DELIVERING A NEW GENERATION OF INTEGRIN MEDICINES

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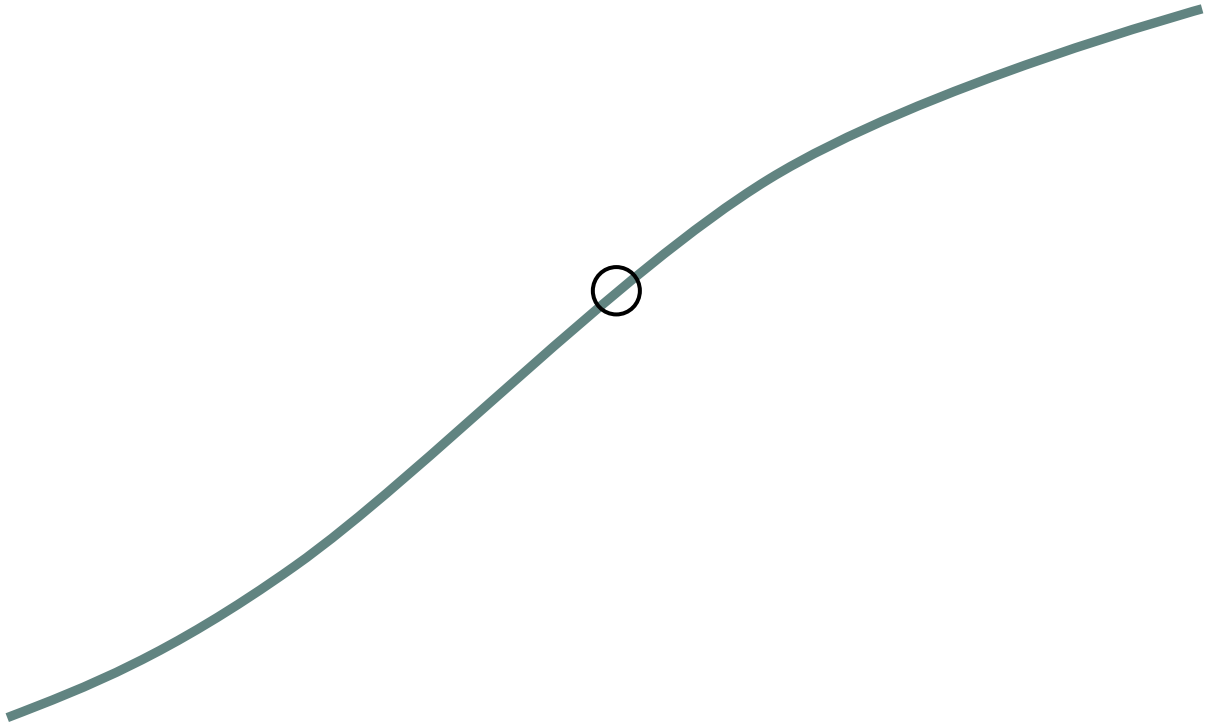
40th Annual J.P. Morgan Healthcare Conference

January 11, 2022

Think Strategically

DAYS

YEARS



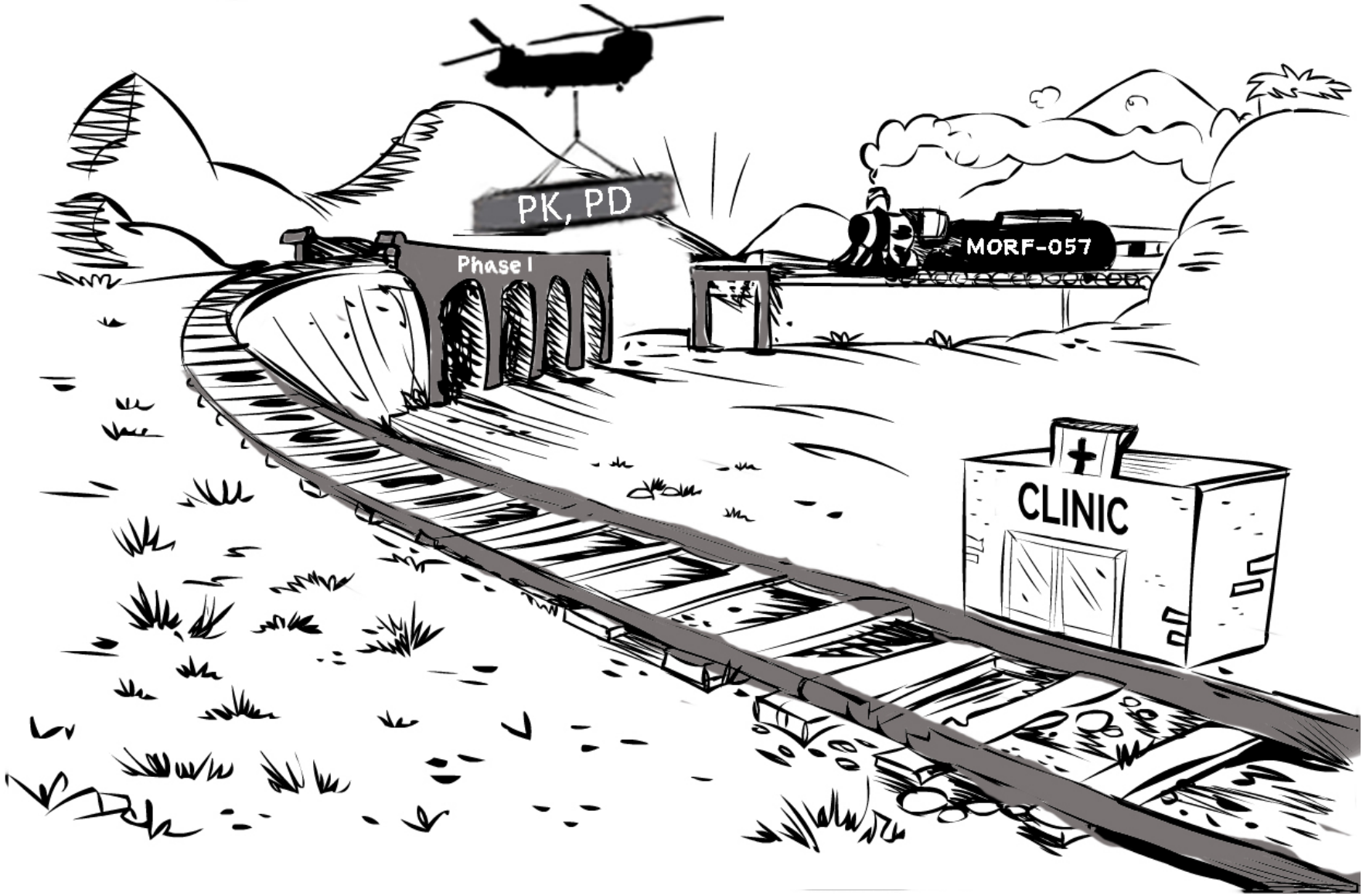
Forward Looking Statements

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 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 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.

