



Corporate Presentation

*August 2021*

# Forward Looking Statement

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*In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These known risks and uncertainties are described in detail in our filings with the Securities and Exchange Commission (the “SEC”) from time to time. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and we undertake no obligation to revise or update this presentation to reflect events or circumstances after the date hereof.*

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# Two Candidates in Ongoing Proof-of-Concept Trials

PROGRAM	CLASS (Route of Admin.)	INDICATION	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	RIGHTS
Seralutinib (GB002)	PDGFR, CSF1R, c-KIT Inhibitor (Inhaled)	Pulmonary Arterial Hypertension (PAH)	Phase 2 Ongoing 1H22 Readout*					Worldwide
GB004	Gut-Targeted, HIF-1α Stabilizer (Oral)	Inflammatory Bowel Disease (IBD) (Ulcerative Colitis, UC)	Phase 2 Ongoing 1H22 Readout*					Worldwide
Research Programs	Multiple Programs	Oncology, Immunology						Worldwide

\*Subject to further developments in the ongoing COVID-19 pandemic.

# 2021 Year of Execution Has Set Stage for Milestones in 2022

## 1<sup>st</sup> Half of 2022\*: Seralutinib Ph. 2 PAH Topline Readout

- Enrolling 80 PAH patients on standard background, including triple therapy
- Patients randomized 1:1 between seralutinib (up to 90mg BID) and placebo
- Primary endpoint: change in PVR from baseline at Week 24

## 1<sup>st</sup> Half of 2022\*: GB004 Ph. 2 UC Topline Readout

- Enrolling 195 mild-to-moderate UC patients, post-5-ASA (pre-biologic)
- Patients randomized 1:1:1 between 2 doses of GB004 and placebo
- Primary endpoint: Clinical remission at Week 12



**TORREY  
STUDY**



# Seralutinib (GB002)

Inhaled PDGFR, CSF1R & c-KIT Inhibitor

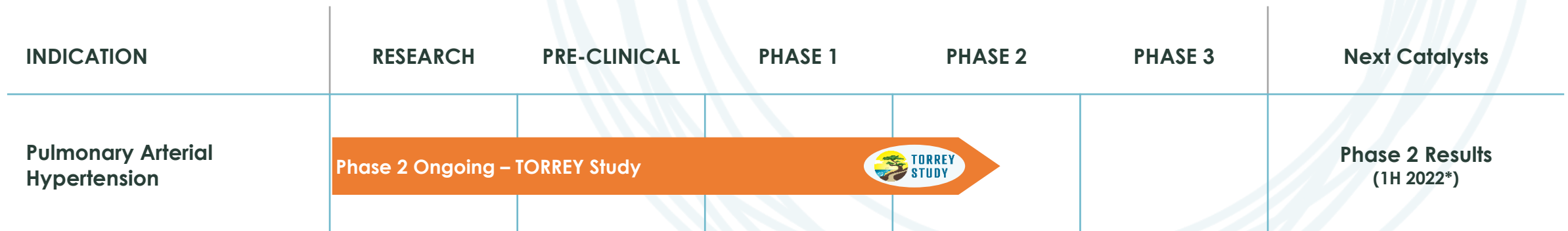
Pulmonary Arterial Hypertension (PAH)



# Seralutinib (GB002): Potential To Deliver Disease-Modifying Effects to Patients with PAH

## Product Candidate Description

- Selective, inhaled PDGF receptor, CSF1R, and c-KIT kinase inhibitor designed to address the disease pathogenesis of PAH
- Kinase inhibition was shown to be clinically significant in Phase 3 PAH trial of imatinib (Gleevec), with systemic toxicities (IMPRES Study)
- Seralutinib formulation and administration via dry powder inhaler (DPI) designed to reach areas of the deep lung; DPI device is small, convenient and currently used in commercial products
- Designed to deposit inhaled seralutinib at site of disease due to proximity of terminal bronchiole and alveolar space to affected pulmonary arteries
- Patent protection to 2039<sup>(1)</sup>; Orphan Drug Designation from FDA and EMA



1) Includes assumption of maximum 5 years of patent term extension. Corresponding patent(s) and patent application(s) with compound-specific claims. Total patent life with patent term extension cannot exceed 14 years from approval.

\*Subject to further developments in the ongoing COVID-19 pandemic.



