

# DELIVERING A NEW GENERATION OF INTEGRIN MEDICINES

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# 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: Morphic’s or our partners’ plans to develop and commercialize oral small-molecule integrin therapeutics and Morphic’s expectations about timing and ability to commence, enroll or complete clinical studies and to obtain regulatory approvals for MORF-057, MORF-720, MORF-627 and other candidates in development, the ability of MORF-057 to treat inflammatory bowel diseases, including ulcerative colitis or Crohn’s disease, the ability of MORF-720 or MORF-627 to treat idiopathic pulmonary fibrosis or liver fibrosis, the ability of our platform to discover additional developable candidates (including against  $\alpha_v\beta_8$  and  $\alpha_v\beta_1$ ) or suitable indications (including in solid tumors or fibrotic diseases), the potential impact of the COVID-19 pandemic and the sufficiency of our cash, cash equivalents and investments to fund our operations.

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.

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The end has to start somewhere, and this time it began with us.



# Biologic Receptors: The Key to Cell Signaling

Ion-channel receptors

GPCRs

Enzyme-linked receptors

Toll-like receptors

T-cell receptors

EGFRs

NMDA receptors

Integrin receptors

Adrenergic receptors

Olfactory receptors

Insulin receptors

RTKs

Neurotrophin receptors

Ephrin receptors

CD28 Receptors

KIRs

LILRs

IL-1 receptors

PDGFRs

Fc receptors

Retinoid receptors

Estrogen receptors

Thyroid receptors

PPARs

GABA receptors

Glycine receptors

Acetylcholine receptors

IP3 receptors

VEGFRs

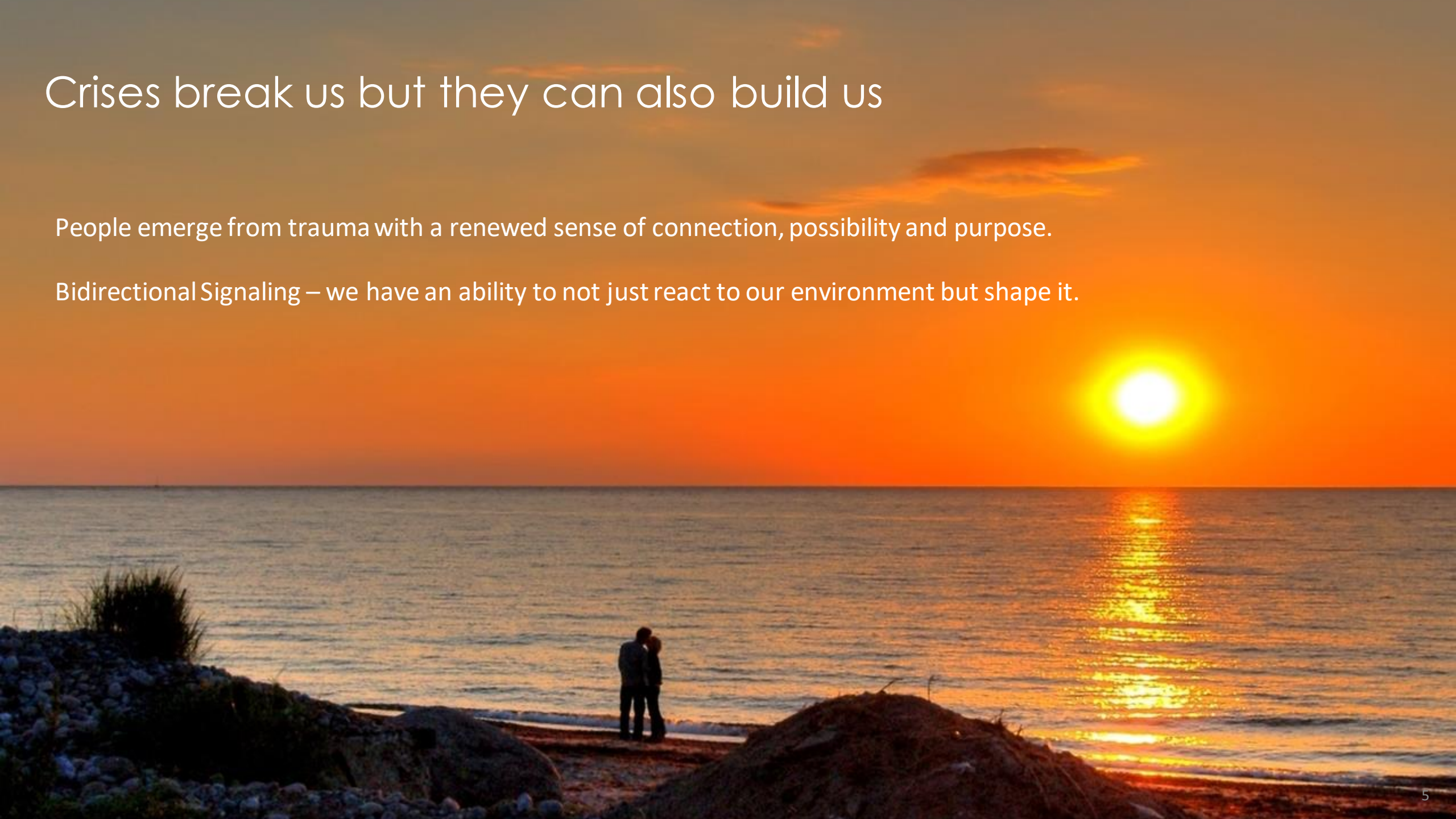
AP receptors



# Crises break us but they can also build us

People emerge from trauma with a renewed sense of connection, possibility and purpose.

Bidirectional Signaling – we have an ability to not just react to our environment but shape it.





# Biologic Receptors: The Key to Cell Signaling

Ion-channel receptors

GPCRs

Enzyme-linked receptors

Toll-like receptors

T-cell receptors

EGFRs

NMDA receptors

**Integrin receptors**

Adrenergic receptors

Olfactory receptors

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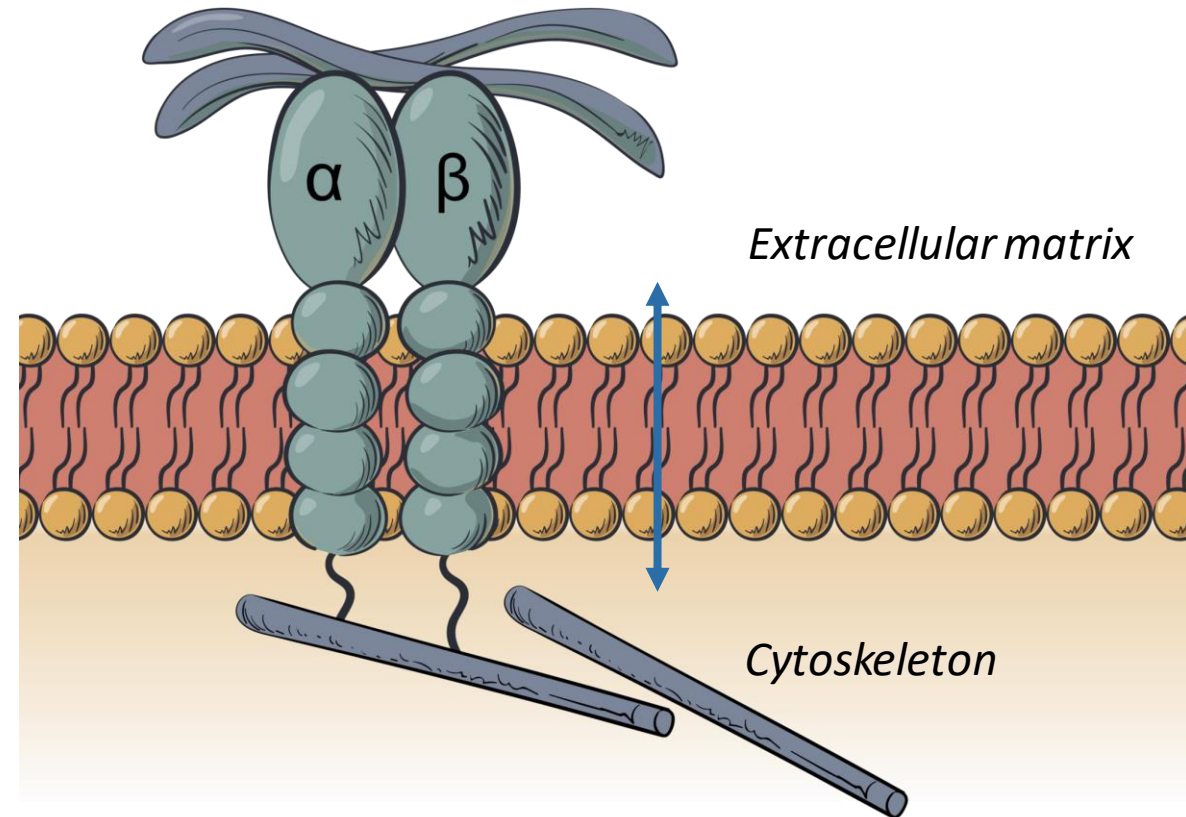
AP receptors