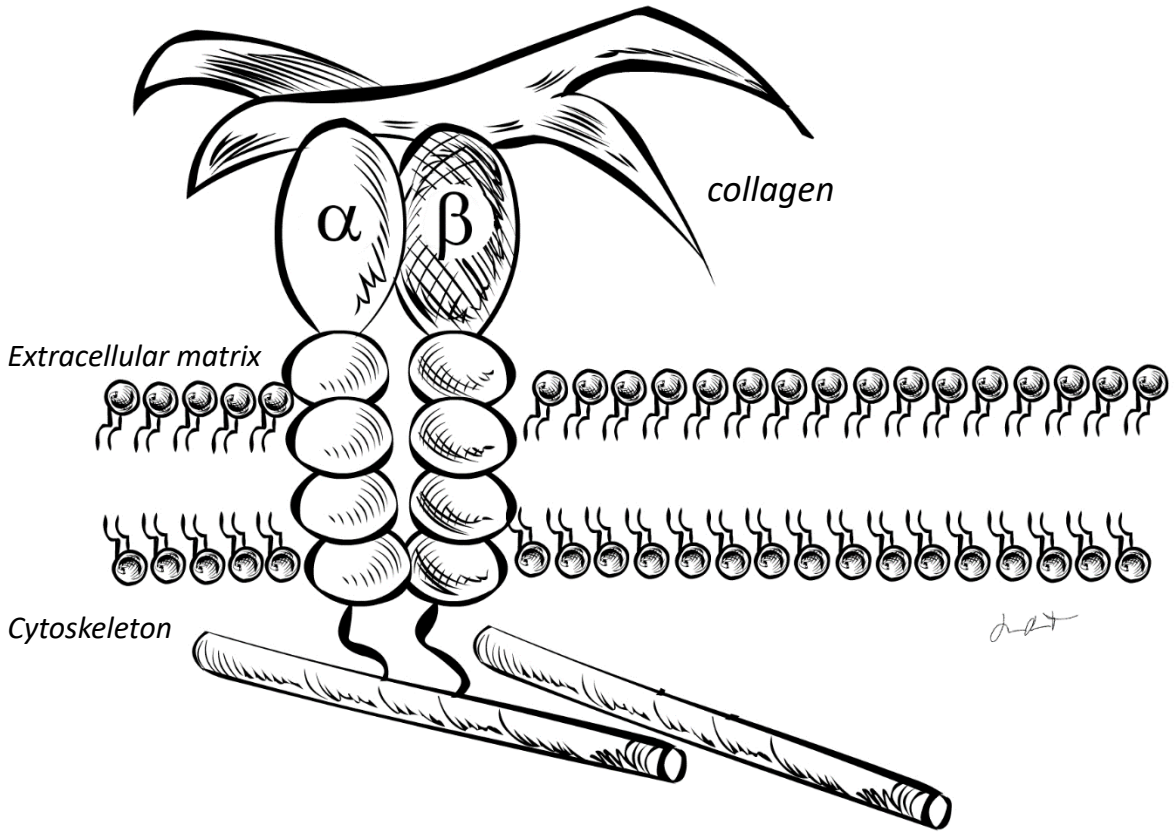
Forward-looking statements are subject to risks and uncertainties that may cause Morphic’s actual activities or results to differ significantly from those expressed in or implied by any forward-looking statement, including risks and uncertainties related to the forward-looking statements in this presentation and other risks set forth in our filings with the Securities and Exchange Commission. 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.

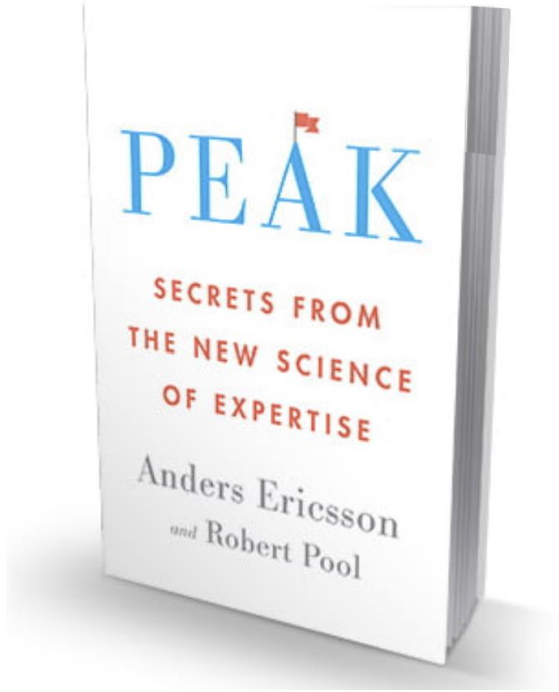
The Situation Last Year…..



The Integrin Receptor Family

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

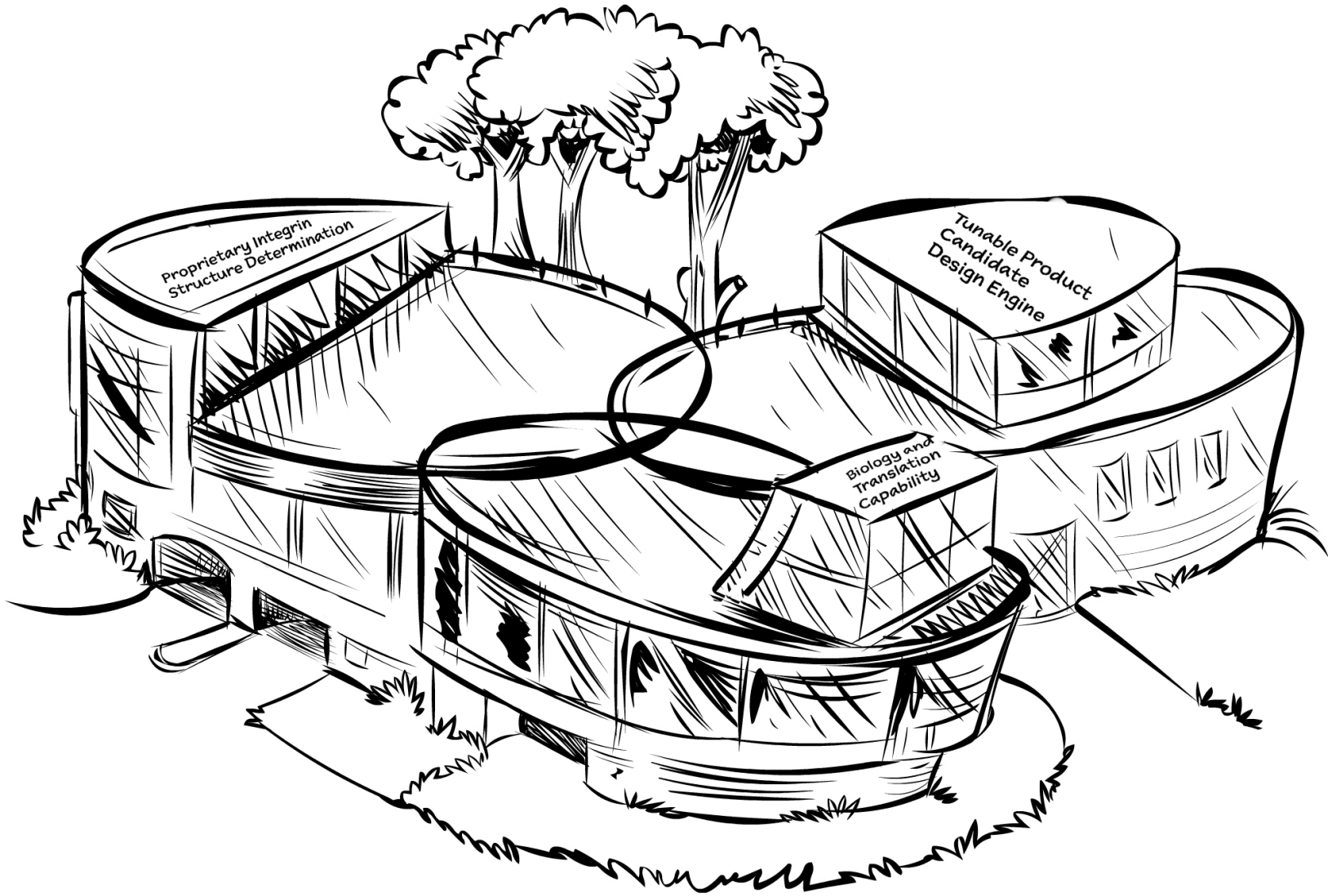




timothy springer @timothyspringer · Nov 20, 2020

Most inspiring **book** ever I read. Peak. Anders Ericsson. New Science of Expertise. Deliberate Practice builds Mental Representations. IQ matters little. All we need is training and practice. Brain changes. Homo exercens not H. sapiens. Thanks @Ptipirneni!