# PAH Has High Unmet Need & Significant Disease Burden

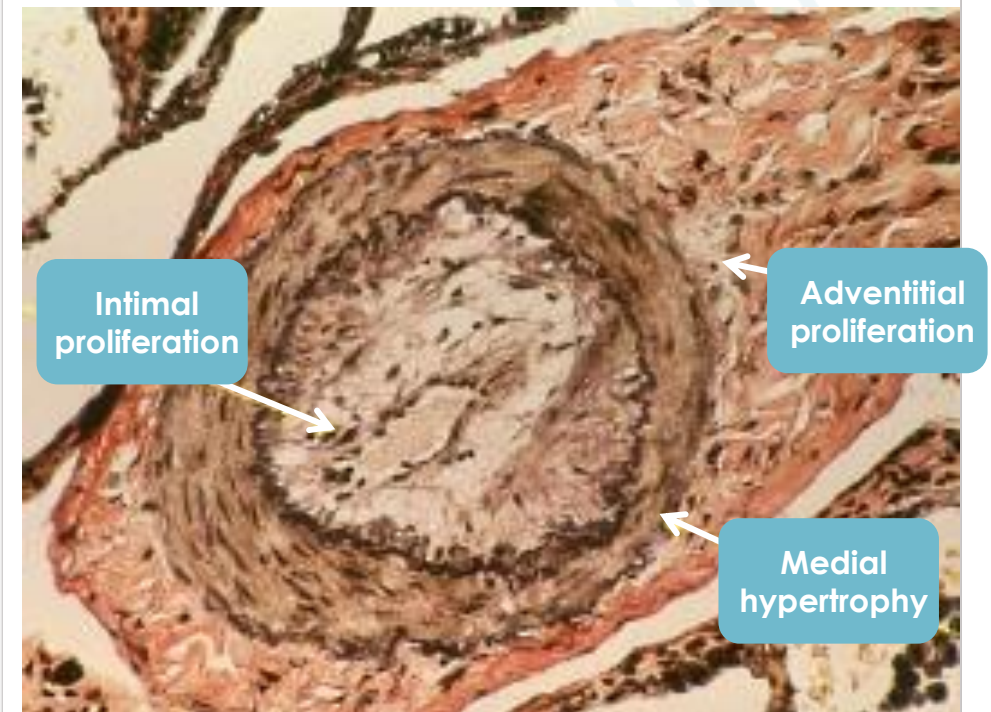
## Pulmonary Arterial Hypertension (PAH)

- Rare, orphan disease
- Characterized by high blood pressure in the blood vessels carrying deoxygenated blood from the right side of the heart to the lungs
- Caused when the arteries in the lungs become narrowed, thickened and / or stiff as a result of pathological remodeling and vasoconstriction
- Heart works harder to pump blood to the lungs, potentially leading to right heart failure
- Progressive disease and often fatal

## Symptoms

- Dyspnea
- Fatigue
- Dizziness
- Chest pressure / pain
- Edema in ankles, legs, abdomen
- Cyanosis
- Heart palpitations