# The Integrin Receptor

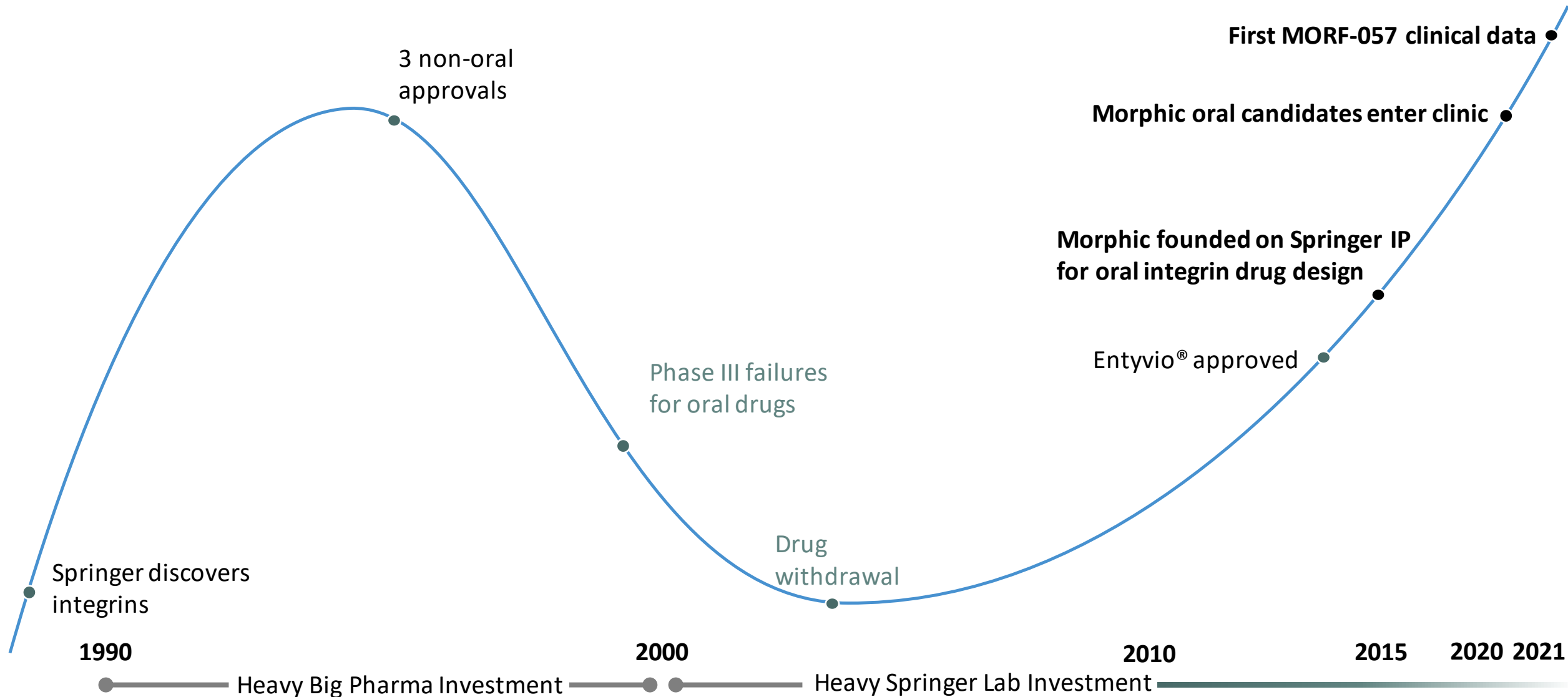
A family of cell surface receptors with unique ability to signal **bi-directionally**

Named integrins because they **'integrate'** extracellular and intracellular stimuli