MInT: The Morphic Integrin Technology Platform



A Recent a4B7 Structure Breakthrough

Cheng 11:37 AM

Thursday, January 6th

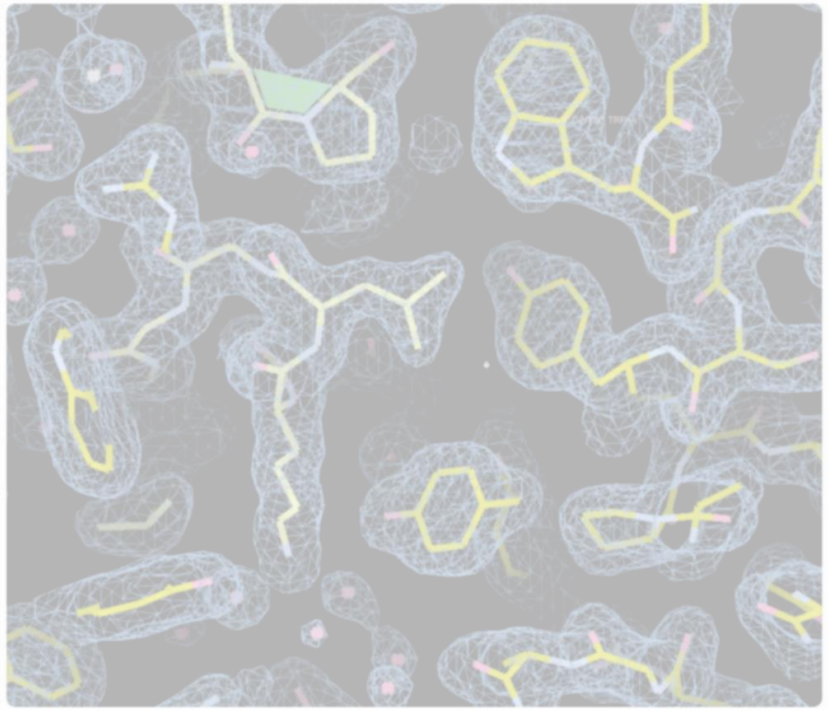
First shoutout of the year goes to @Qi Qiao @Meghan Monroy (she/her) and @Percy for keeping me barely slept last night. Overexcited.

Reason being, the Structure Biology group in Protein Science team has successfully presented **a sub 2A resolution of a4b7 crystal structure**! This is a huge deal for compound design. And this has been the dream of the team since Day 1 of the project, especially @Albert Lin!

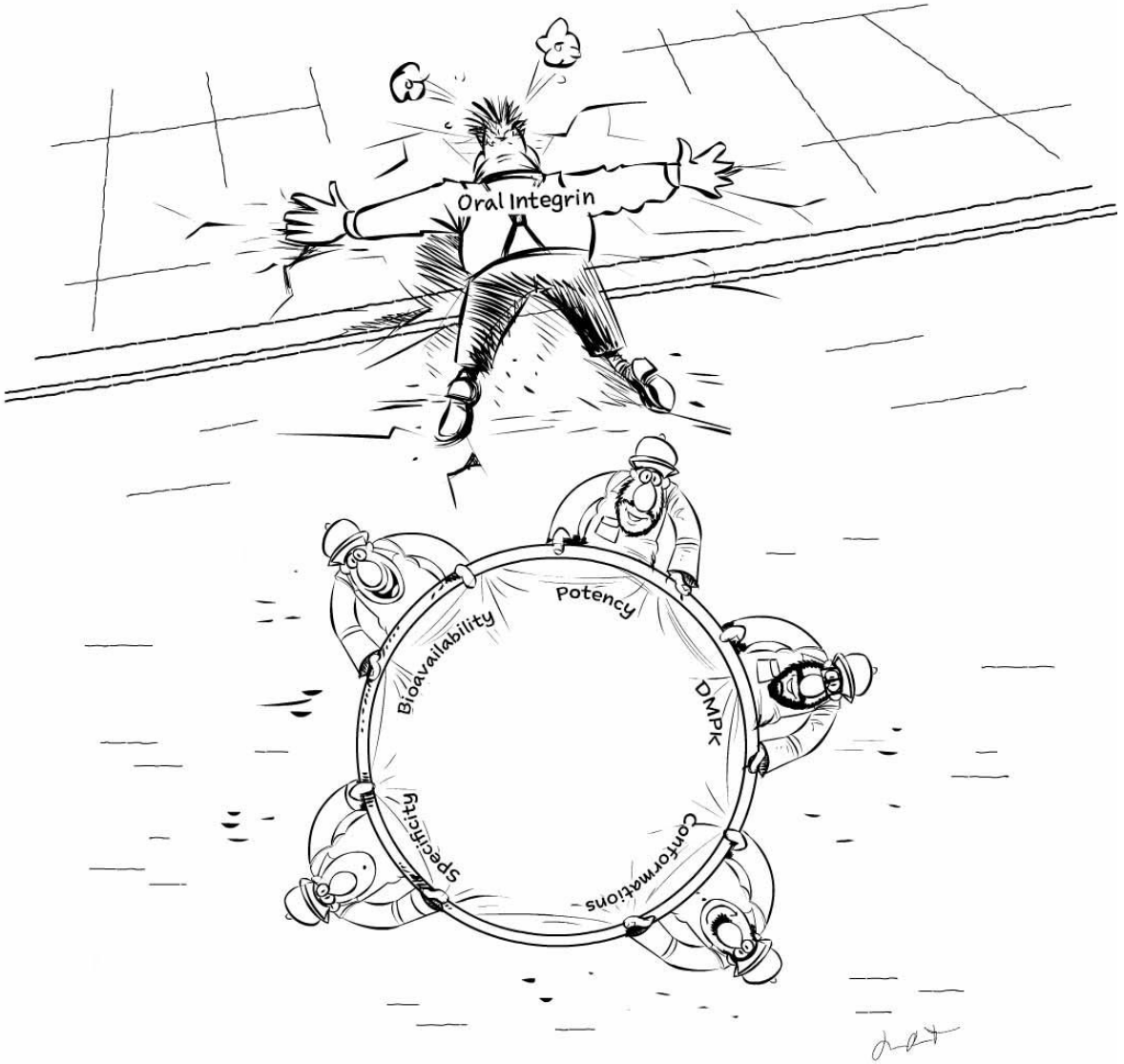
Kudos to the Structure Biology group! No doubt, high resolution crystals of many programs are expected and sure to be accomplished.

Dare to dream, and chase it. (edited)

