response (mMCS)[2], n (%)	16 (45.7)	11 (52.4)	5 (35.7)	9 (50)	7 (41.2)
Clinical remission (mMCS)[3], n (%)	9 (25.7)	9 (42.9)	0	6 (33.3)	3 (17.6)
Symptomatic remission[4], n (%)	11 (31.4)	10 (47.6)	1 (7.1)	7 (38.9)	4 (23.5)
Endoscopic response / improvement[5], n (%)	9 (25.7)	9 (42.9)	0	6 (33.3)	3 (17.6)
Change in SF, mean ± SD	-0.8 ± 1.1	-1.0 ± 1.2	-0.5 ± 0.7	-0.9 ± 1.3	-0.6 ± 0.8
Change in RB, mean ± SD	-1.1 ± 0.8	-1.1 ± 0.9	-0.9 ± 0.8	-1.4 ± 0.8	-0.7 ± 0.7

AT, advanced therapy; MCS, Mayo Clinic Score; mMCS, modified MCS; RHI, Robarts histopathology index; SF, Stool Frequency; RB, Rectal Bleeding; SD, standard deviation
1. RHI Remission: RHI ≤ 2
2. Clinical response (mMCS): decrease from baseline in the mMCS ≥2 points and ≥30% from baseline, plus a decrease in rectal bleeding subscore ≥1 or an absolute rectal bleeding subscore ≤1
3. Clinical remission (mMCS): rectal bleeding subscore of 0; a stool frequency subscore of ≤1; and an MES of ≤1 without friability
4. Symptomatic remission: SFS = 0 (or = 1 with ≥ 1 point decrease from baseline) and RBS = 0
5. Endoscopic response/improvement: MES ≤1

Consistent "Across-the-Board" Efficacy Signals Observed

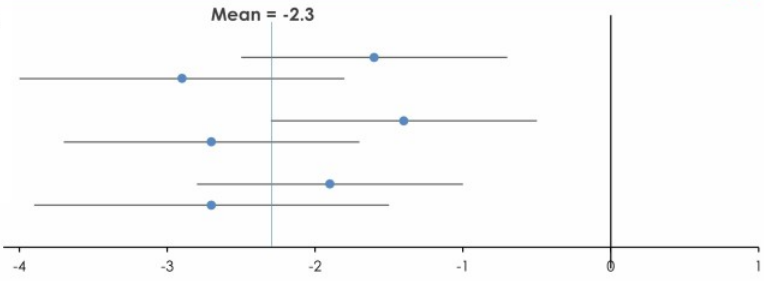
Robarts Histopathology Index (RHI)

Subgroup	Mean Change (95% CI)
AT-Experienced	
Yes (n=14)	**-4.8 (-10.7, 1.1)**
No (n=21)	**-7.4 (-12.8, -2.0)**
Corticosteroid Use at Baseline	
Yes (n=9)	**-5.2 (-11.1, 0.7)**
No (n=26)	**-6.8 (-11.7, -1.8)**
Baseline MES	
3 (n=17)	**-5.8 (-11.1, -0.4)**
2 (n=18)	**-6.9 (-13.0, -0.9)**



Modified Mayo Clinical Score (mMCS)

Subgroup	Mean Change (95% CI)
AT-Experienced	
Yes (n=14)	**-1.6 (-2.4, -0.7)**
No (n=21)	**-2.9 (-3.9, -1.8)**
Corticosteroid Use at Baseline	
Yes (n=9)	**-1.4 (-2.3, -0.6)**
No (n=26)	**-2.7 (-3.6, -1.7)**
Baseline MES	
3 (n=17)	**-1.9 (-2.9, -1.0)**
2 (n=18)	**-2.7 (-3.9, -1.6)**



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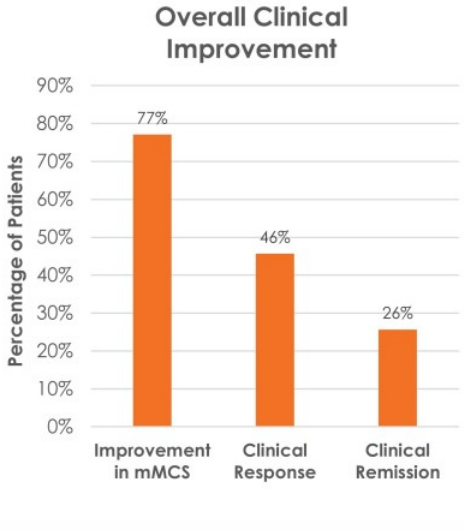
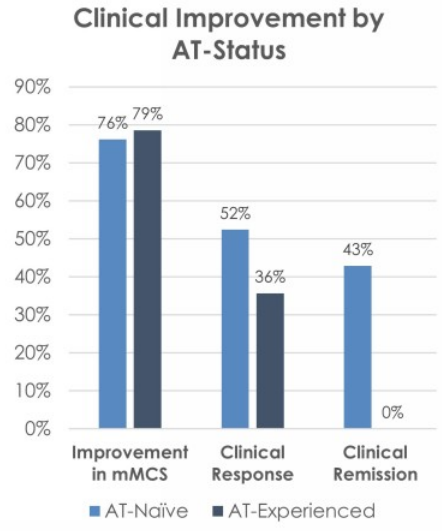
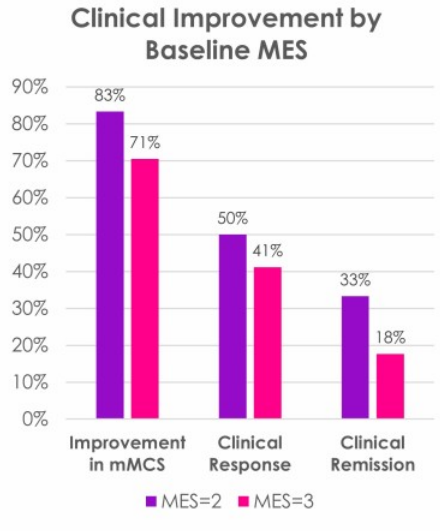
Clinical Improvement in >75% of All Patients, Regardless of Prior Therapy and Baseline MES



N=35



AT-Naïve: n=21; AT-Experienced: n=14



Baseline MES=2: n=18; Baseline MES=3: n=17

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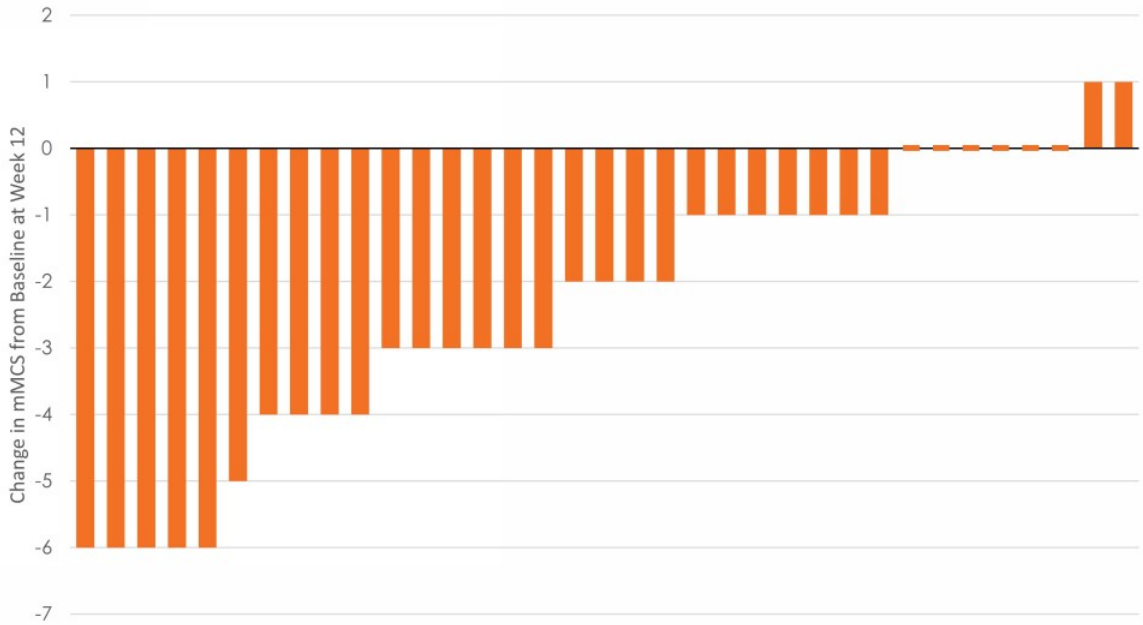
Change in Central mMCS By Patient from Baseline at Week 12