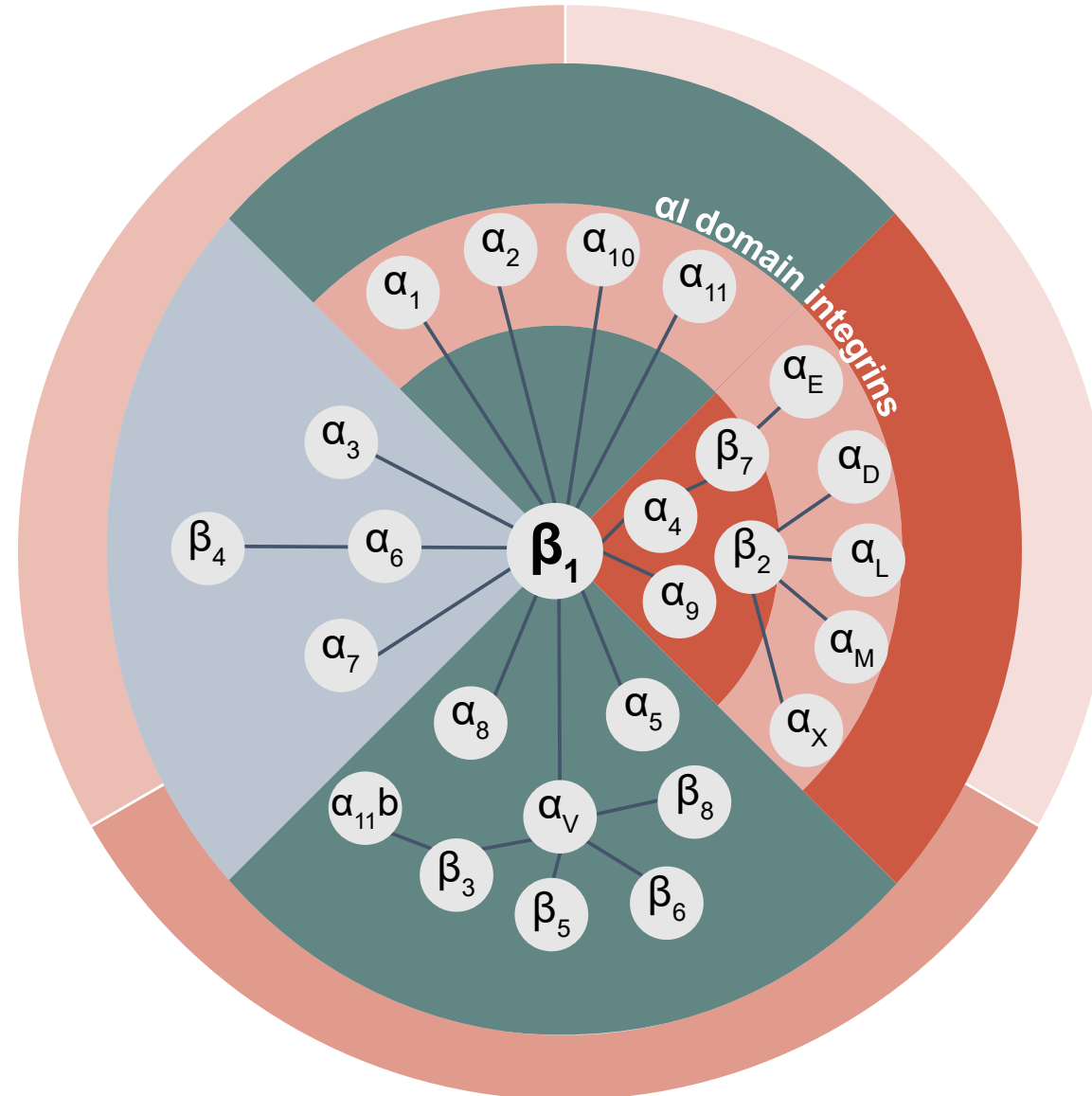


# Morphic: A New Chapter In Integrin History



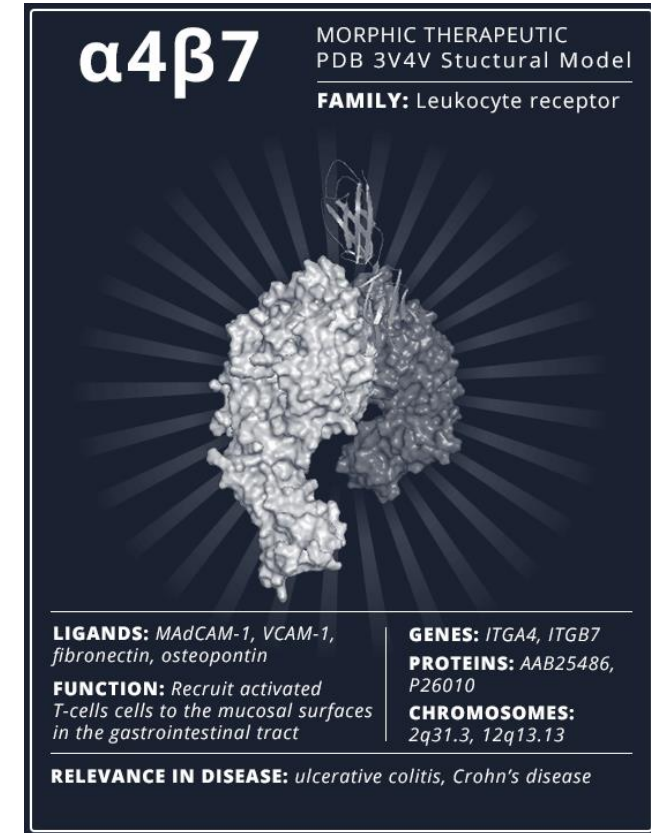
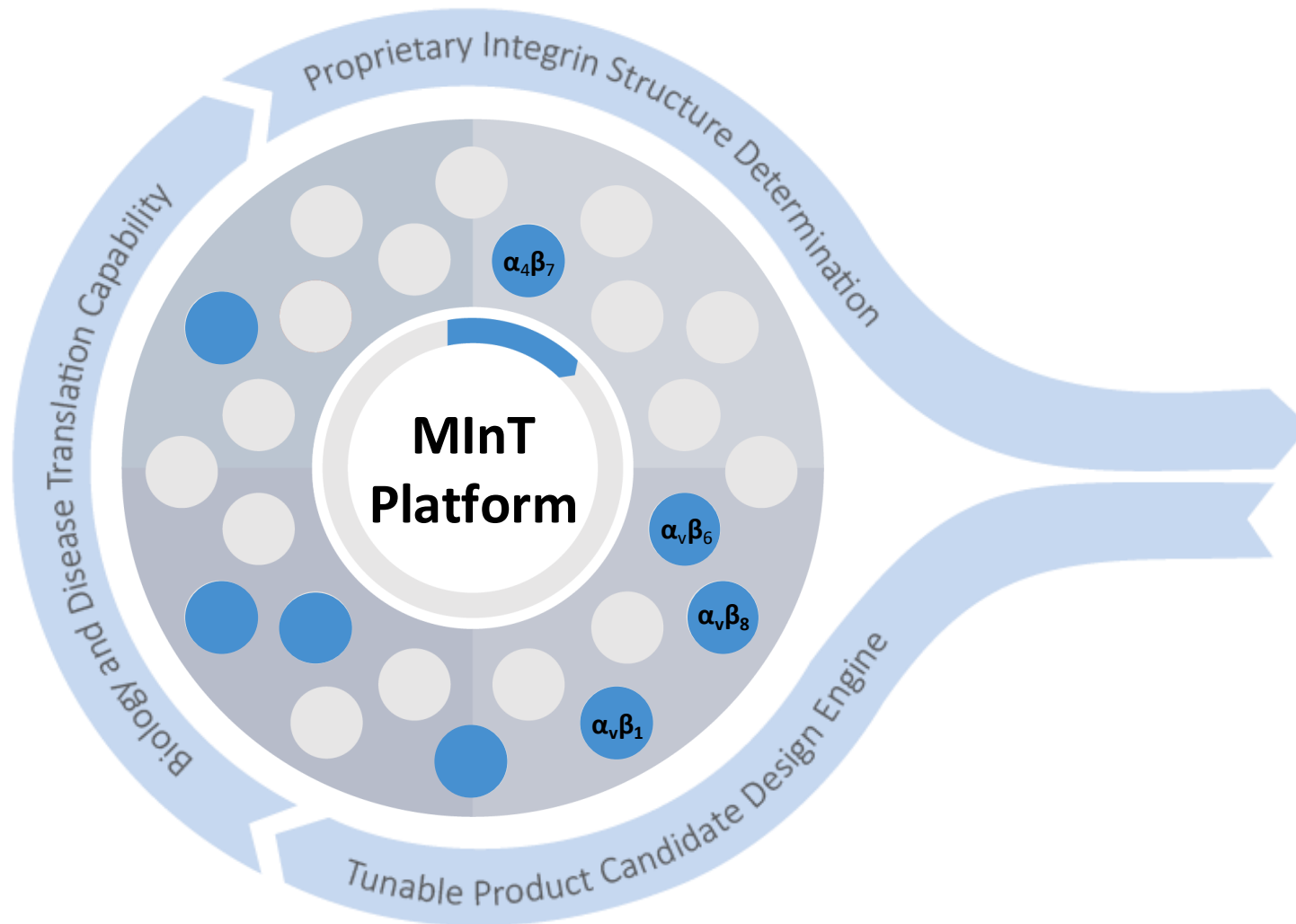


# The Integrin Target Class





# Morphic Integrin Technology (MInT) Platform: Building Knowledge Through Iteration








*J Cell Biol, 2012*







# Morphic: A Deep Proprietary & Partnered Pipeline

## Proprietary Pipeline

Target (Program)	Indication	Status		
		Preclinical	Phase 1	Phase 2
$\alpha_4\beta_7$ (MORF-057)	Ulcerative colitis		Data anticipated 1H21	Planned adaptive trial
	Other indications, including Crohn's disease			
$\alpha_v\beta_1$	Fibrotic diseases			
$\alpha_v\beta_8$	Solid tumors			
Undisclosed targets	Multiple indications			

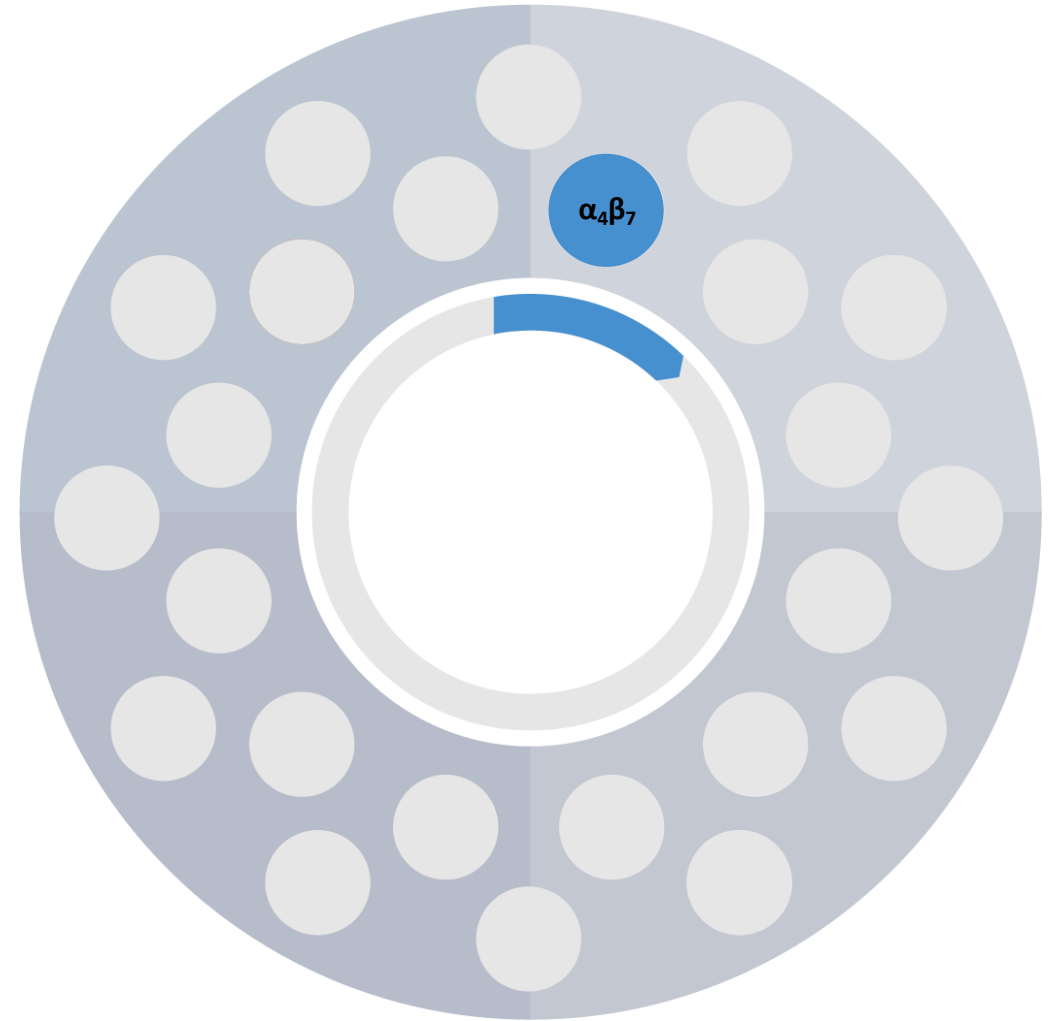
## Partnered Pipeline

Target (Program)	Indication	Status		
		Preclinical	Terms	Partner
$\alpha_v\beta_6$ (MORF-720 & MORF-627)	Idiopathic pulmonary fibrosis and fibrotic diseases		AbbVie paid \$100M for exclusive option to multiple targets, \$20M to exercise $\alpha_v\beta_6$ option	abbvie
Undisclosed targets	Fibrotic diseases			
Undisclosed targets	Cardio/Renal/Metabolic		Janssen paid \$15M for multiple novel targets	janssen 



# MORF-057

Targeting  $\alpha_4\beta_7$ , a validated mechanism, for  
Inflammatory Bowel Disease