sub 2A a4b7.png



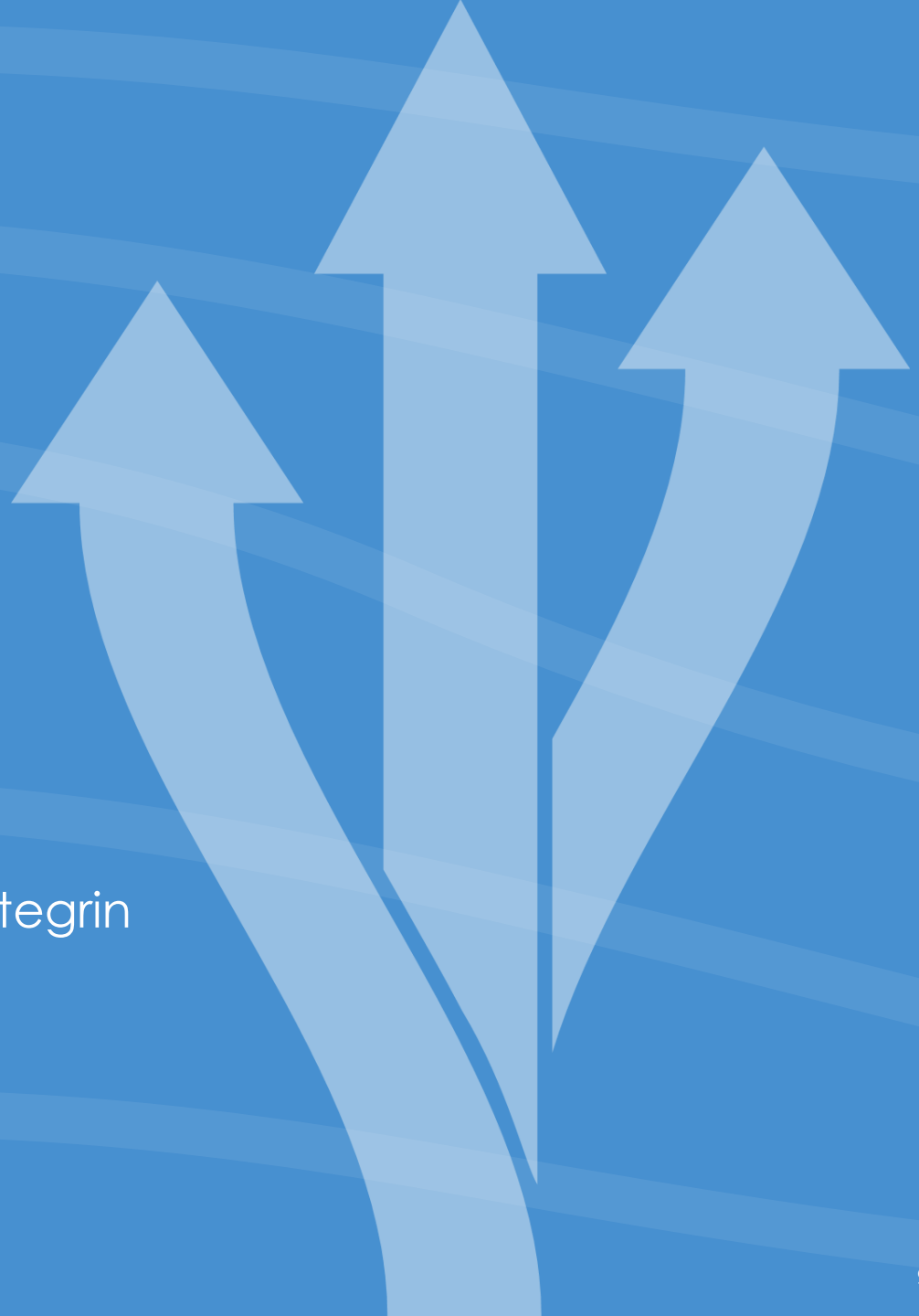
Drug Candidate Requirements



- High potency ✓
- Proprietary crystal structures complexed with lead compounds ✓
- High selectivity ✓
- Desired Pharmaceutical Properties ✓
- Oral Bioavailability ✓
- Proprietary conformation / functional understanding ✓

PROPRIETARY PIPELINE

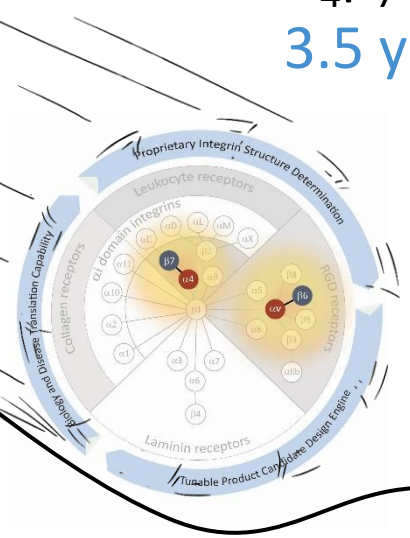
Creating the next generation of proprietary integrin inhibitor candidates