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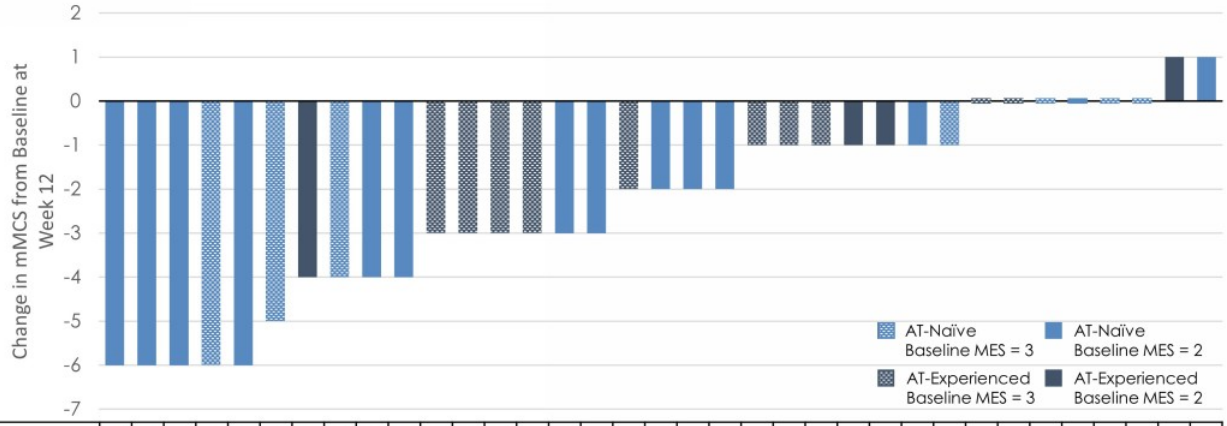
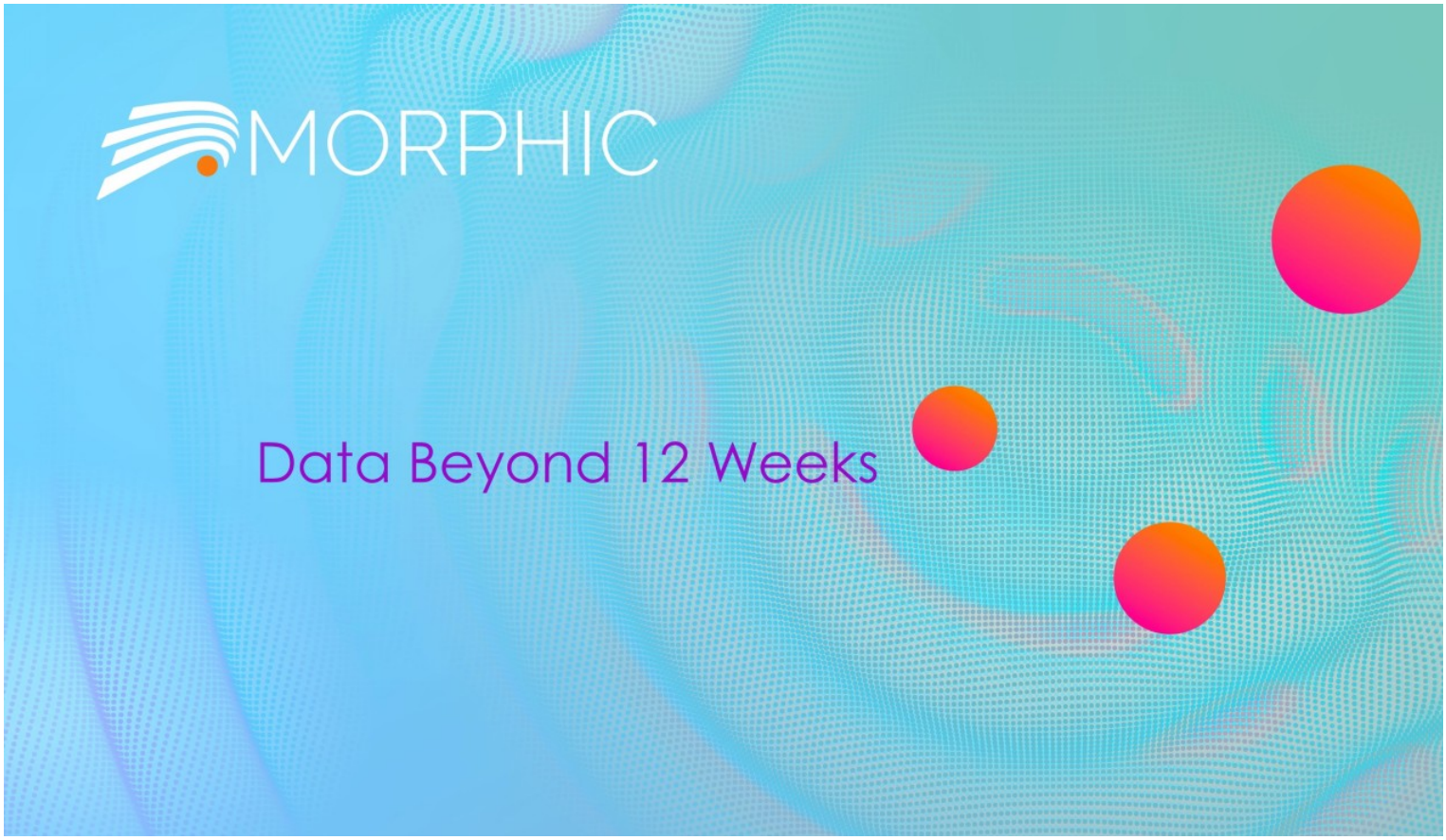
Change in Central mMCS from Baseline by Subgroup at Week 12



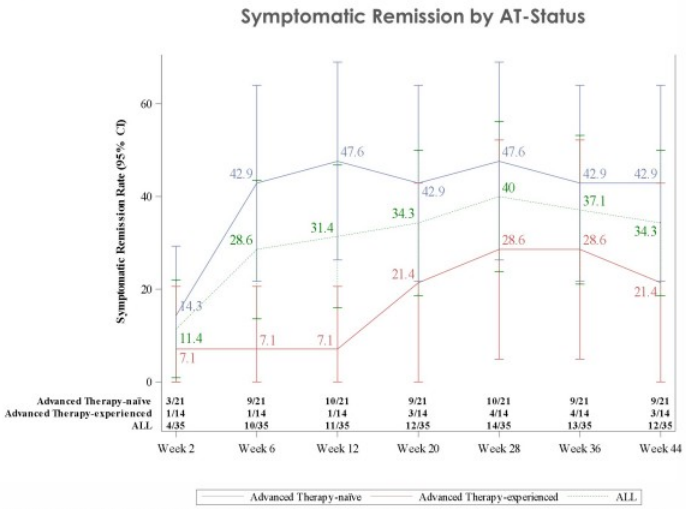
Response	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			✓														
Remission	✓	✓	✓	✓	✓	✓		✓	✓						✓																	
RHI decrease from baseline ≥ 7	✓	✓		✓	✓	✓	✓	✓						✓	✓	✓		✓			✓			✓	✓	✓	✓			✓					
Steroid Use	N	N	N	N	N	N	N	N	N	N	N	N	Y	N	Y	N	Y	Y	N	N	N	N	Y	Y	N	N	Y	N	Y	N	Y	N	N	N	N
Baseline MES	2	2	2	3	2	3	2	3	2	2	3	3	3	3	2	2	3	2	2	2	3	3	3	2	2	2	3	3	3	3	2	3	3	2	2
# Prior AT							1				2	2	1	1			1				2	2	1	1	2			1	1					1	

AT, advanced therapy; RHI, Robarts histopathology index; MES, Mayo endoscopic score


MORPHIC
Data Beyond 12 Weeks

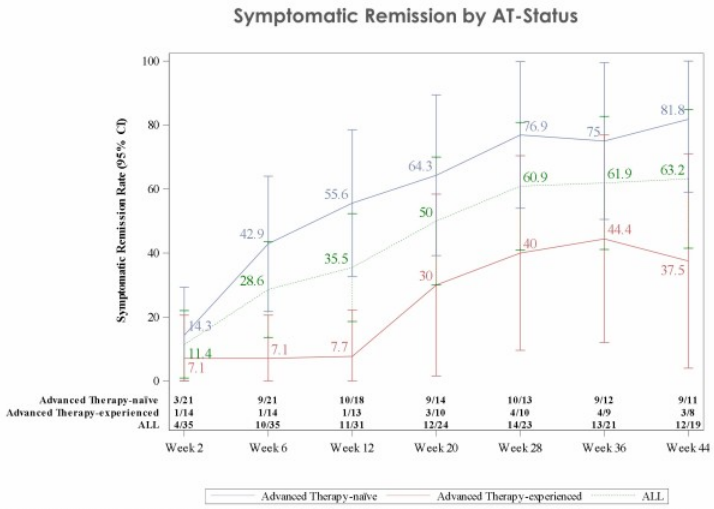
Symptomatic Remission By AT-Status: Week 44

Intent to Treat (ITT): Denominator includes all enrolled patients (N=35)



Symptomatic remission is defined as an stool frequency subscore=0 (or =1 with a >=1-point decrease from baseline) and rectal bleeding subscore=0

As observed: Denominator includes only patients who completed the visit



Symptomatic remission is defined as an stool frequency subscore=0 (or =1 with a >=1-point decrease from baseline) and rectal bleeding subscore=0

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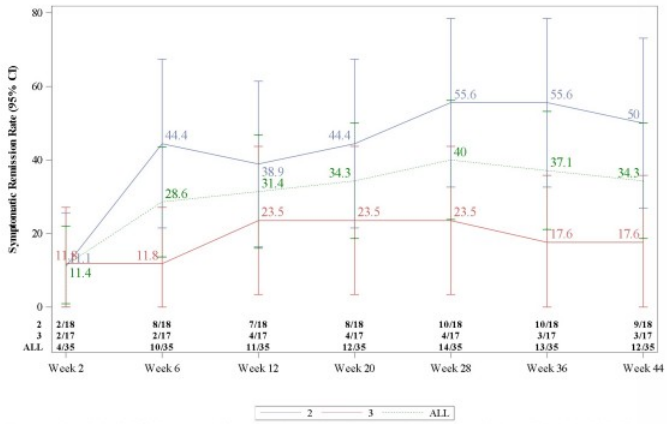
Note: These are ad hoc analyses and are subject to change during the quality control and trial completion processes

Symptomatic Remission By Baseline MES: Week 44

ITT: Denominator includes all enrolled patients (N=35)