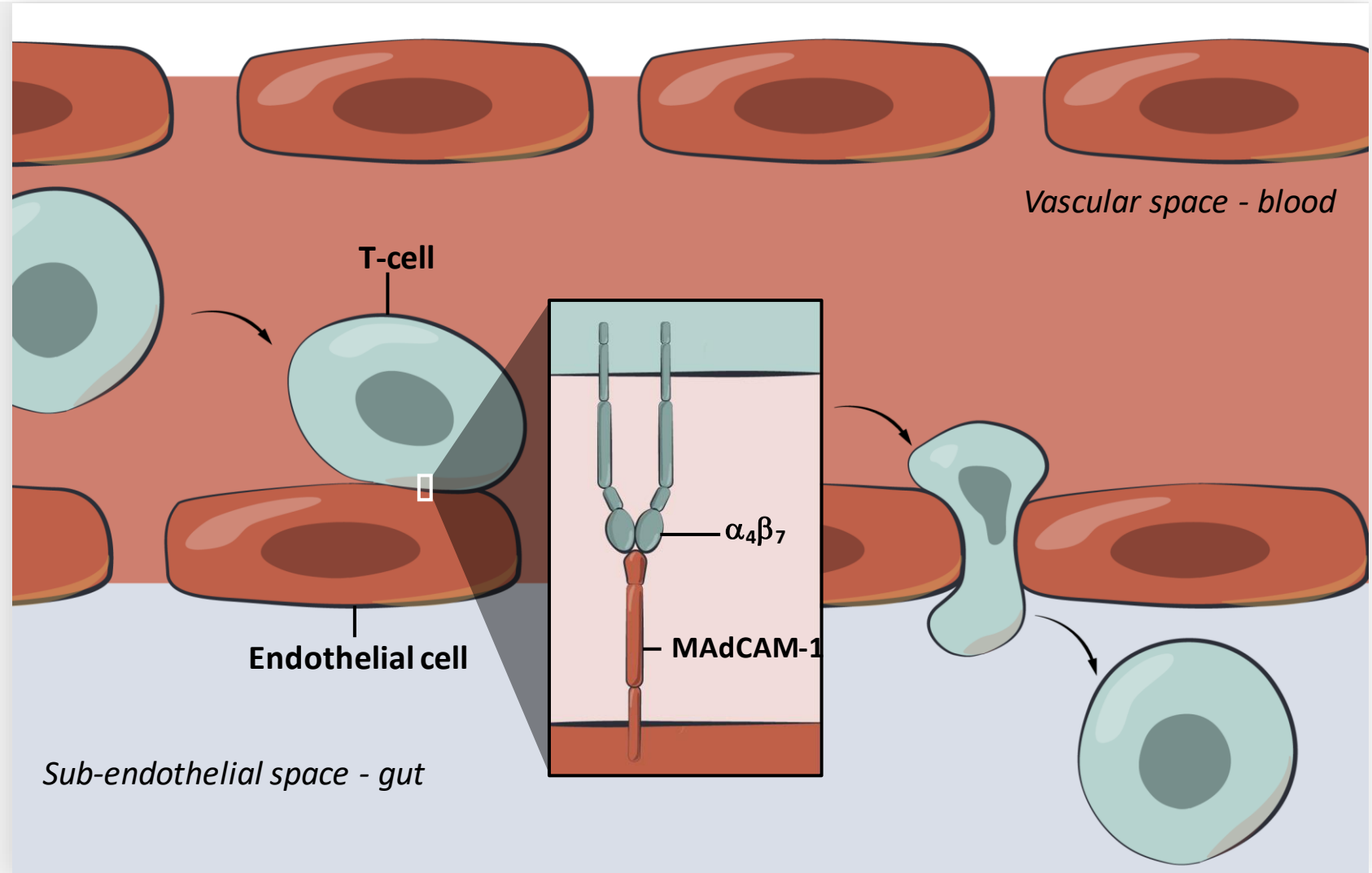




# $\alpha_4\beta_7$ Inhibition is a Proven Mechanism to Treat IBD

## Approved antibody Entyvio® (vedolizumab)

- $\alpha_4\beta_7$ + T-cells are trafficked to gut tissue via MAdCAM-1 binding. These T-cells cause inflammation that leads to inflammatory bowel disease.
- 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, >150,000 patients have received Vedolizumab<sup>1</sup>
- Vedolizumab generated \$3.1B sales in FY19<sup>2</sup>



<sup>1</sup>Takeda

<sup>2</sup>Global Data

ENTYVIO® is a registered trademark of Millennium Pharmaceuticals, Inc.



# Challenges in Drug Design

$\alpha_4\beta_7$

High potency

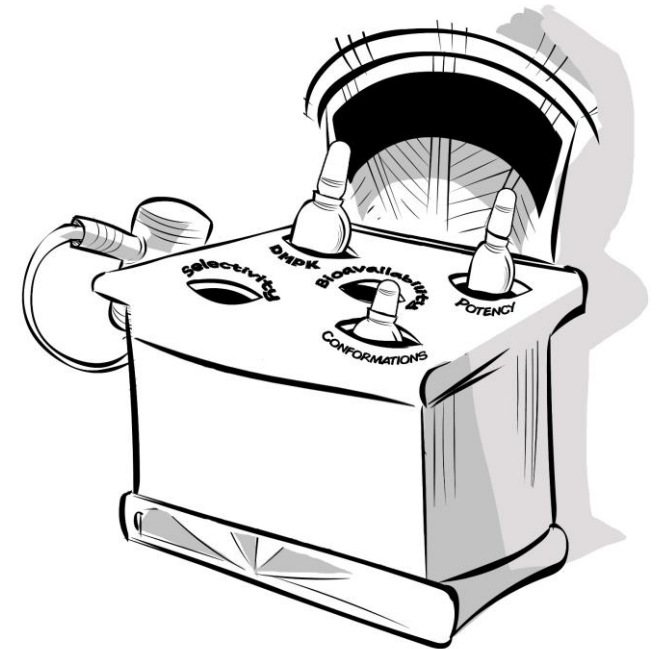
Proprietary crystal structures complexed with lead compounds

High selectivity

Desired DMPK Properties

Oral Bioavailability

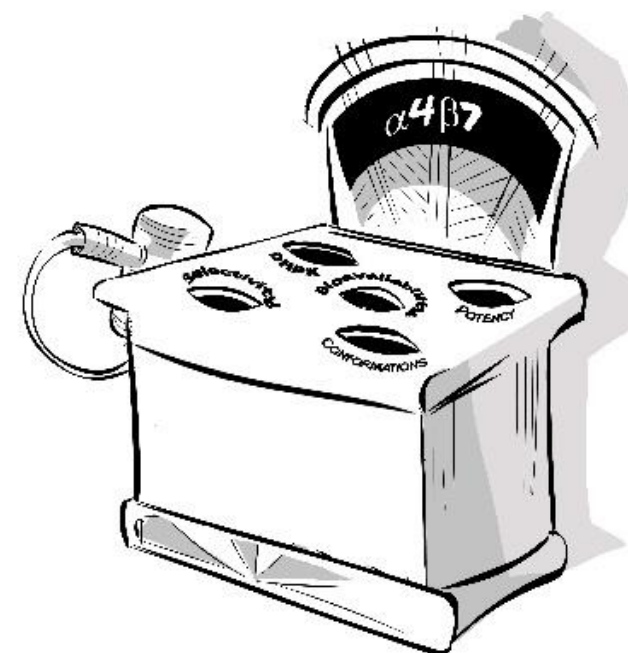
Proprietary conformation / functional understanding





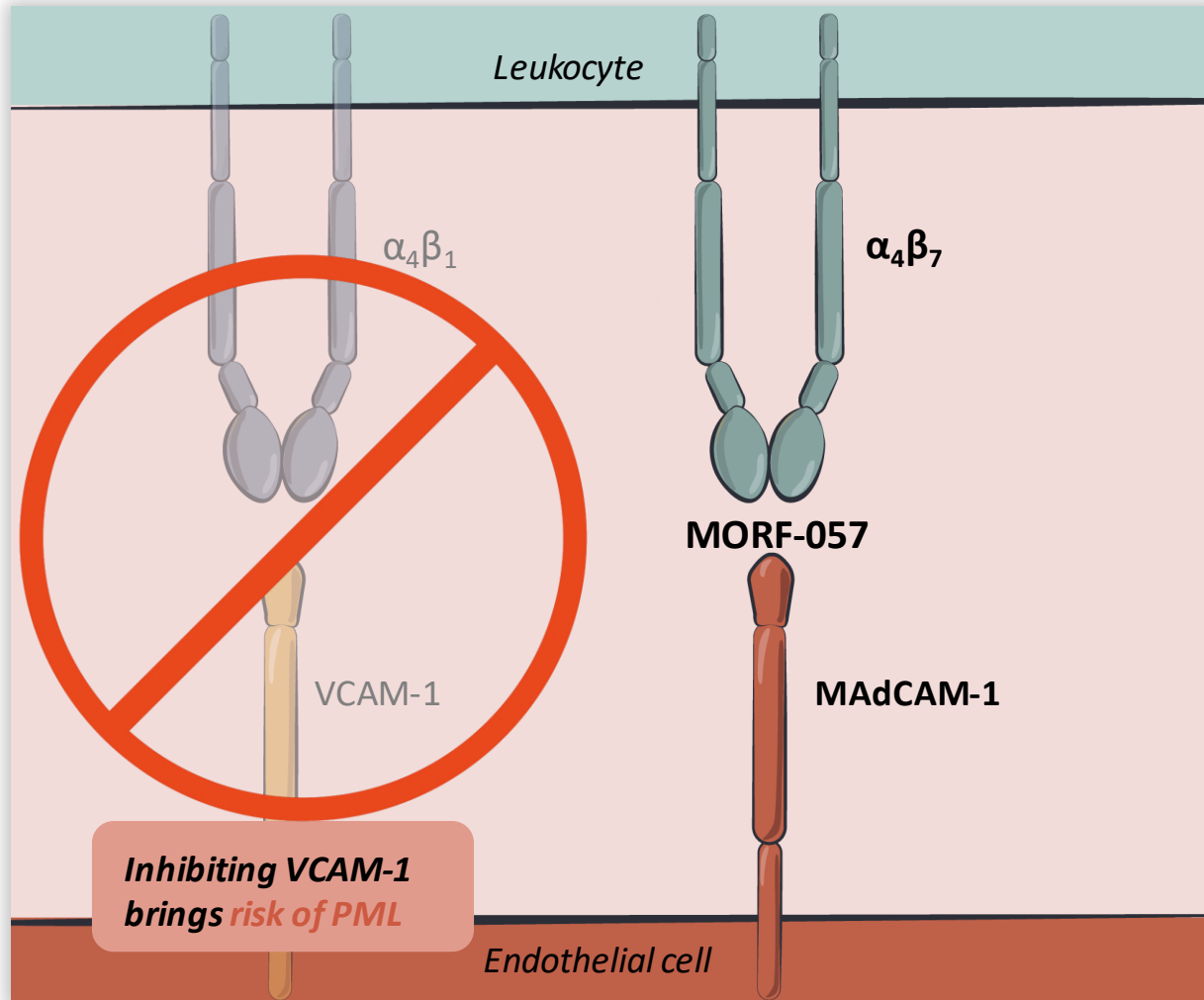
# MInT: Overcoming Challenges in Drug Design