Increasing Returns from the MInT Platform

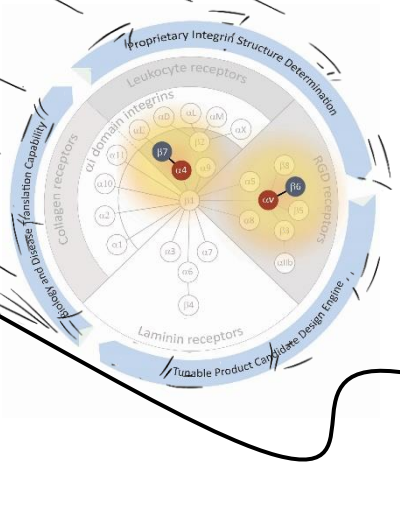
$\alpha_4\beta_7$

3.5 years Lead Optimization to Development Candidate



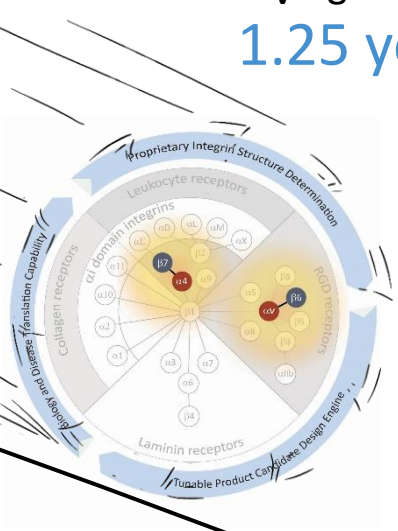
$\alpha_v\beta_6$

2 years LO to DC

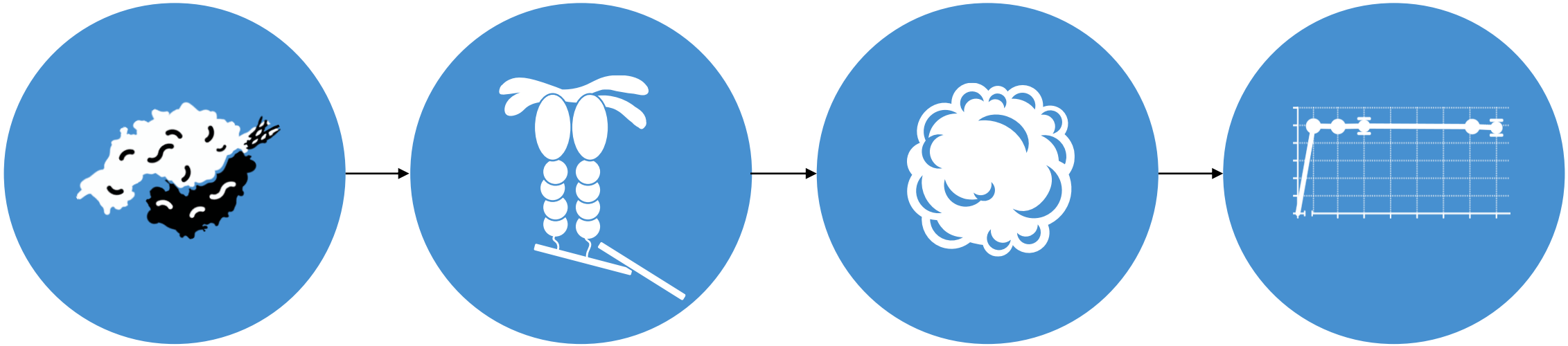


$\alpha_v\beta_8$

1.25 years LO to DC



avβ8 Small Molecule Integrin Inhibitor Immuno-oncology Program



Avβ8 Program

Small molecule inhibitors of the αvβ8 integrin in preclinical development

Mechanism

αvβ8 inhibition suppresses activation of TGFβ isoforms 1 and 3

Indications

Solid tumors, which make up approximately 90% of all adult human cancers

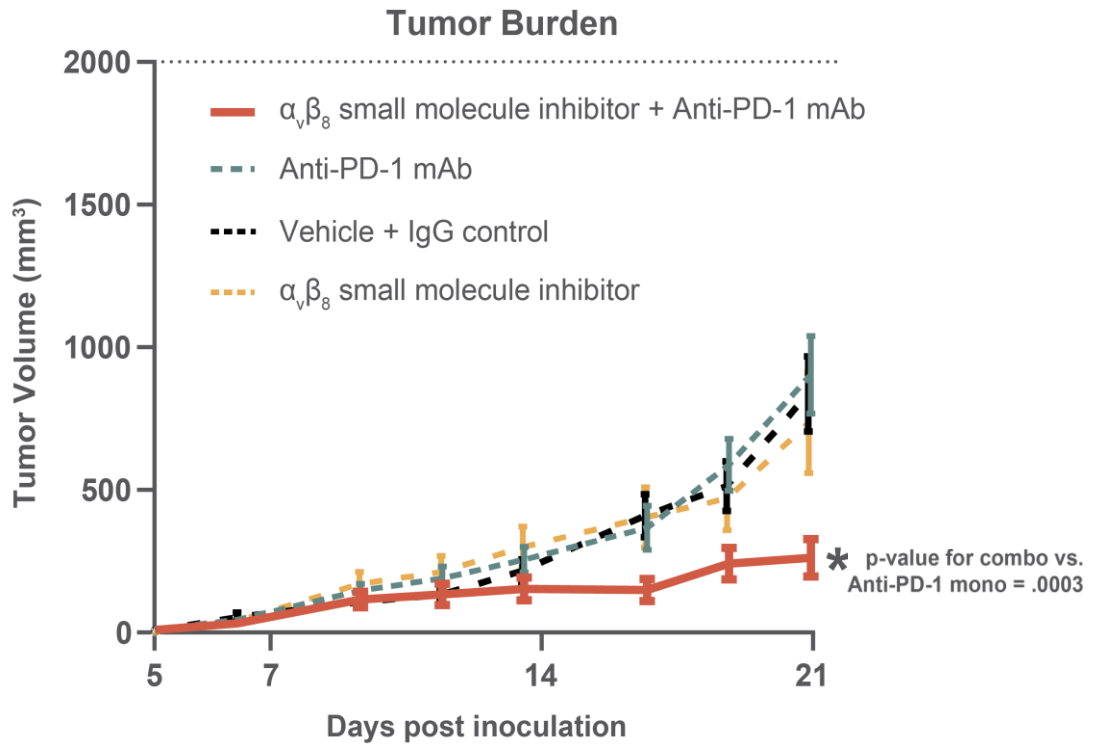
Data

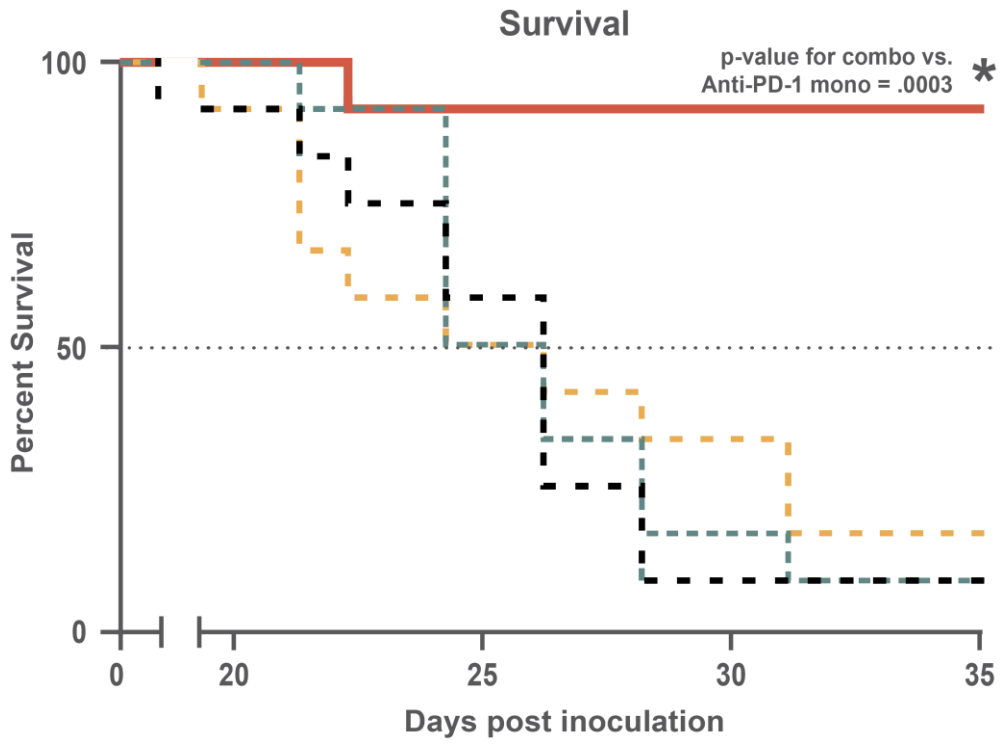
Oral inhibitor αvβ8 integrin , in combination with anti-PD-1, drives efficacy across mouse models of treatment-resistant breast cancer including the EMT6 and PyMT syngeneic breast cancer models

avβ8 Small Molecule Inhibitor Enhances Checkpoint Inhibitor Response in Immune Refractory Model

αvβ8 inhibition blocks activation of TGF-b, a key regulator of tumor formation, progression, and metastasis