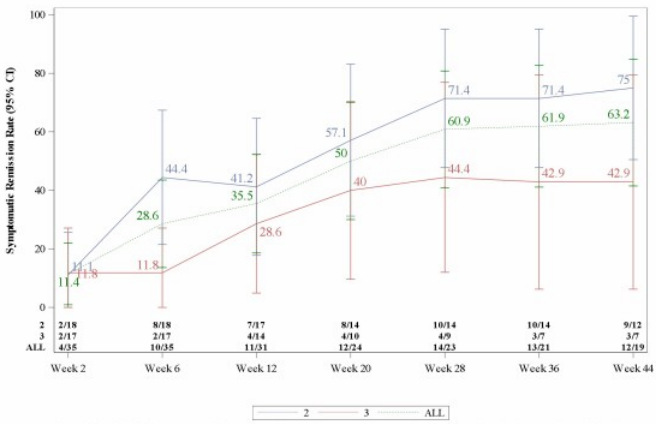
Symptomatic Remission by Baseline Endoscopy Score



Symptomatic remission is defined as an stool frequency subscore=0 (or =1 with a >=1-point decrease from baseline) and rectal bleeding subscore=0

As observed: Denominator includes only patients who completed the visit

Symptomatic Remission by Baseline Endoscopy Score



Symptomatic remission is defined as an stool frequency subscore=0 (or =1 with a >=1-point decrease from baseline) and rectal bleeding subscore=0

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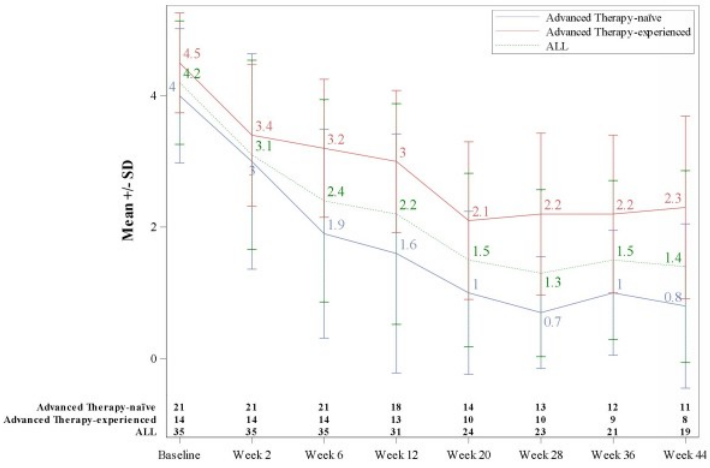
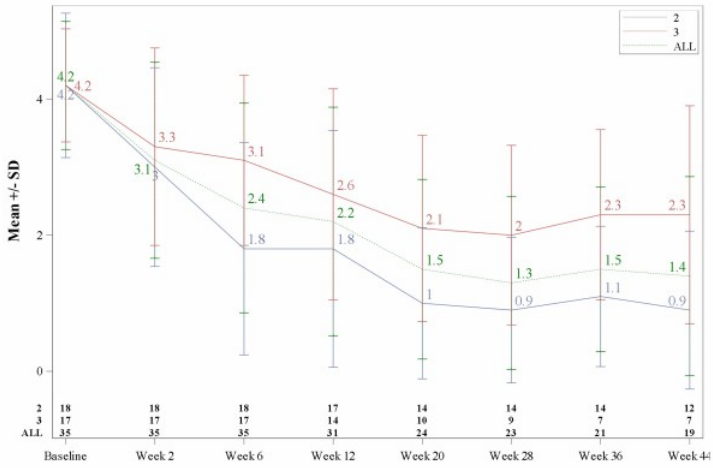
Note: These are ad hoc analyses and are subject to change during the quality control and trial completion processes

PRO2 (SFS+RBS) Scores by Subgroup: Week 44

PRO2 (Sum of Stool Frequency and Rectal Bleeding Scores) by AT-Status



PRO2 (Sum of Stool Frequency and Rectal Bleeding Scores) by Baseline Endoscopy Score



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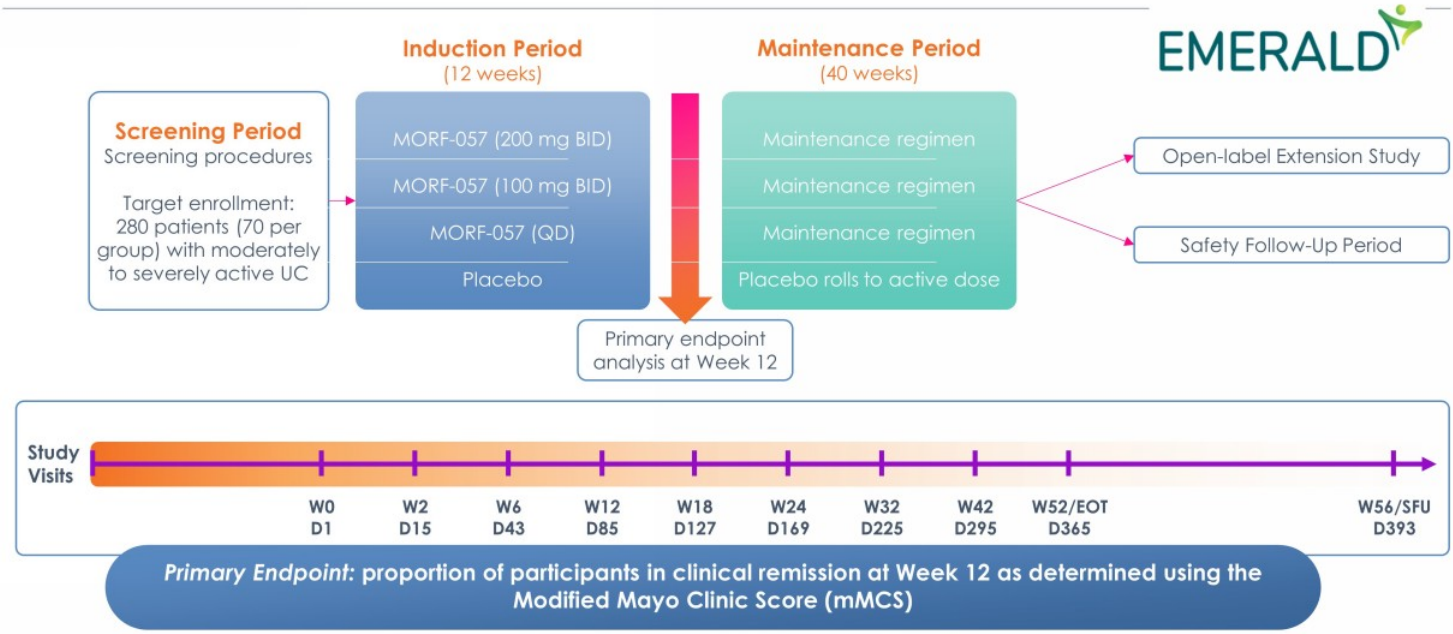
Note: These are ad hoc analyses and are subject to change during the quality control and trial completion processes

MORF-057 Phase 2b: EMERALD-2 Study in Moderate to Severe UC



MORF-057 Phase 2b Study in Crohn's Disease

GARNET

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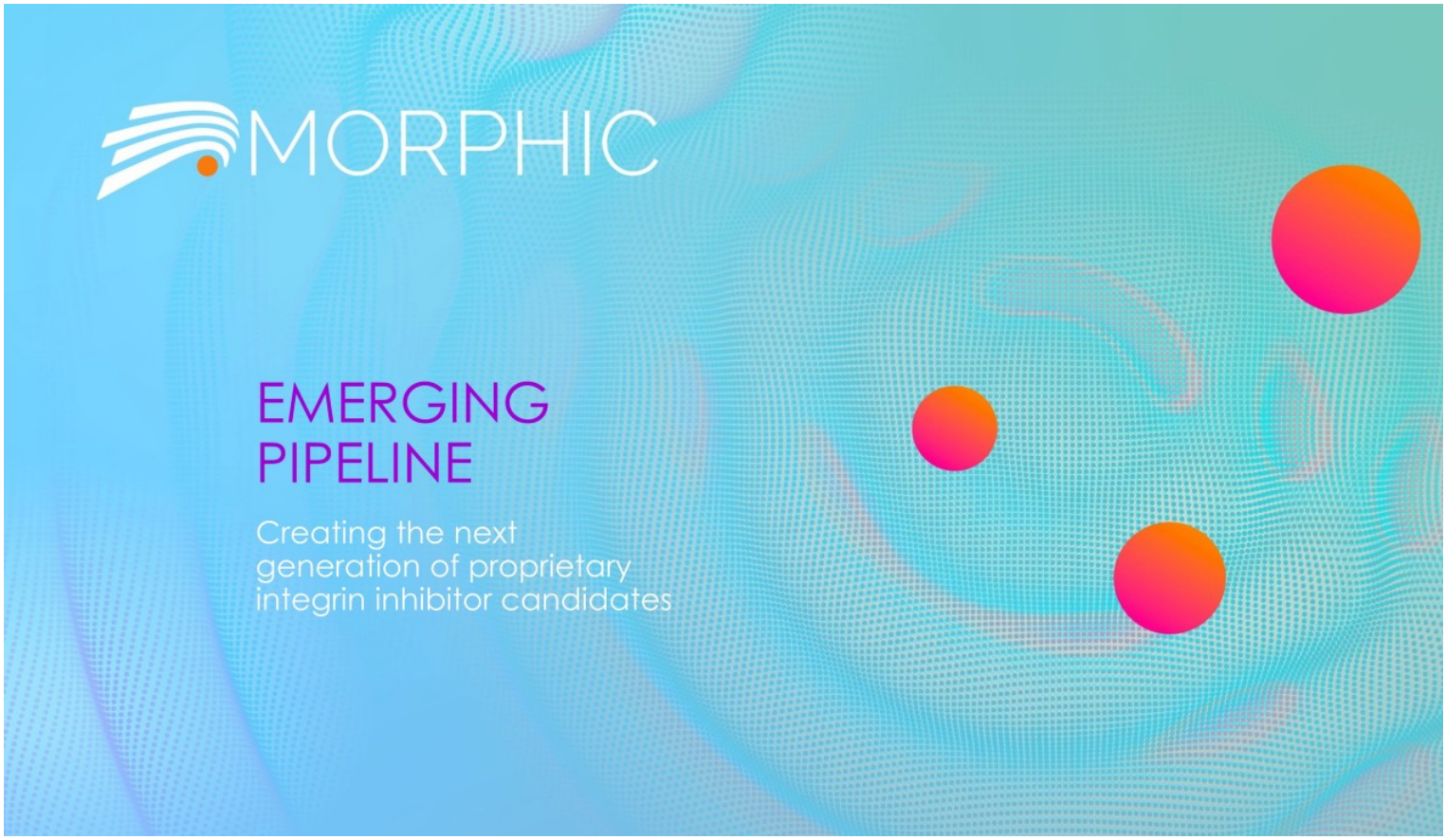
GARNET Launch Activities Underway