	$\alpha_4\beta_7$
High potency	✓
Proprietary crystal structures complexed with lead compounds	✓
High selectivity	✓
Desired DMPK Properties	✓
Oral Bioavailability	✓
Proprietary conformation / functional understanding	✓





# MORF-057 Has Inherently High Selectivity for $\alpha_4\beta_7$ Versus Other Integrins



Inhibitor	$\alpha_4\beta_7$ IC <sub>50</sub> <sup>a</sup> RPMI8866 MAdCAM in 50% serum	$\alpha_4\beta_7/\alpha_4\beta_1$ Fold selectivity	$\alpha_4\beta_7/\alpha_E\beta_7$ Fold selectivity
MORF-057	1.2 nM	>3,000	>143,000
Vedolizumab	0.035 nM	>3,000	-
Natalizumab	0.166 nM	1-12	-
AJM300	93 nM	8-45	-
Etrolizumab	0.019	>10 <sup>6</sup>	14

- 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 has high selectivity against other integrins in fluorescence polarization assays with purified proteins

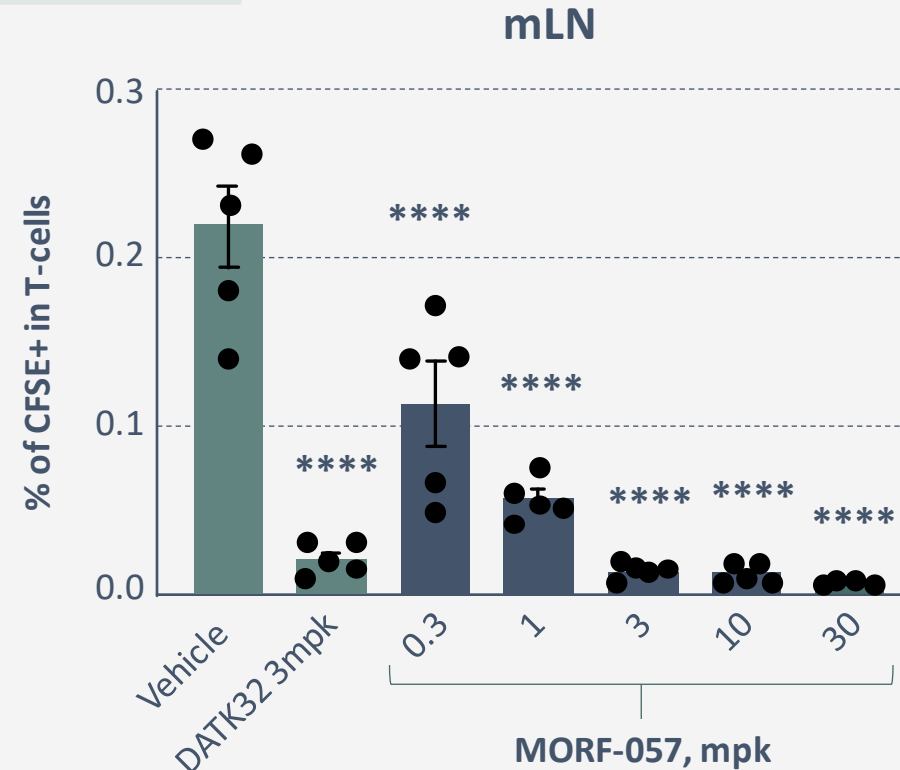
<sup>a</sup> Cell line characteristics: Jurkat cells have been traditionally used for specifically assessing  $\alpha_4\beta_1$  potency, as these cells do not express  $\alpha_4\beta_7$ . RPMI8866 cells have lower levels of  $\alpha_4\beta_1$  that likely better approximate expression levels in human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



# MORF-057 Shows Dose-dependent Anti-inflammatory Activity in Pre-clinical Studies

T lymphocyte homing into mesenteric lymph nodes (mLN)

Mean  $\pm$  SEM



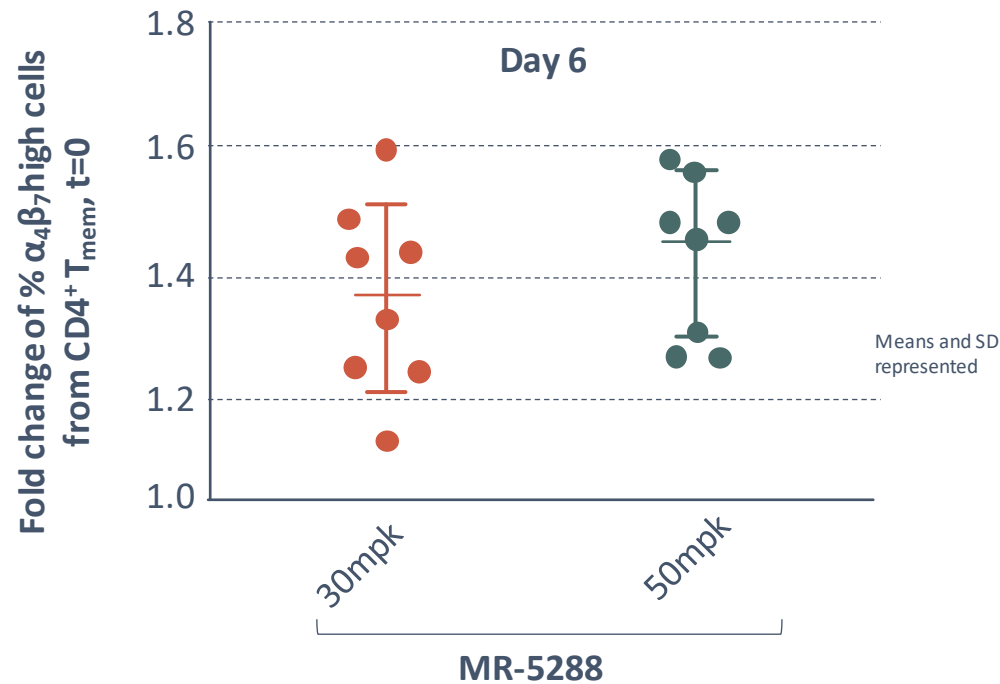
- \*\*\*\*p<0.0001 vs. vehicle by One Way Anova followed by Dunnett's multiple comparisons
- DATK32 is a mouse surrogate of the  $\alpha_4\beta_7$  antibody vedolizumab



# MORF-057 and Related Compounds Impact $T_{\text{mem}}$ Biomarker in a Dose-dependent Manner

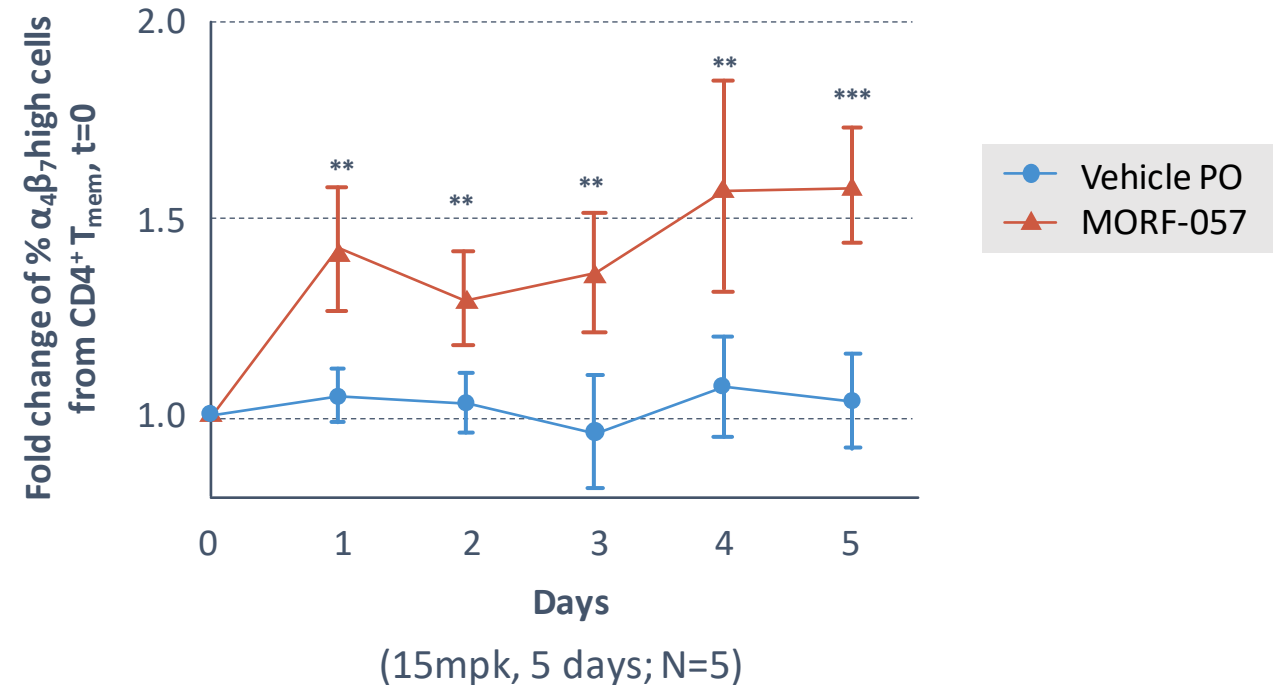
Increase in circulating  $T_{\text{mem}}$  demonstrates  $\alpha_4\beta_7$  mechanistic activity: T cells are prevented from migrating through mucosa thus reducing IBD-associated inflammation