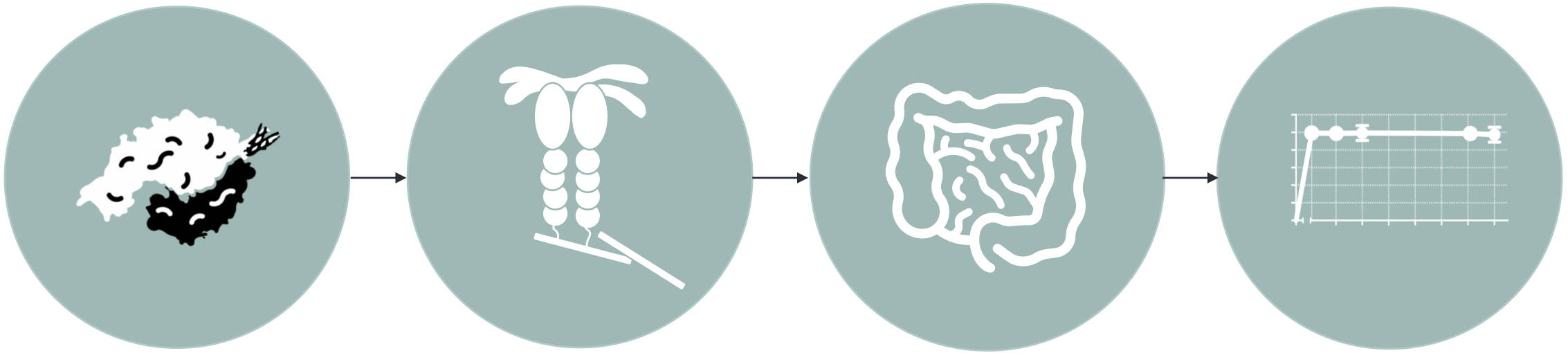
EMT6 Murine Breast Cancer Model





EMT-6 inoculation on day 0. Dosing window days 6 through 27

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



Candidate: 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 Program

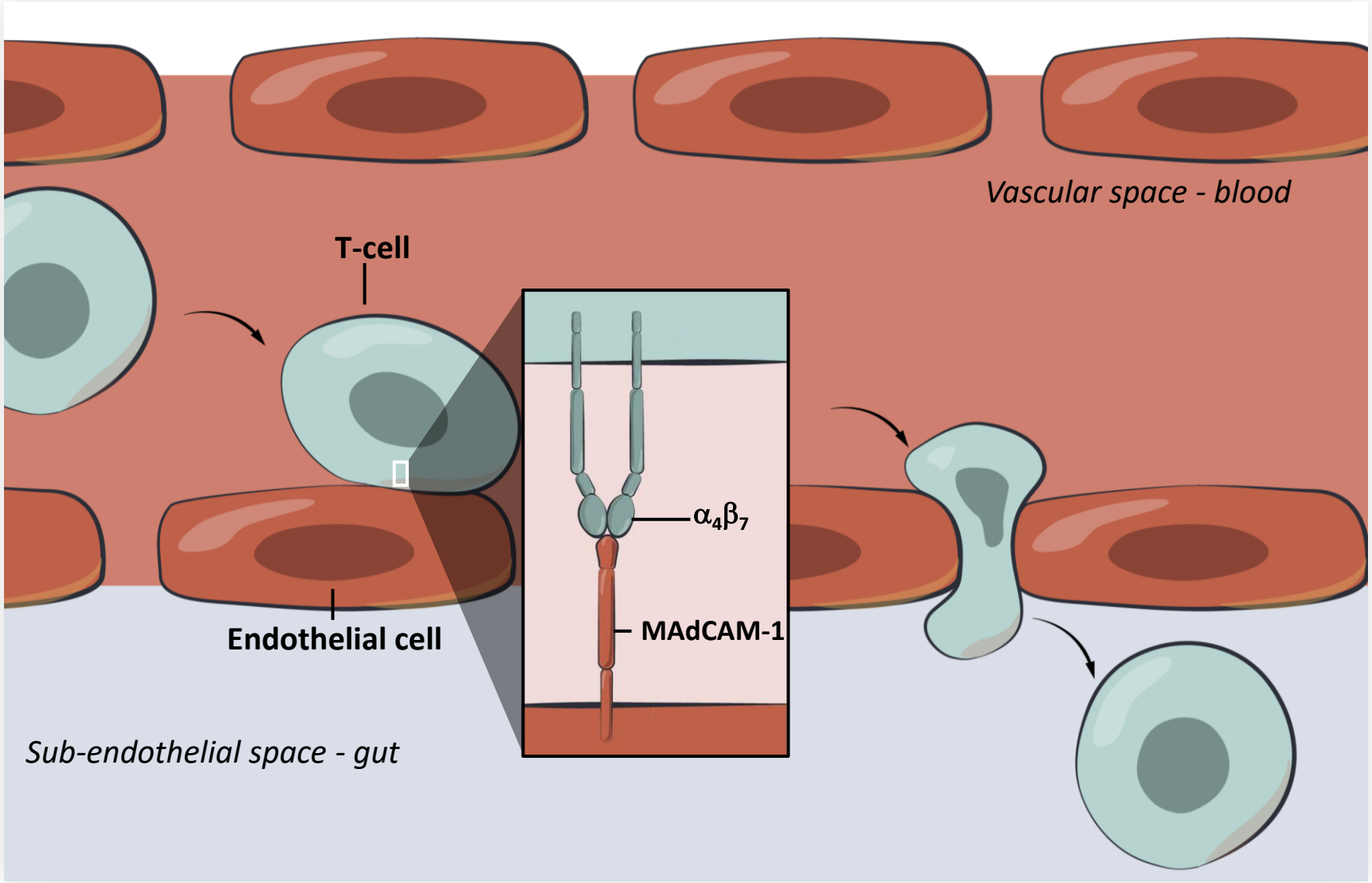
Well tolerated across 3 phase 1 trials, dose dependent and consistent PK, $\alpha_4\beta_7$ receptor saturation at 100 mg BID

No quantifiable levels of α4β1 RO observed

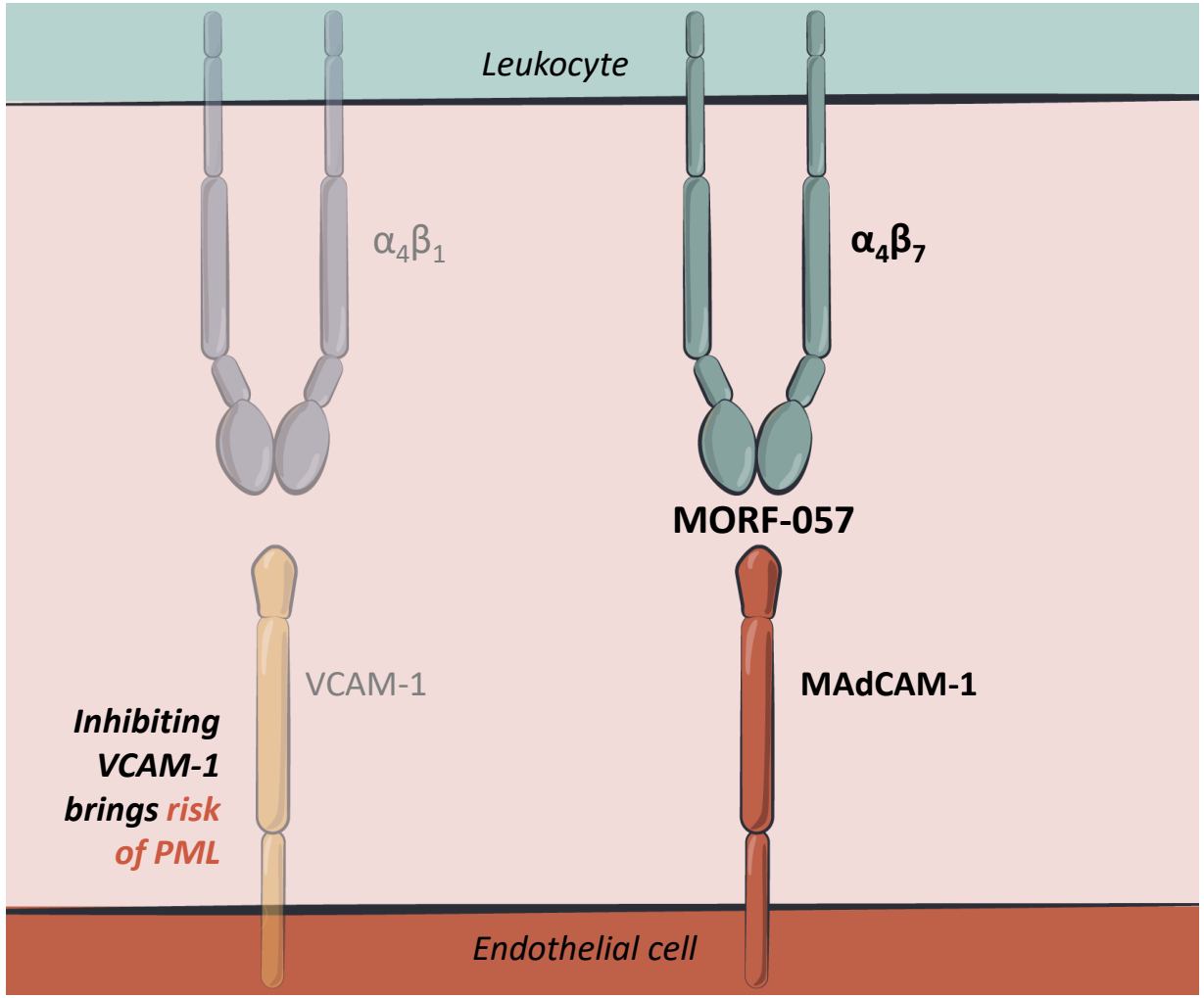
Phase 2 program beginning 1Q22 with open-label phase 2a, randomized controlled phase 2b trial to follow