- Global, randomized phase 2b trial of MORF-057 in patients with moderately to severely active Crohn's disease
- Primary endpoint: proportion of participants in endoscopic response (>=50% reduction) at week 14 as determined using SES-CD
- 210 patients
  - 70 patients 200 MG BID MORF-057
  - 70 patients 100 MG BID MORF-057
  - 70 patients placebo
- Anticipate first patient enrolled 1H24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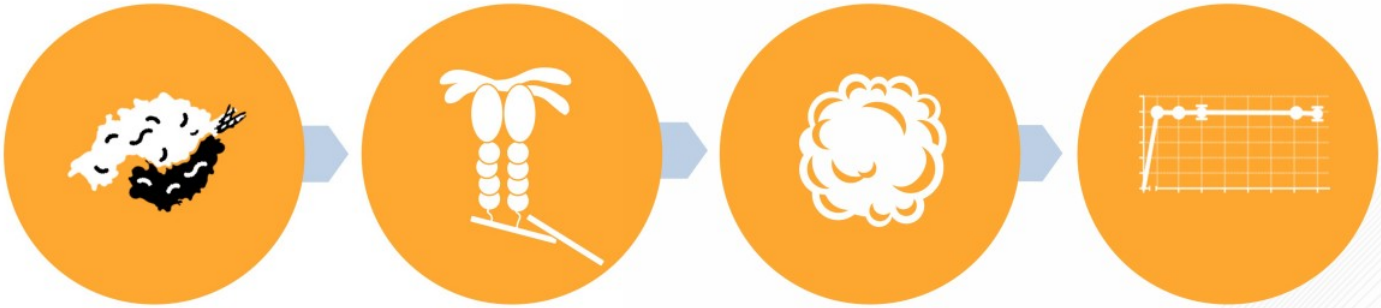
EMERGING
PIPELINE
Creating the next
generation of proprietary
integrin inhibitor candidates

$\alpha_v\beta_8$ Small Molecule Integrin Inhibitor Program for Myelofibrosis and Immuno-oncology



αvβ8 Program

Small molecule inhibitors of the $\alpha_v\beta_8$ integrin in preclinical development

Mechanism

$\alpha_v\beta_8$ inhibition suppresses activation of TGFβ isoforms 1 and 3

Indications

Myelofibrosis;
Combination therapy for solid tumors

Data

Oral $\alpha_v\beta_8$ inhibitor, in combination with anti-PD-1, drives efficacy across mouse models of treatment-resistant breast cancer;
Myelofibrosis: $\alpha_v\beta_8$ inhibition drives increase in platelet production in published literature

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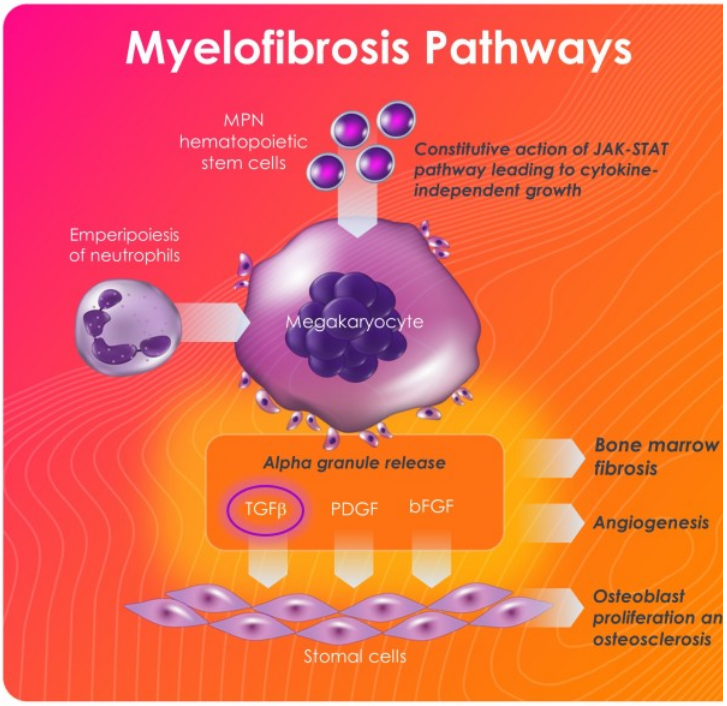
MORF-088: $a_v\beta_8$ Inhibitor for Myelofibrosis (MF)

- MF: multi-mechanistic etiology including TGF-B
- Blockbuster rare disease indication
  - Jakafi $1 billion MF sales alone
- No disease modifying Tx except allogeneic hematopoietic stem cell transplant
- Current SoC has multiple deficiencies
  - Toxicity: anemia and thrombocytopenia
  - Intolerance or resistance to therapy develops over time
  - Not disease modifying
- $a_v\beta_8$ Smi offers potential to increase platelet counts



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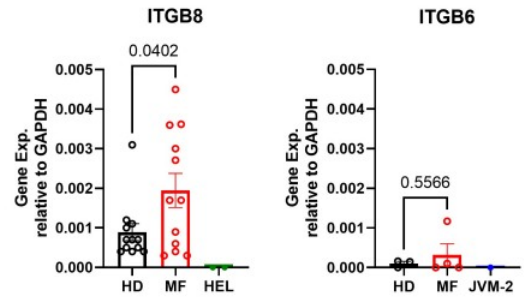
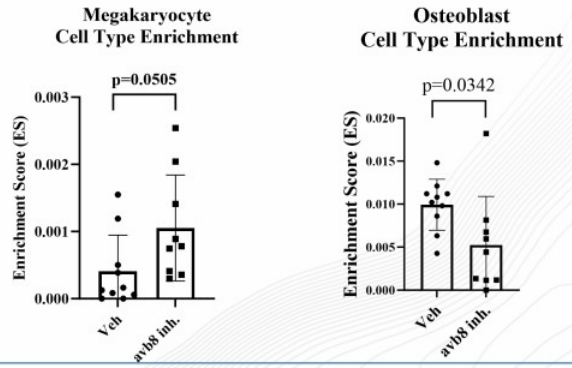
$\alpha_v\beta_8$ Inhibition: Central Role in TGF-β Modulation

$\alpha_v\beta_8$ is the dominant TGF-β forming integrin in human bone marrow



Healthy donor (HD) and myelofibrosis (MF) CD34+ HSC[1]

$\alpha_v\beta_8$ inhibition *in vivo* leads to enrichment of megakaryocytes and decreased osteoblasts, suggesting a healthier bone marrow niche



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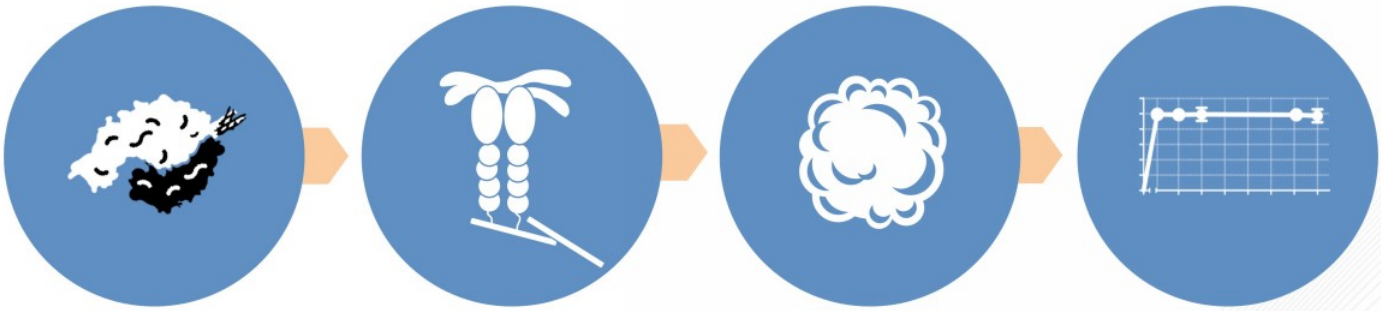
[1]The HEL 92.1.7 (HEL) and JVM-2 cell lines were used as a negative controls for ITGB8 and ITGB6 expression, respectively.