## MR-5288 Dose Response, N=8



The biomarker response with MR-5288 (closely related tool compound of MORF-057) is dose responsive

## MORF-057 inhibits $\alpha_4\beta_7^+$ $CD4^+$ T cell trafficking to mucosal sites in NHP

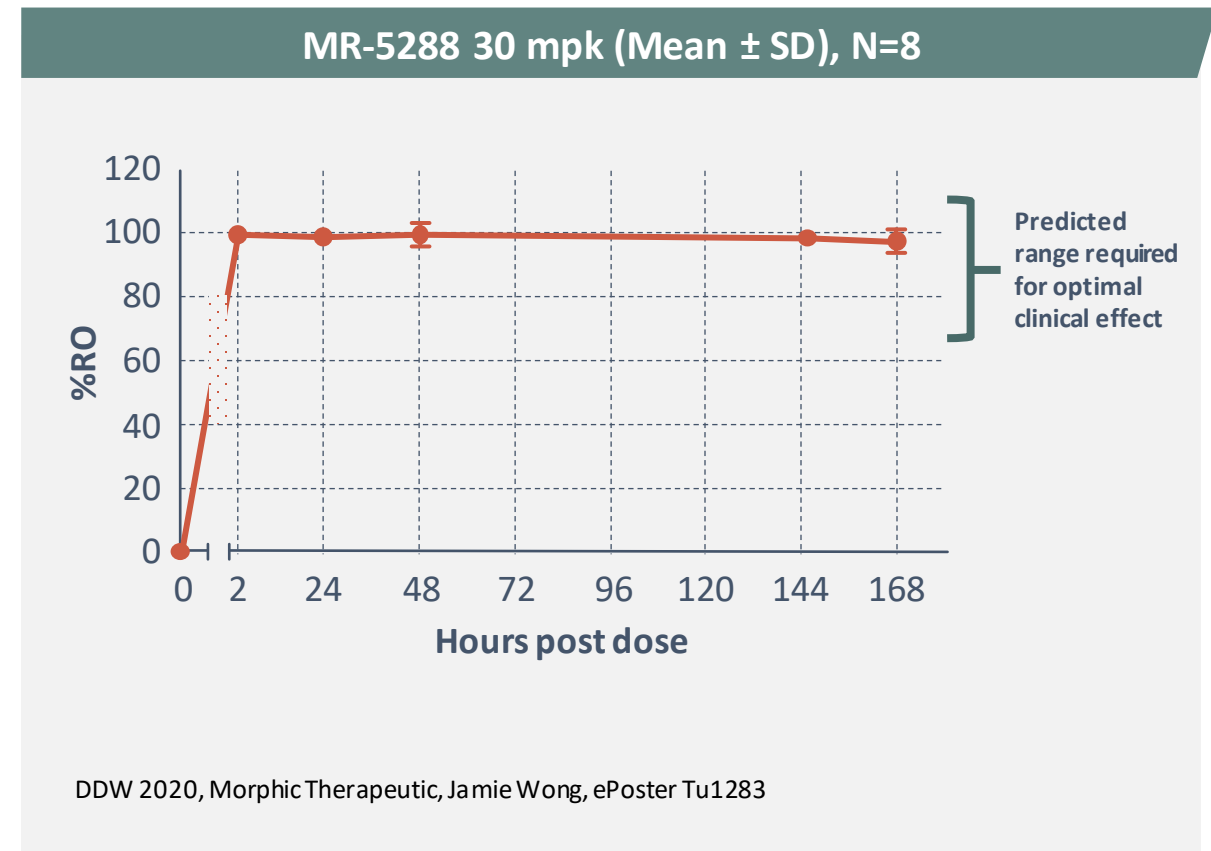
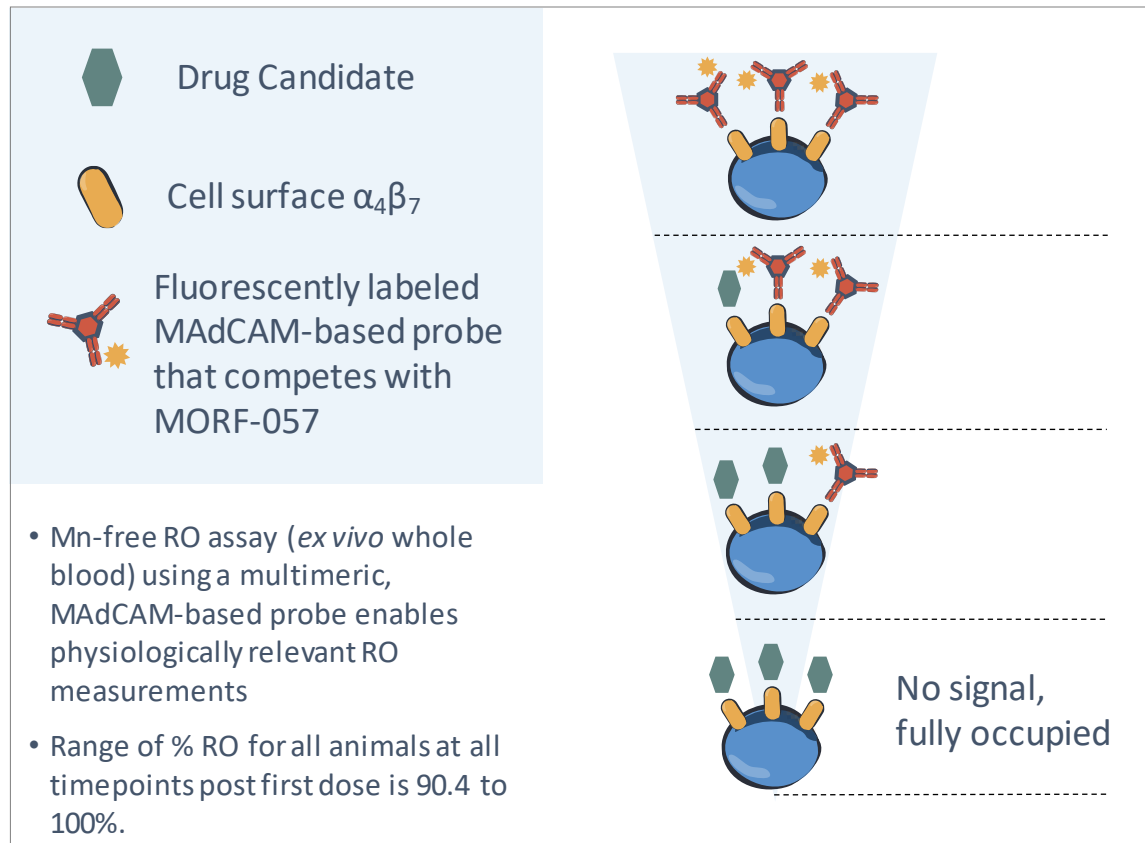


Means and SD of data normalized per individual at timepoint 0h (first dose administration).  
T test analysis was performed at each timepoint  
Statistical significance determined using the Holm-Sidak method, with alpha = 0.05. \*\* p < 0.01,  
\*\*\* p < 0.001



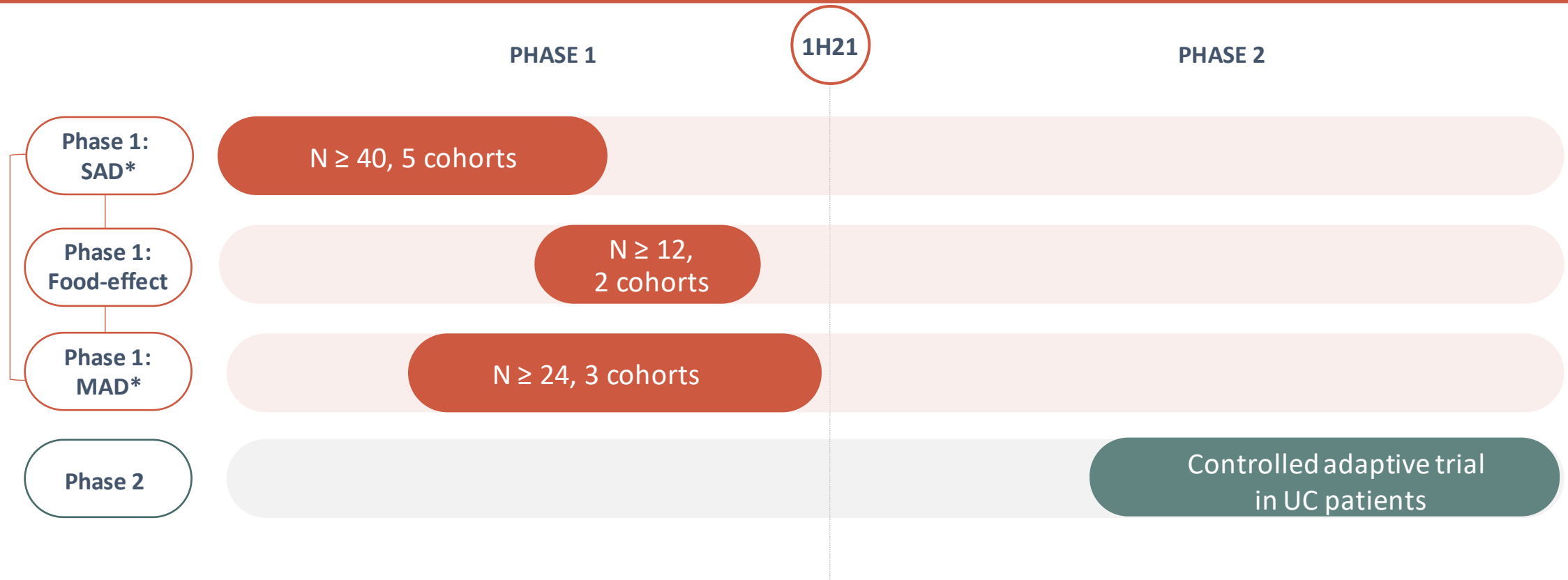
# Morphic Oral Inhibitor Saturates $\alpha_4\beta_7$ Receptor in Non-human Primate Study