[1]*Chrohn's and Colitis Foundation of America*

α4β7 Inhibition is a Proven Mechanism to Treat IBD



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

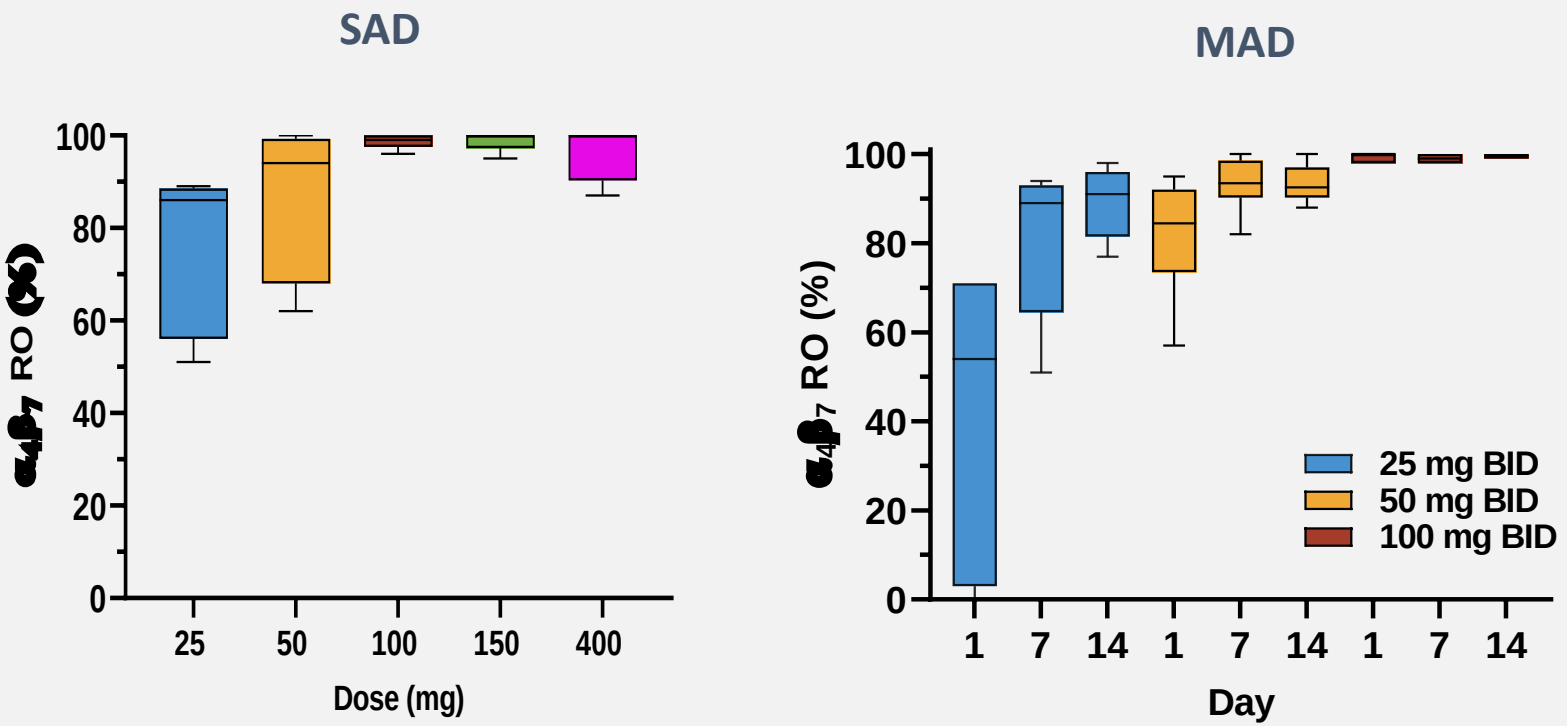
[a] Cell line characteristics: Jurkat cells have been traditionally used for specifically assessing $\alpha_4\beta_1$ potency, as these cells do not express $\alpha_4\beta_7$. RPMI8866 cells have lower levels of $\alpha_4\beta_1$ that likely better approximate expression levels in human blood.

DDW 2020, Morphic Therapeutic, Jamie Wong, ePoster Tu1283

MORF-057 Saturates the a4β7 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

$\alpha_4\beta_7$ RO vs. MORF-057 Plasma Concentration and Dose

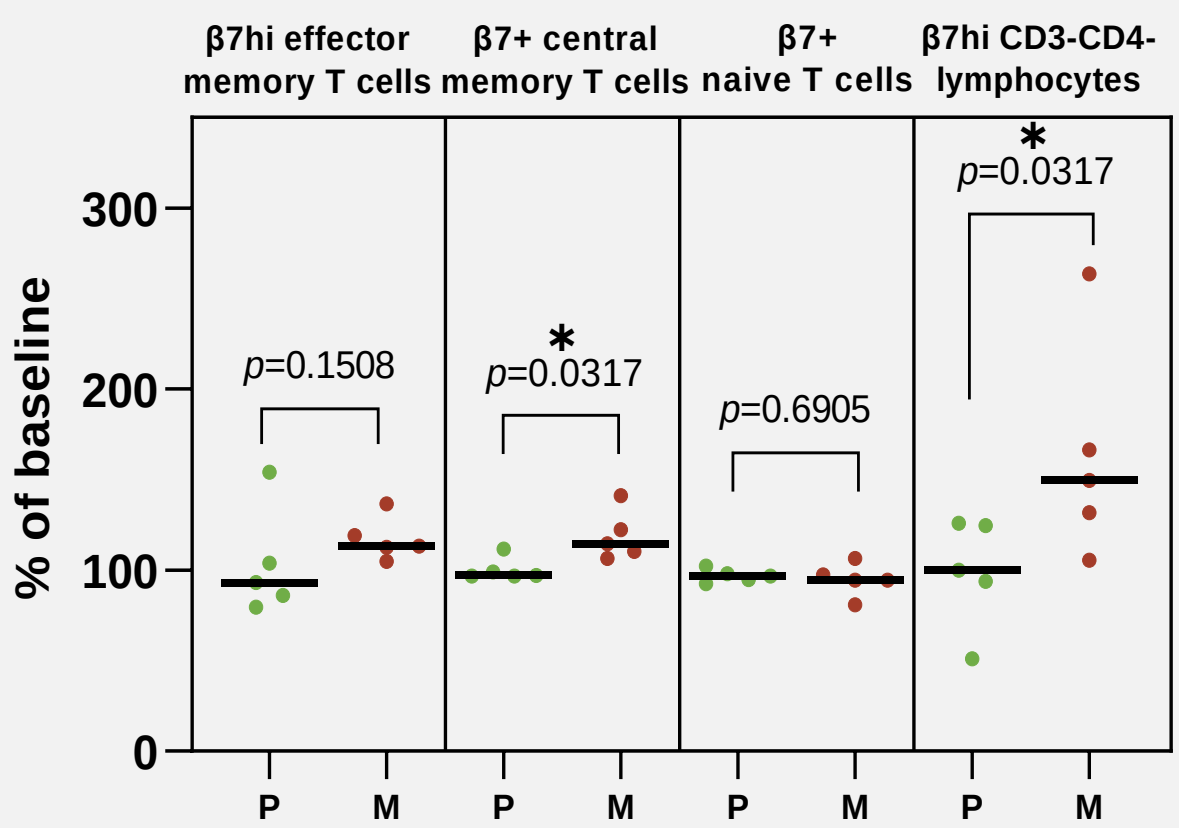


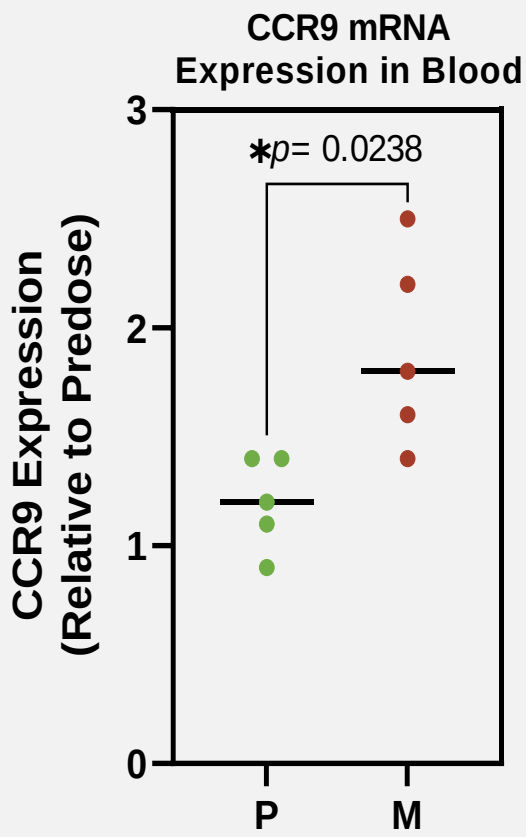
Ray, et al, ECCO 2021

Changes in Lymphocyte Subsets Consistent with Activity of Approved Mabs Inhibiting a4β7