$\alpha_5\beta_1$: Small Molecule Integrin Inhibitor for Pulmonary Hypertensive Diseases



Program

Small molecule inhibitors of fibronectin integrins in preclinical development

Mechanism

Fibronectin integrin inhibition suppresses pulmonary arterial smooth muscle cell proliferation

Indications

Multiple pulmonary hypertensive diseases

Data

Preclinical data demonstrating improved cardiac output and reversal of vascular remodeling

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$\alpha_5\beta_1$ Integrin Inhibition for Pulmonary Hypertensive Diseases

- Potential applications in severely underserved pulmonary hypertensive diseases
- In preclinical studies, $A_5\beta_1$ inhibition may drive multiple independent processes:
  - Reverses remodeling in pulmonary vasculature
  - Directly prevents right ventricle fibrosis
  - Improves cardiomyocyte efficiency
- $A_5\beta_1$ inhibition holds potential for true disease-modifying activity

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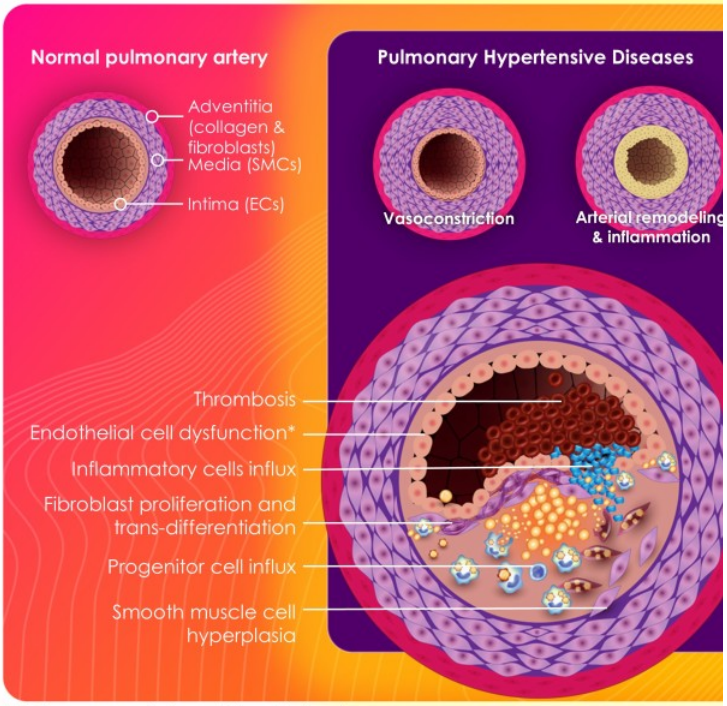
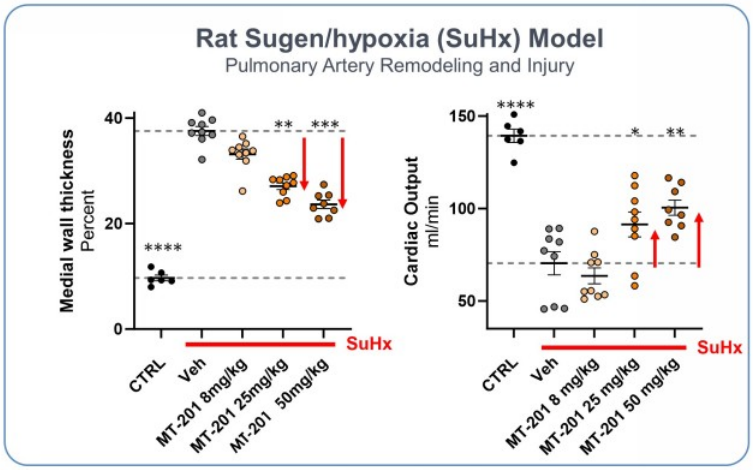
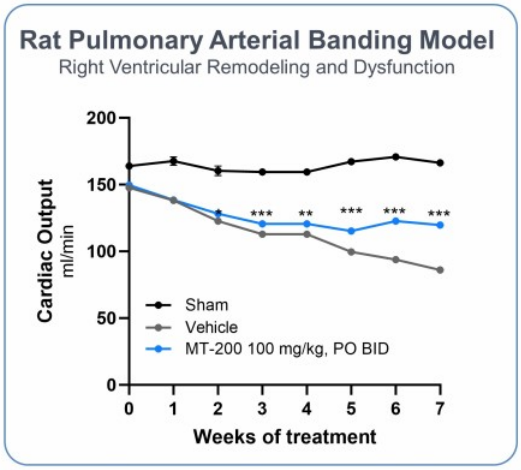


*FDA approved drugs (Vasodilators)

Modified from Pharmacol Ther. 2013 Jun;138(3):409-17

α5b1 Inhibition Improves Pulmonary Artery Remodeling and Cardiac Function





α5β1 inhibition Improves Pulmonary Artery Remodeling and prevents right ventricle failure in preclinical models

Potential differentiation from TGF-β family inhibitors, which did not show improvement in cardiac output in patients

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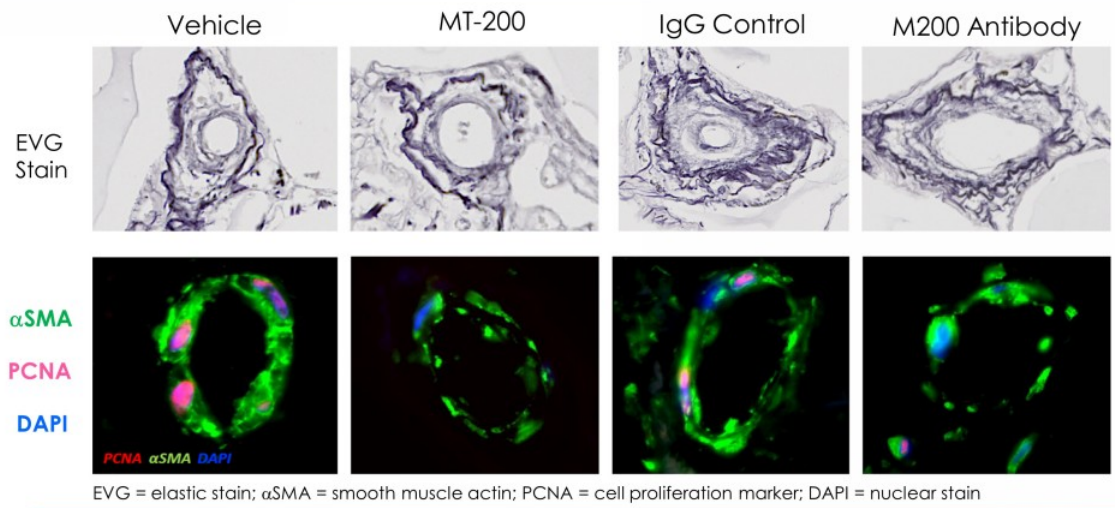
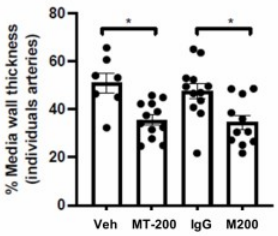
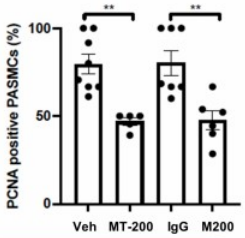
MT-200 = α5β1/αv small molecule inhibitor; (100 mg/kg, PO BID). SOC = Macitentan (Endothelin receptor antagonist, 1 mg/kg, PO BID), Tadalafil (phosphodiesterase type 5 inhibitor , 10 mg/kg, PO BID). MT-201 = α5β1 small molecule inhibitor (PO BID)

Data generated by Sebastien Bonnet, Laval Unive
Mean ± SEM. *p<0.05; **p<0.01; ***p<0
One-way ANOVA followed by Dunnett's test vs. Ve

$\alpha_5\beta_1$ Inhibition Blocks Pulmonary Artery Smooth Muscle Cell Proliferation in Human PAH Lung Slices







EVG = elastic stain; αSMA = smooth muscle actin; PCNA = cell proliferation marker; DAPI = nuclear stain

Study assessed the use of precision cut lung slices (PCLS) from human PAH patients to assess vascular remodeling *ex vivo*

Impressive inhibition of pulmonary artery remodeling achieved in this human system

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MT-200 = α5β1 small molecule inhibitor; M200 = Volociximab, α5β1-specific antibody

Data generated by Sebastien Bonnet, Laval Universi

Deep Specialist Expertise Across Management, and Board of Directors

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Chief Executive Officer

Bruce Rogers, PhD
President

Marc Schegerin, MD
Chief Financial Officer
Chief Operating Officer

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and Secretary

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Praveen Tipirneni, MD CEO Morphic Therapeutic