Receptor Occupancy (RO) measured at  $C_{\text{trough}}$  in non-human primates dosed with selective  $\alpha_4\beta_7$  inhibitor, MR-5288, a tool compound related to MORF-057





# MORF-057: Phase 1 Trial with Biomarkers Provides Opportunity for Early Proof of Concept



## Three-part Phase 1 Design:

1. SAD cohort: safety, tolerability, and PK/PD
2. Food Effect Cohort to determine PK of a single, projected clinically relevant dose
3. MAD cohort: safety, tolerability, and PK/PD, including receptor occupancy data

\*SAD: single ascending dose

\*\*MAD: multiple ascending dose



SENDHIL MULLAINATHAN  
ELDAR SHAFIR

# Scarcity

'A captivating book that just  
might change the way you live'

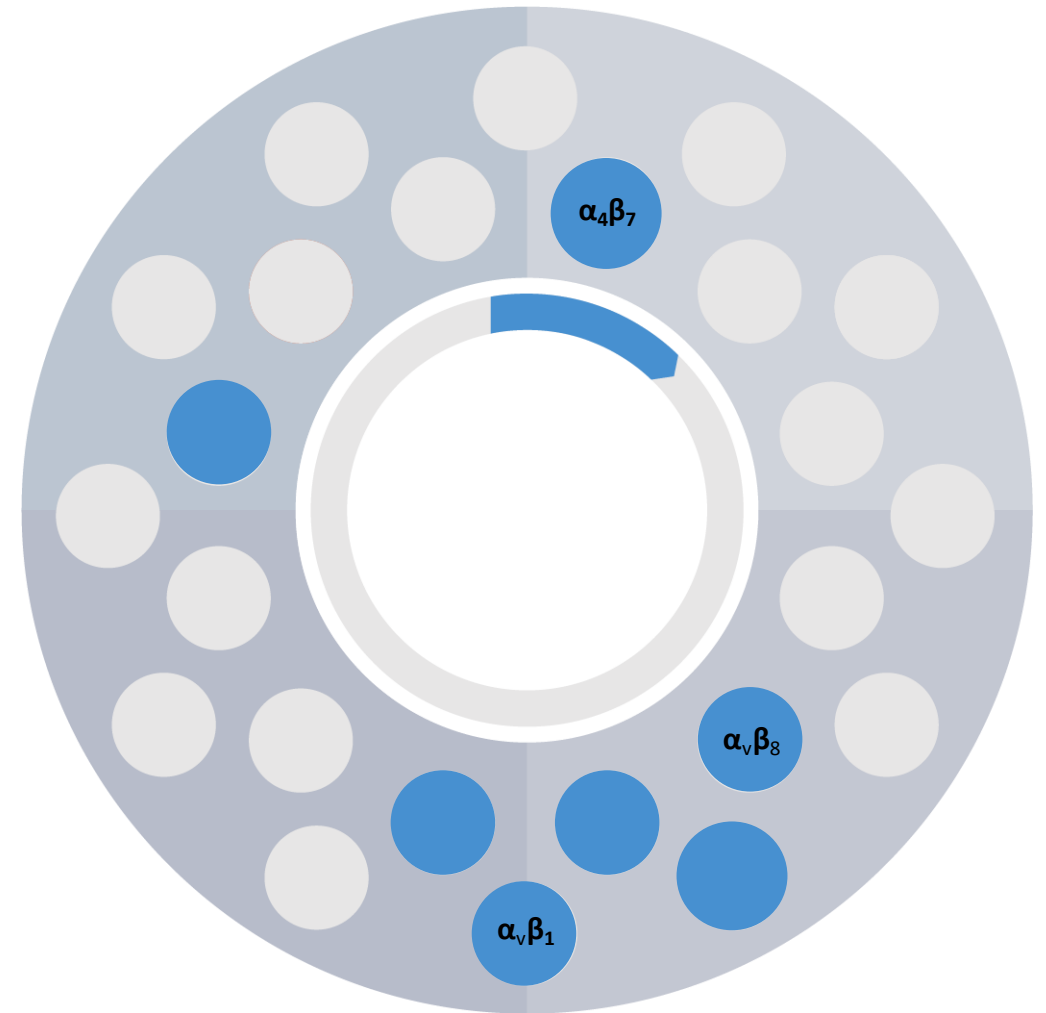
Steven D. Levitt, co-author of *Freakonomics*





# Proprietary Pipeline

Creating the next generation of proprietary integrin inhibitor candidates

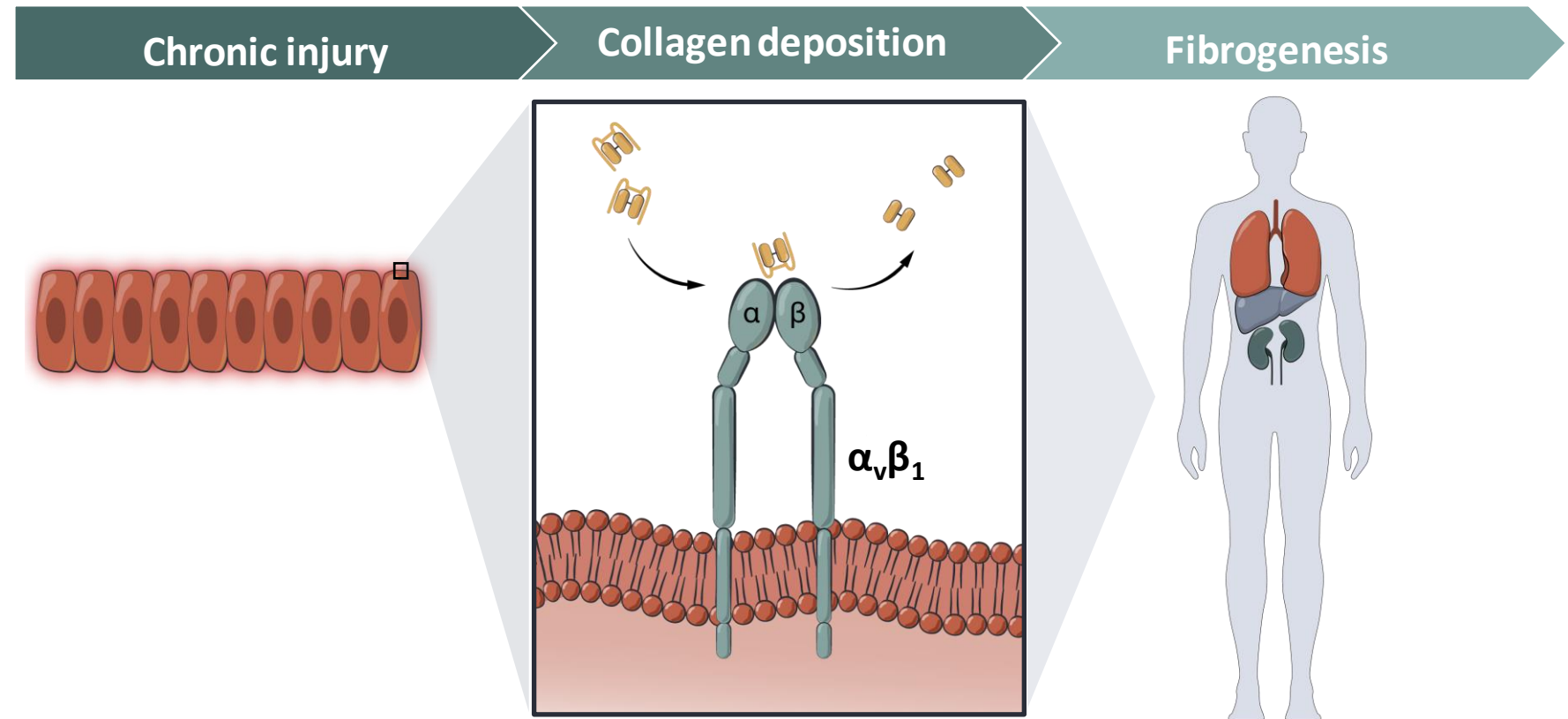




# $\alpha_v\beta_1$ Inhibition: Potential to Treat Fibrosis Across Multiple Organ Systems

$\alpha_v\beta_1$  inhibition reduces collagen deposition that drives fibrosis through multiple mechanisms

- Morphic lead compounds active across multiple animal models of fibrosis
- Extends and leverages Morphic development expertise in fibrosis