Changes in lymphocyte migration patterns are correlated with reduced inflammation in other IBD therapeutics including vedolizumab[1]

Statistically Significant Changes in Key Pharmacodynamic Biomarkers[2]





*statistically significant

- **β7 high** = expressing high levels of integrin β7
- **β7+** = expressing β7
- **P** =placebo
- **M** =MORF-057; D= day
- **CCR9** = inflammatory marker

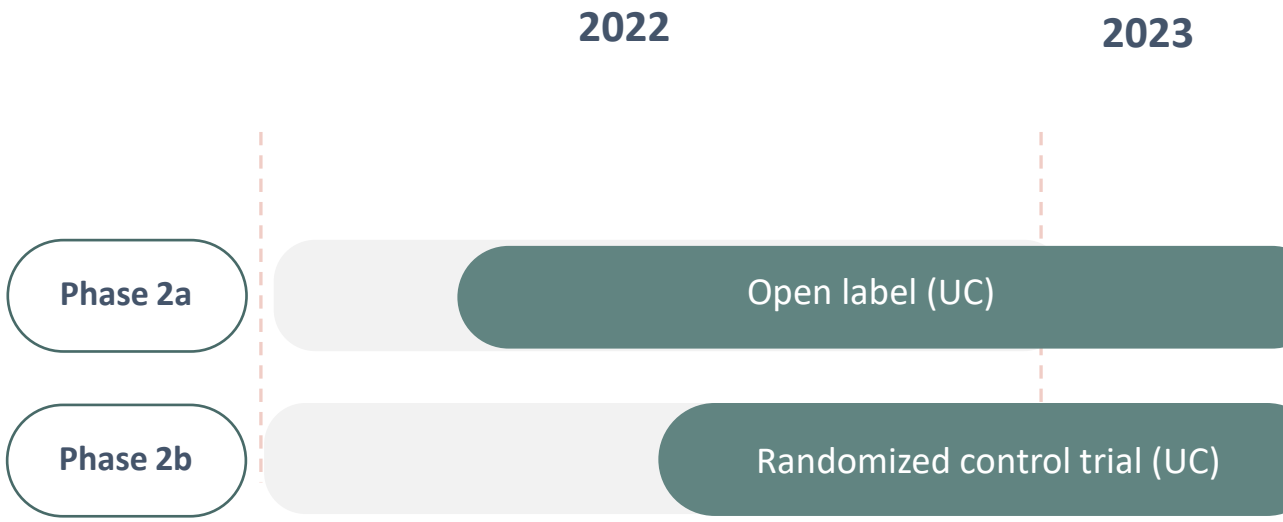
[1] *Veny et al, J. Crohn's and Colitis, 2021, 441–452*
[2] *Ray, et al, ECCO 2021*

MORF-057 Clinical Development Program

Phase 2a

Provide rapid proof of concept for MORF-057 as an $\alpha_4\beta_7$ inhibitor comparable or superior to vedolizumab in patients suffering from UC

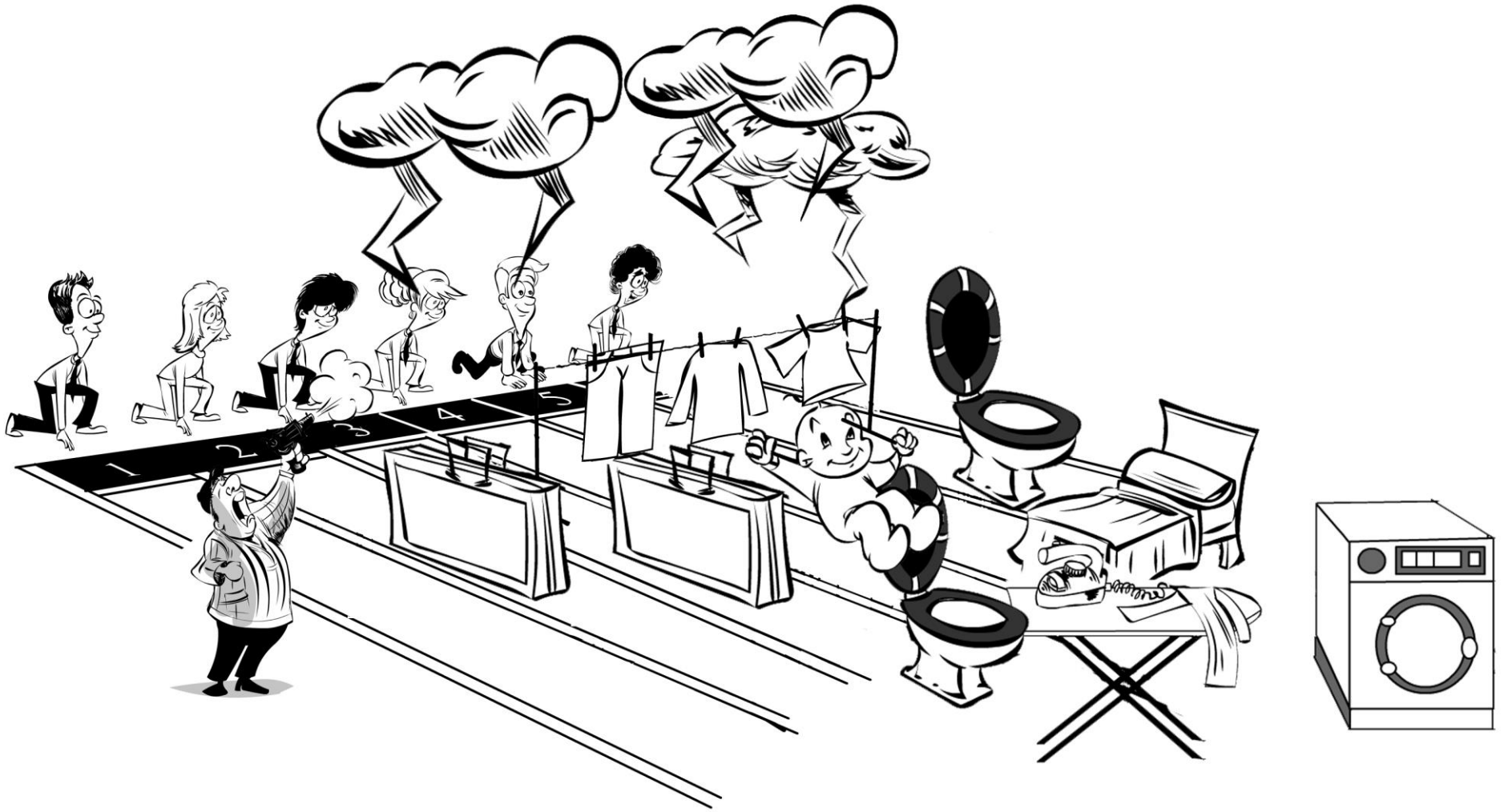
- Open label (n=35)
- 100mg BID MORF-057
- Deep data set including safety, PK/PD and multiple clinical measures



Phase 2b Randomized Controlled Trial

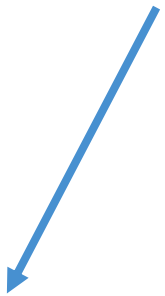
- Double-blind, placebo-controlled, randomized trial
- Dose ranging efficacy and safety to inform Phase 3 design

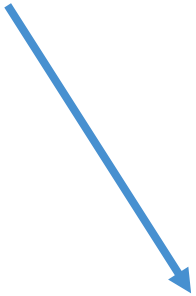
The Difference Between “Broke” and “Poor”



Bayes Theorem

Posterior odds = Prior odds * Likelihood Ratio





Base Rates

Information Specific to the Situation Being Examined

MORPHIC THERAPEUTIC

DELIVERING A NEW GENERATION OF INTEGRIN MEDICINES

Thank You