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THANK YOU

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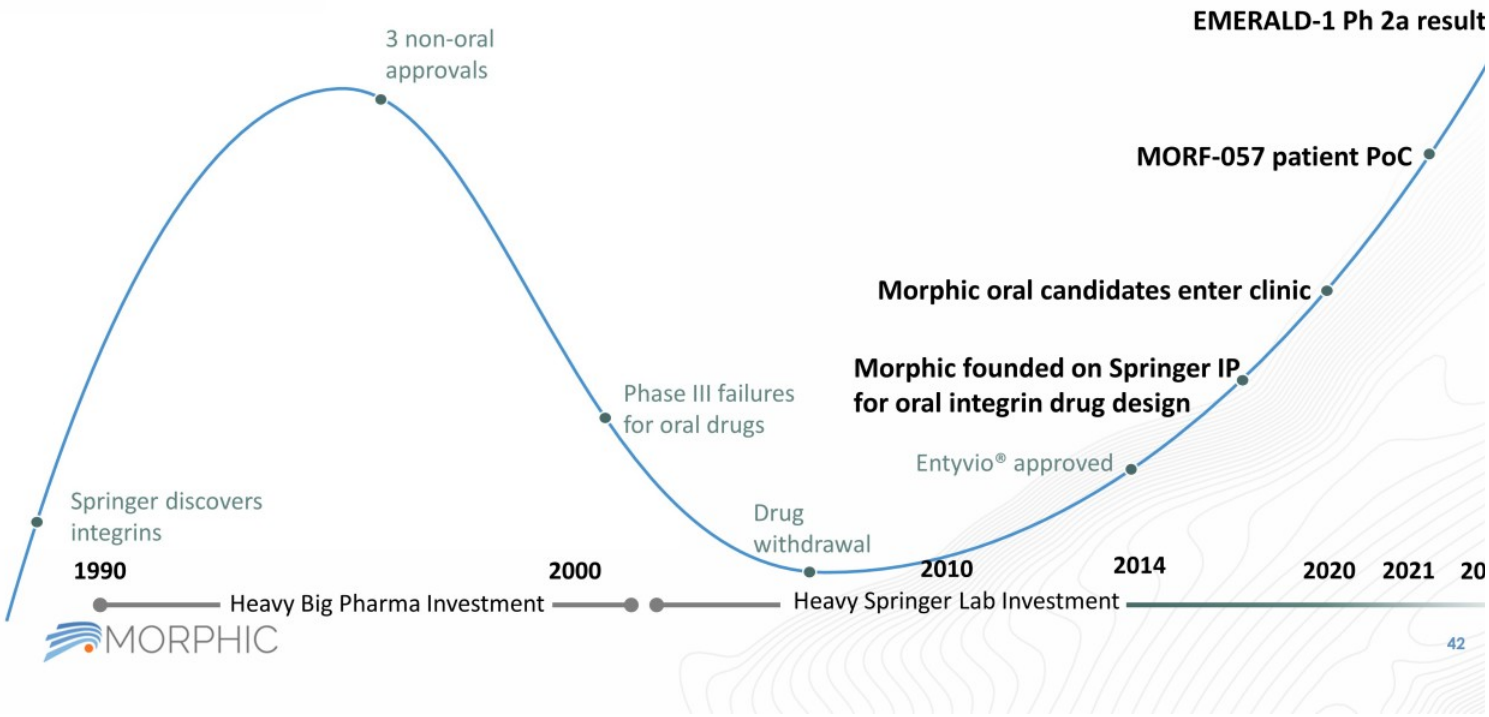
Delivering A New Generation Of Integrin Medicines

Appendix

Morphic: A New Chapter In Integrin History



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Horizons of IBD Treatment

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IBD Current Landscape

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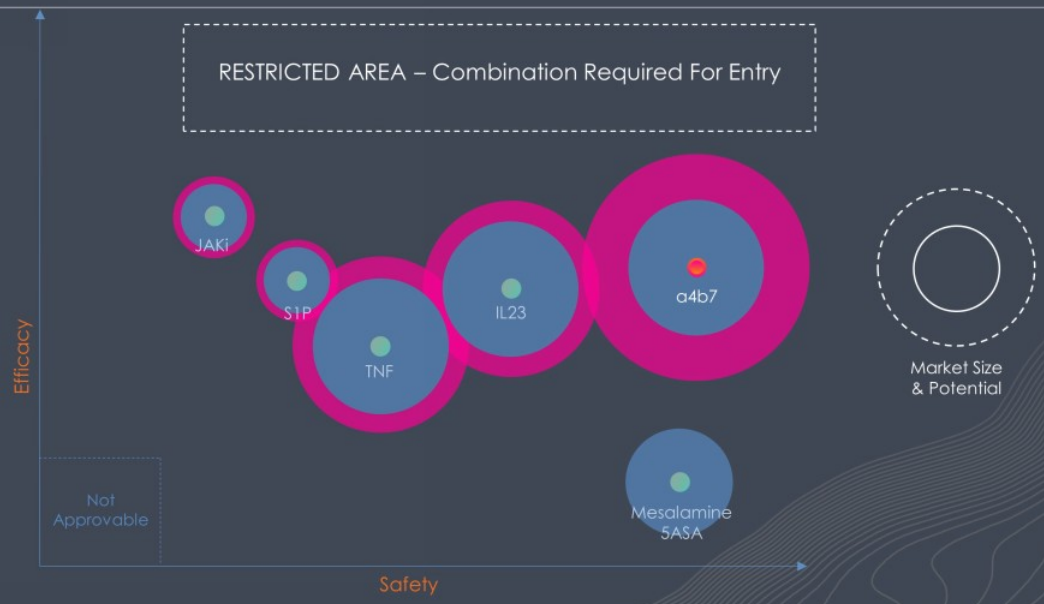
Illustrative representation: for discussion purposes

IBD Opportunity: Future Expansion



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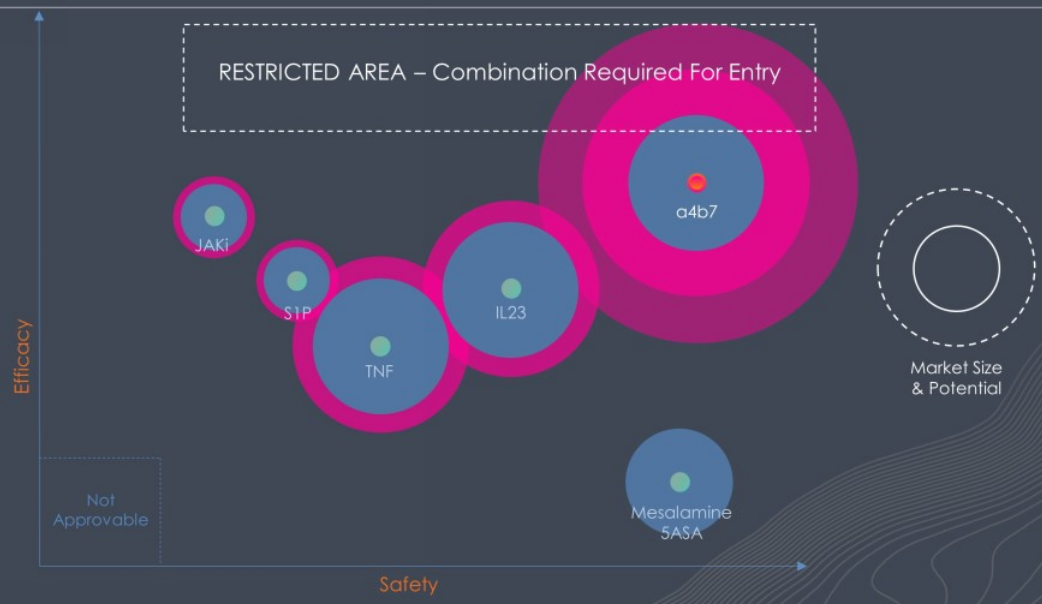
Illustrative representation: for discussion purposes

IBD Opportunity: Oral Combination Potential



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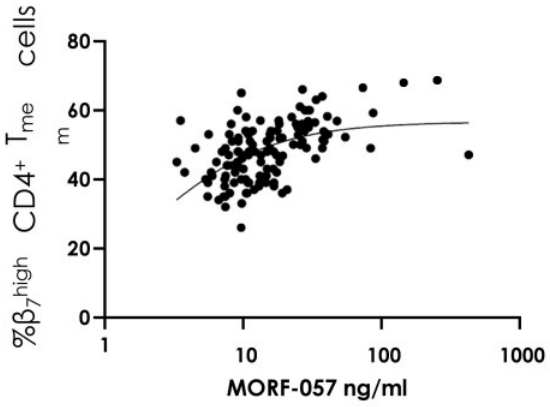
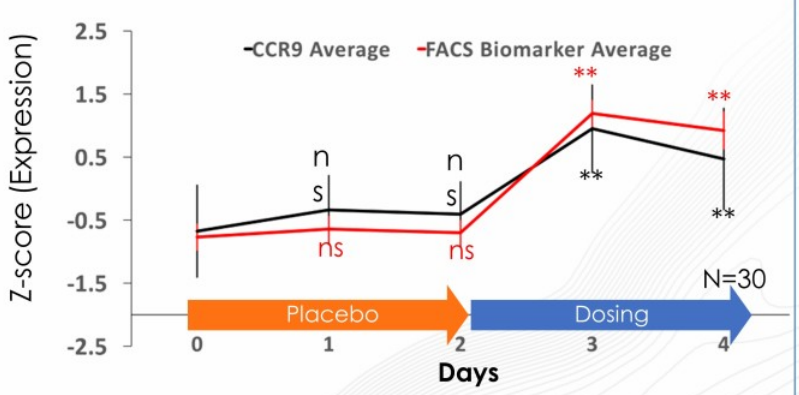
Illustrative representation: for discussion purposes

T_{mem} cell and CCR9 blood biomarkers increase with MORF-057 exposure

T_{mem} biomarker data from all studies



Comparison of CCR9 and T_{mem} biomarker changes



β_7^{high} CD4+ T_{mem} biomarker increases with plasma exposure and dosing correlated with elevated CCR9 transcript