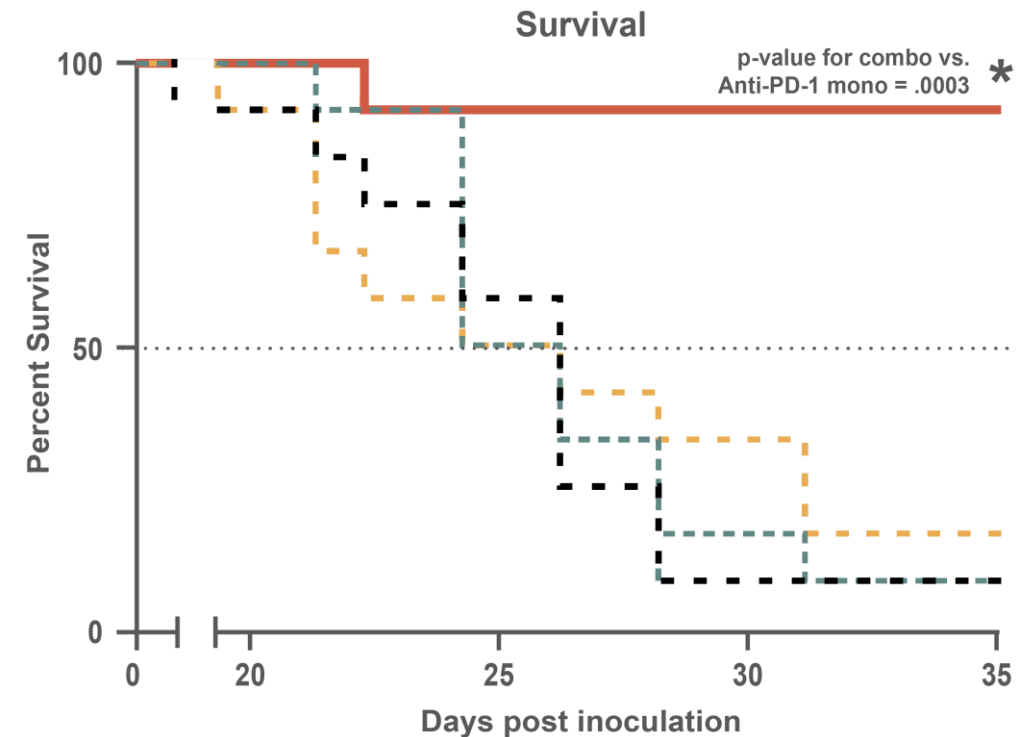
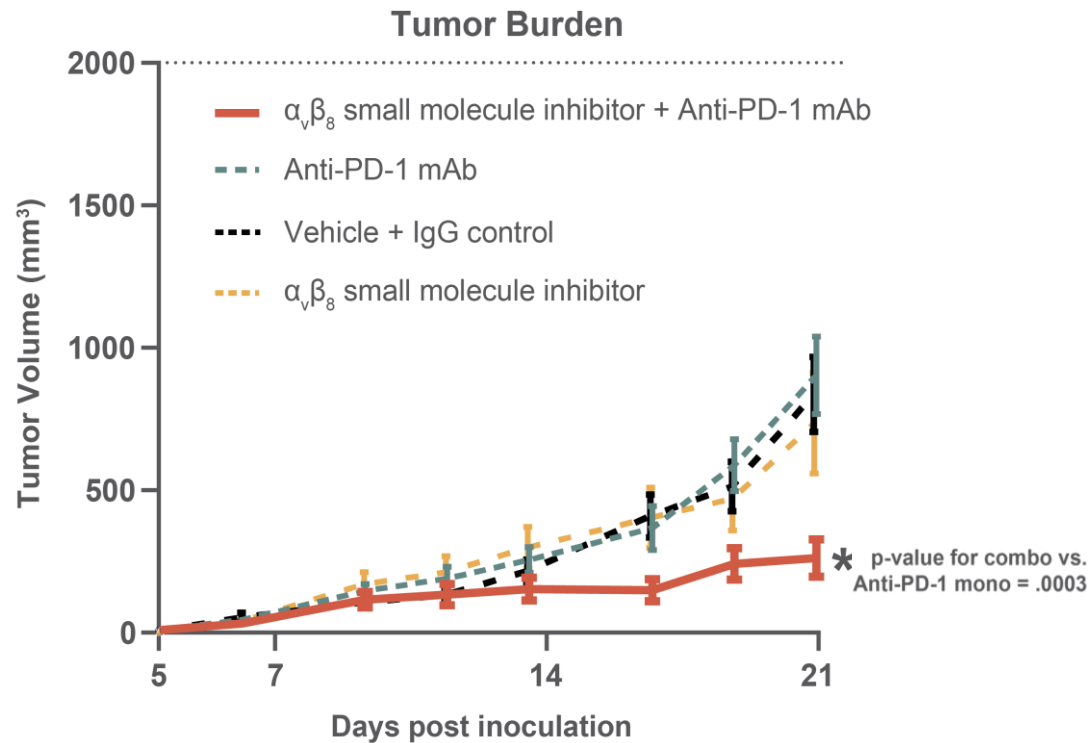




# $\alpha_v\beta_8$ Small Molecule Inhibitor Enhances Checkpoint Inhibitor Response in Immune Excluded Model

$\alpha_v\beta_8$  inhibition blocks activation of TGF- $\beta$ , a key regulator of tumor formation, progression, and metastasis

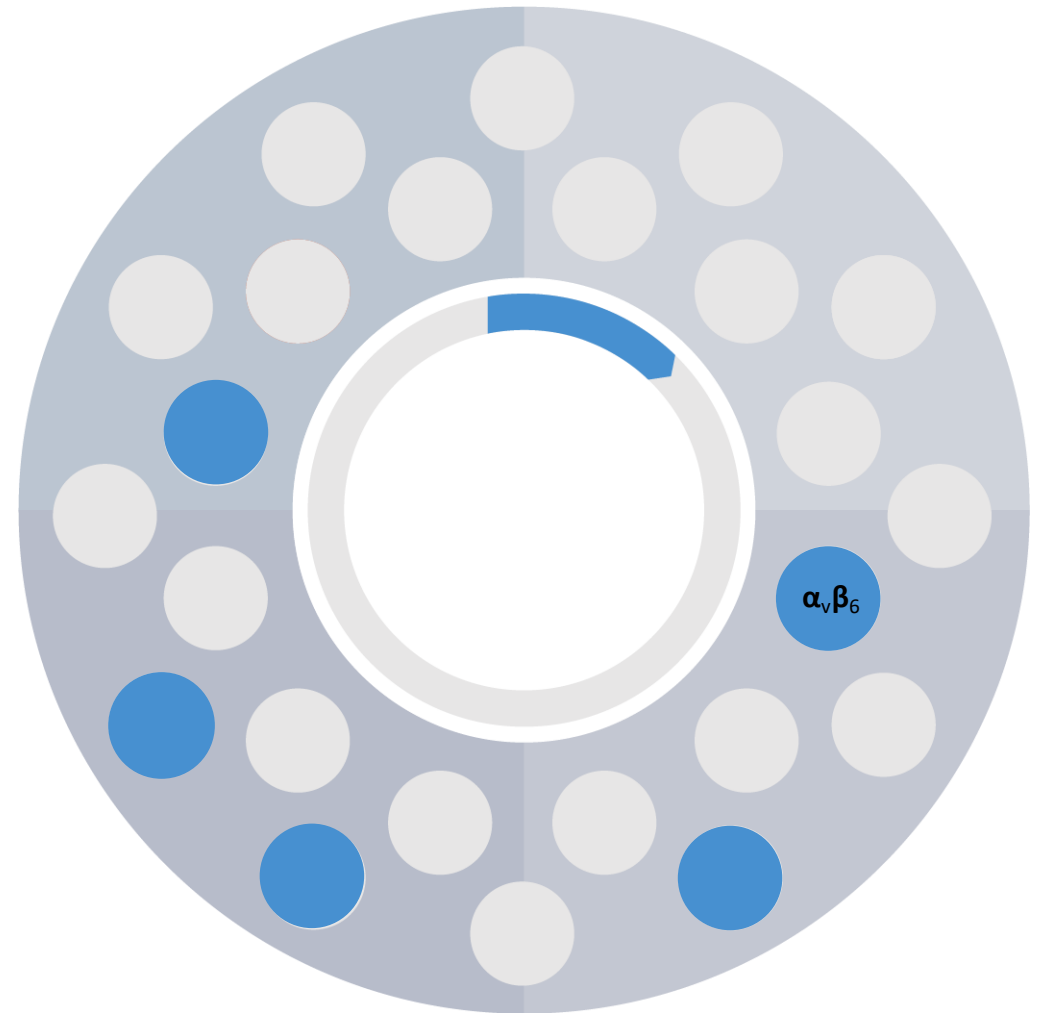
## EMT6 Murine Breast Cancer Model





# Partnered Programs

Leveraging the MInT platform to create new oral integrin candidate for premier collaborators





# Platform-validating Partnerships



- \$100 million upfront partnership agreement to develop multiple selective orally available small molecule integrin inhibitors
- Initial focus on  $\alpha_v\beta_6$  inhibition to prevent TGF- $\beta$  activation and collagen deposition leading to fibrosis
- AbbVie exercised \$20 million option for  $\alpha_v\beta_6$  inhibitors, MORF-720 and MORF-627
- Morphic is entitled to milestones and royalties on commercialized products and retains opt-in rights for certain indications



- Novel target discovery collaboration
- Undisclosed targets in cardio/renal/metabolic space
- \$10 million upfront payment
- Milestones and royalties on commercial products
- Recent expansion of collaboration to include antibody activator



# Morphic: "Cracking the Code" of Oral Integrin Therapies



Unique MInT Platform to Access the Integrin Target Class



Lead Asset in IBD Targeting Validated Biology in Blockbuster Space



Broad Preclinical Pipeline Addressing Multiple Disease Areas



Never underestimate the resilience of the human spirit  
We respond to our environment; but we also shape it







# **DELIVERING A NEW GENERATION OF INTEGRIN MEDICINES**