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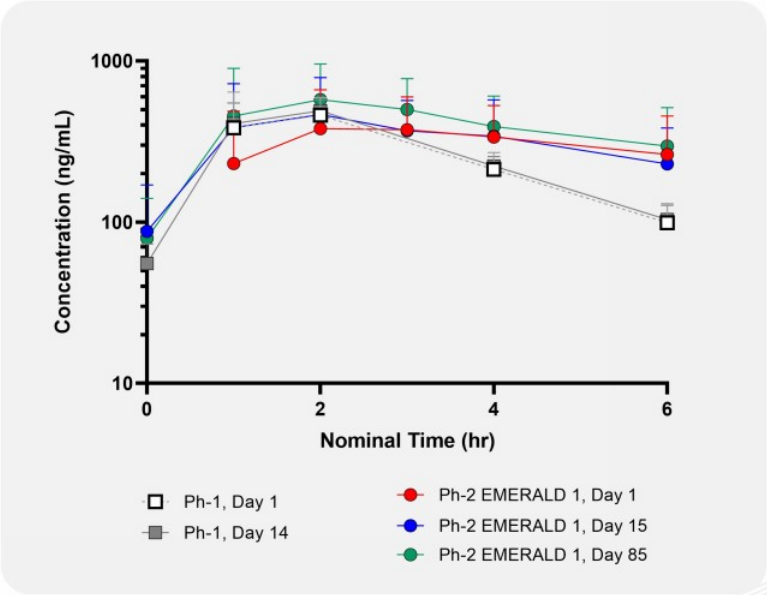
*CD4+ T memory cells defined by: $CD45^+CD3^+CD20^-$ $CD4^+CD8^-CD45RA^-$
**Circulating CCR9 mRNA levels were measured in comparison with housekeeping genes (ACTB, IPO8, B2M, TBP)

Patient PK Consistent with Healthy Volunteer PK



- Serum drug concentrations conform highly to Phase 1 healthy volunteer data
- Mean PK data demonstrate consistency from start of dosing through week 12
- MORF-057 trough concentrations sufficient for saturation of α4β7 receptor in the blood

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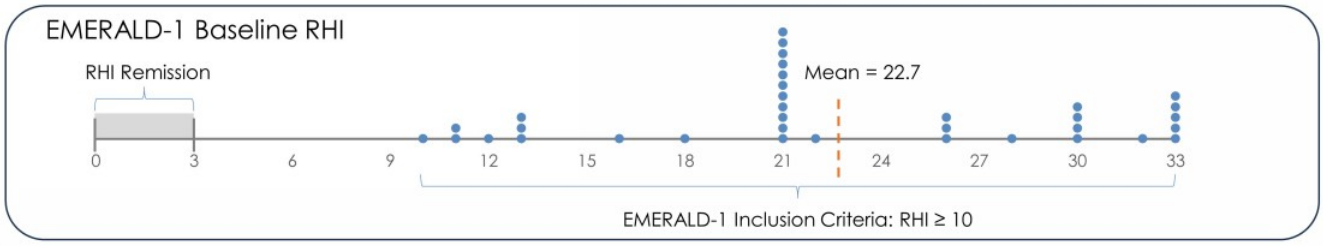
Robarts Histopathology Index for UC

- RHI: a validated histology index derived from the Geboes Score and designed to be reproducible and responsive to clinically meaningful change in disease activity in UC over time
- Calculated by evaluating 4 centrally read, individually weighted histologic items, each on a scale from 0 to 3
- RHI = (1 × chronic inflammatory infiltrate score) + (2 × lamina propria neutrophils score) + (3 × neutrophils in epithelium score) + (5 × erosion or ulceration score)
  - Thus, total RHI Score ranges from 0 (no disease activity) to 33 (severe disease activity)
- Remission: RHI ≤ 3



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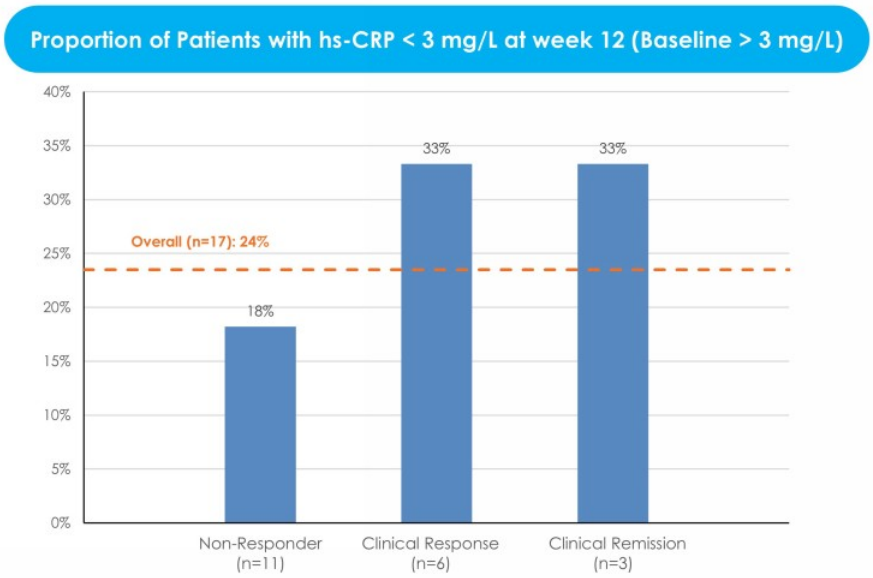
Modified Mayo Clinic Score for UC

Stool Frequency (SFS)	
0	Normal
1	1-2/day > Normal
2	3-4/day > Normal
3	5+/day > Normal
Rectal Bleeding (RBS)	
0	None
1	Streaks
2	Obvious
3	Mostly Blood
Endoscopy / Mucosa (MES)	
0	Normal
1	Mild Friability
2	Moderate Friability
3	Spontaneous Bleeding
0-9	Total

- **Modified Mayo Clinic Score (mMCS)**
  - Three component score
  - 0 to 9 scale with moderate to severe UC 5 to 9
  - Clinical Remission
    - SFS ≤ 1
    - RBS = 0
    - MES ≤ 1 without friability
  - Endoscopic Response / Improvement: MES ≤ 1
  - Symptomatic Remission: SFS = 0 (or = 1 with ≥ 1 point decrease from baseline) and RBS = 0
  - PRO2: SFS + RBS

Expected Changes in C-Reactive Protein Observed



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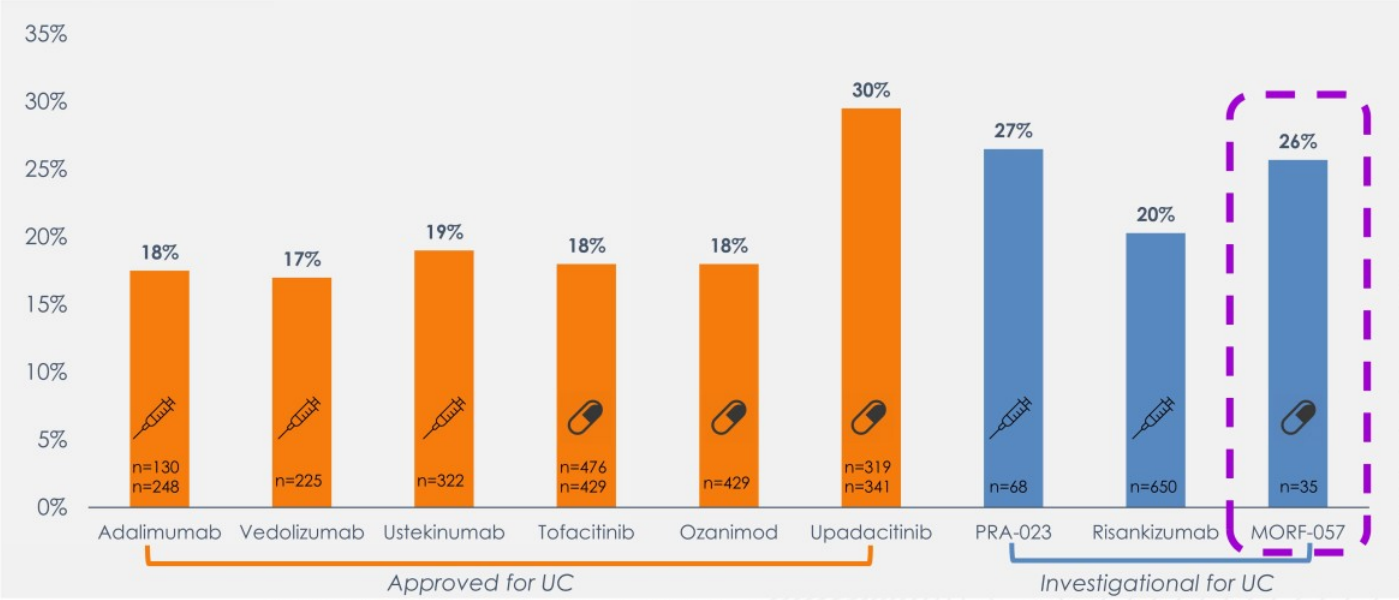
No inclusion/exclusion criteria for CRP levels: n= 17 pts with baseline > 3 mg/L
Patients experiencing clinical remission also included in clinical response

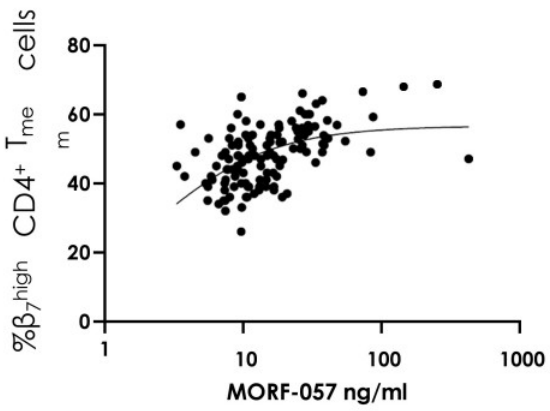
UC Absolute Clinical Remission Data at Induction Selected Approved and Investigational Agents



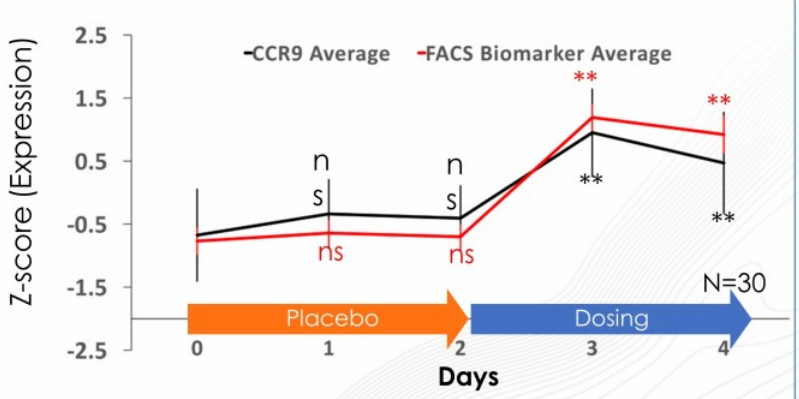
- PRA-023 and MORF-057 data from Phase 2 trials; all other data from RCT Phase 3 studies. Graphic is not meant to represent a head-to-head study. Comparing the results from different trials may be unreliable due to different protocol designs, trial designs, patient selection and populations, number of patients, trial endpoints, trial objectives and other parameters that may not be the same between trials. Therefore, cross-study comparisons provide very limited information about the efficacy or safety of a drug.
- Remission data is based on mMCS for all drugs except adalimumab, vedolizumab, and tofacitinib, which are based on tMCS
- MORF-057 EMERALD-1 study consisted of n=35, a significantly smaller number of patients than reflected in the other datasets represented on this slide. In larger trials of MORF-057 the clinical activity suggested by our EMERALD-1 trial may not be replicated.
- N's are from active arms only, data sourced from following trials respectively: UC-1/UC-2, Gemini-1, UC-1,/UC-1, UC-2, TRUE NORTH, , U_ACHIEVE-1/U-ACHIEVE-2, APOLLO-UC, INSPIRE and EMERALD-1

T_{mem} cell and CCR9 blood biomarkers increase with MORF-057 exposure

T_{mem} biomarker data from all studies



Comparison of CCR9 and T_{mem} biomarker changes



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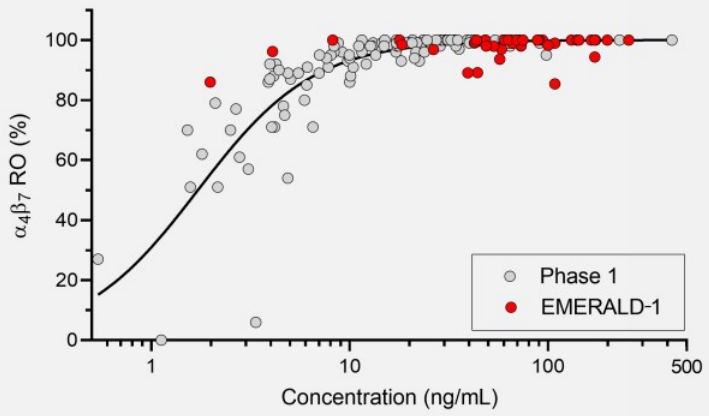
*CD4+ T memory cells defined by: $CD45^+CD3^+CD20^-CD4^+CD8^-CD45RA^-$
**Circulating CCR9 mRNA levels were measured in comparison with housekeeping genes (ACTB, IPO8, B2M, TBP)

Patient α4β7 Receptor Occupancy (RO) Consistent with Healthy Volunteer RO



α4β7 selectivity over α4β1 consistent with Phase 1 results

RO at 12 weeks		
	α4β7	α4β1
Mean	**>98%**	BLQ
Median	**>99%**	BLQ

- α4β7 RO achieved early and sustained saturating levels
- α4β1 RO remained at low levels
- No lymphocytosis or changes to circulating naïve T-cells were observed
- α4β1 projected RO was below the limit of quantitation with mean trough value estimated to be <15%

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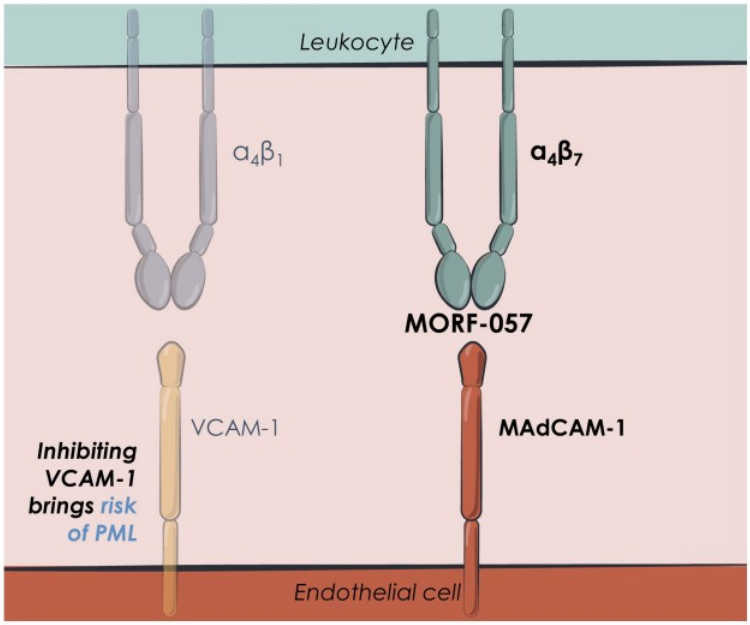
MORF-057 Has Inherently High Selectivity for α4β7 Versus Other Integrins



Inhibitor	$\alpha_4\beta_7$ IC_{50}[a] RPMI8866 MAdCAM in 50% serum	$\alpha_4\beta_7/\alpha_4\beta_1$ Fold selectivity
MORF-057	1.2 nM	**>3,000**
Vedolizumab	0.035 nM	**>3,000**
Natalizumab	0.166 nM	**1-12**
AJM300	93 nM	**8-45**
Etrolizumab	0.019	**$>10^6$**

- MORF-057 is highly selective for $\alpha_4\beta_7$ over $\alpha_4\beta_1$ in cell adhesion assays in 50% human serum (over 3 orders of magnitude)
- MORF-057 was designed to be a potent and selective oral inhibitor of the integrin $\alpha_4\beta_7$ and not $\alpha_4\beta_1$, a related integrin

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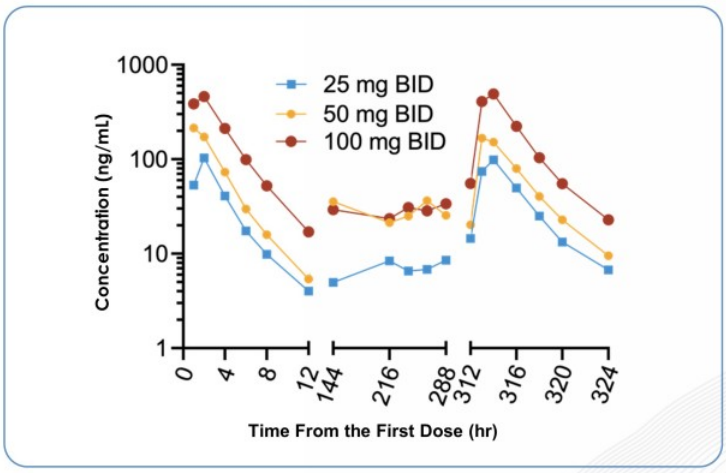
[a] Cell line characteristics: Jurkat cells have been traditionally used for specifically assessing $\alpha_4\beta_1$ potency, as these cells do not express $\alpha_4\beta_7$. RPMI8866 cells have lower levels of $\alpha_4\beta_1$ that likely better approximate expression levels in human blood.

MORF-057 Pharmacokinetics are Dose-Dependent and Predictable

Mean Plasma Concentration of MORF-057/Time



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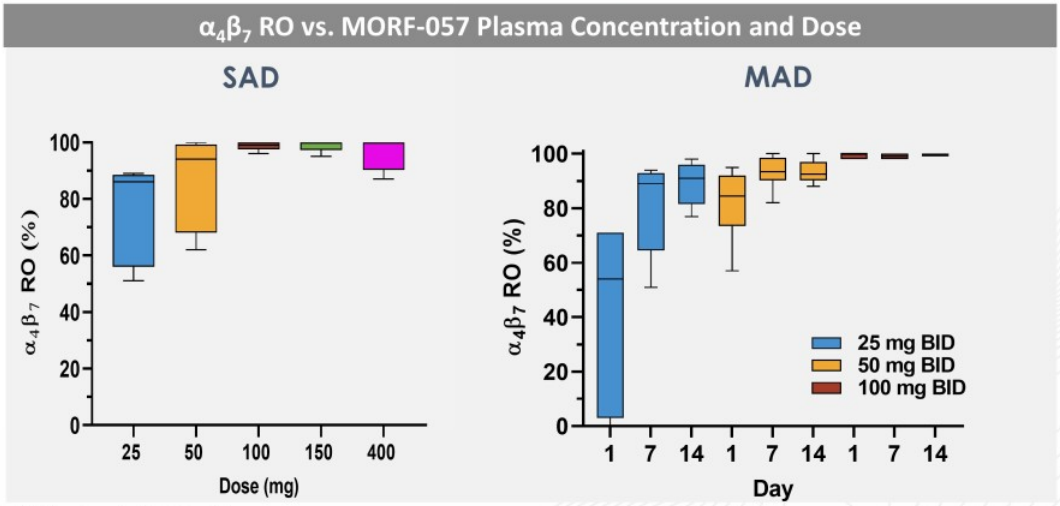
MORF-057 Saturates the α4β7 Receptor in a Time and Dose Dependent Fashion

MORF-057 achieved >95% mean receptor occupancy (RO) of the $\alpha_4\beta_7$ integrin at three highest dose levels and demonstrated ability to saturate $\alpha_4\beta_7$ receptor in individual subjects in dose cohorts above 25 mg



Ray, et al, ECCO 2021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