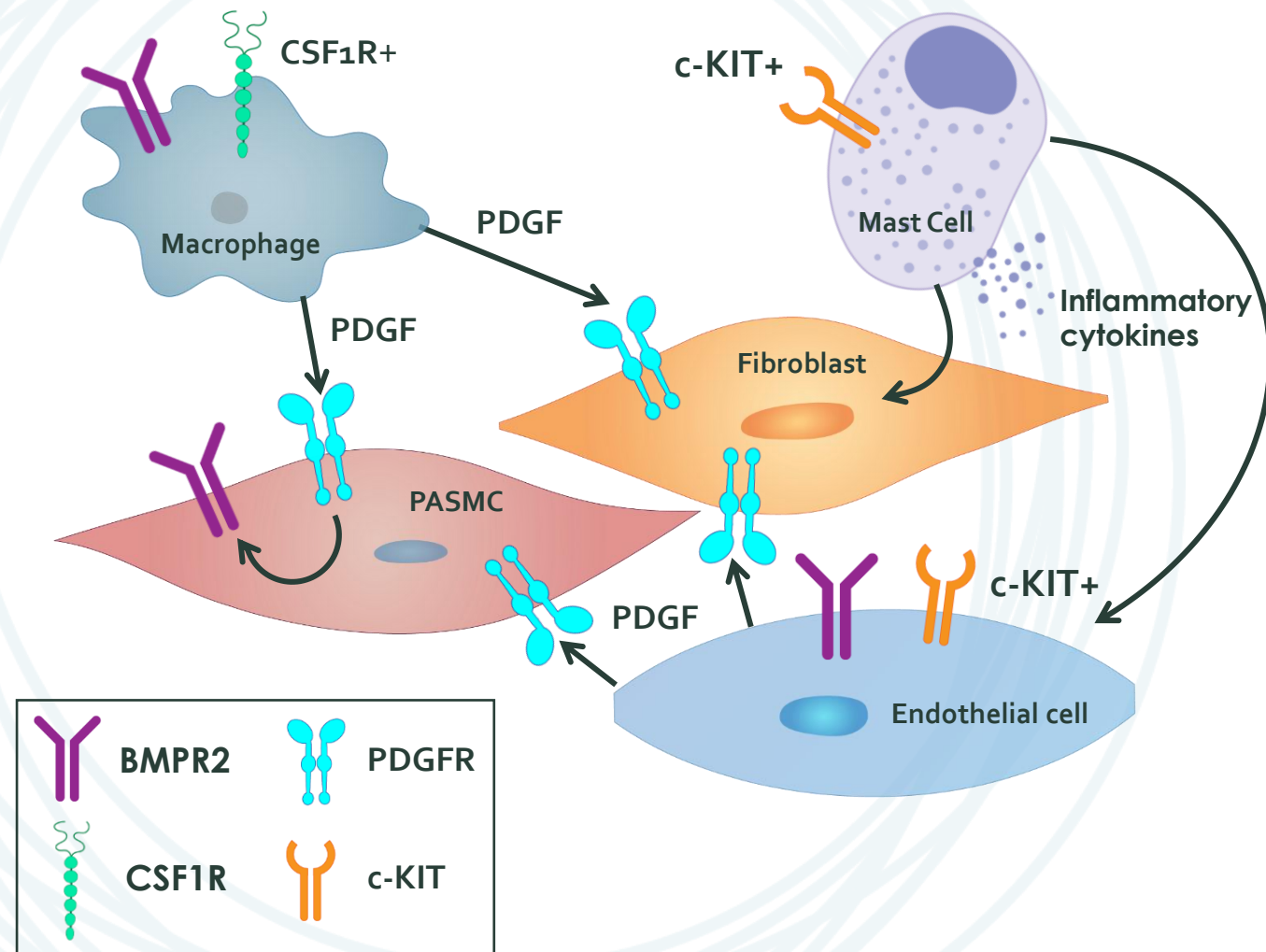
## PAH is Characterized by Vascular Remodeling



Muscular pulmonary artery from iPAH patient<sup>1</sup>

# PDGFR, CSF1R, and c-KIT Activation Play a Role in the Pathological Remodeling of Lung Blood Vessels in PAH and Interact with BMPR2

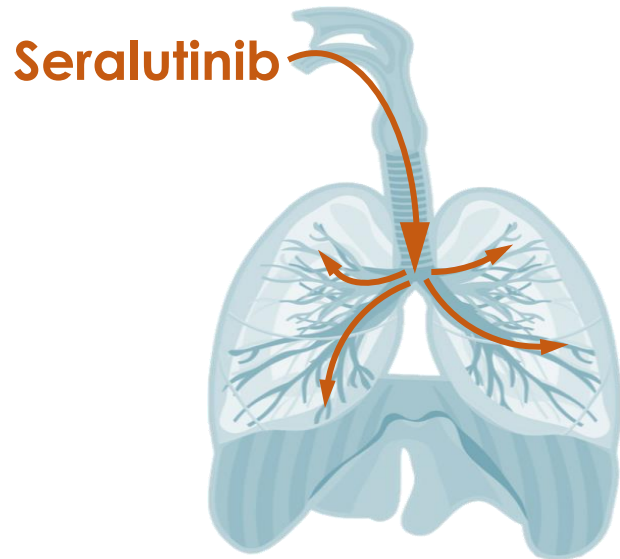
- Aberrant PDGFR signaling drives overgrowth of smooth muscle cells myofibroblasts leading to medial hypertrophy, neointimal lesions, and fibrosis
- CSF1R<sup>+</sup> macrophages secrete PDGF and contribute to inflammation and vascular remodeling
- c-KIT<sup>+</sup> cells are increased and further drive the inflammatory and proliferative disease process
- PDGF activation decreases BMPR2, which further drives PASMC proliferation





# Seralutinib Administration via Dry Powder Inhaler is Designed to Be Convenient and to Deliver Drug Directly to the Site of Disease

## Dry Powder Inhaler from Plastiapne



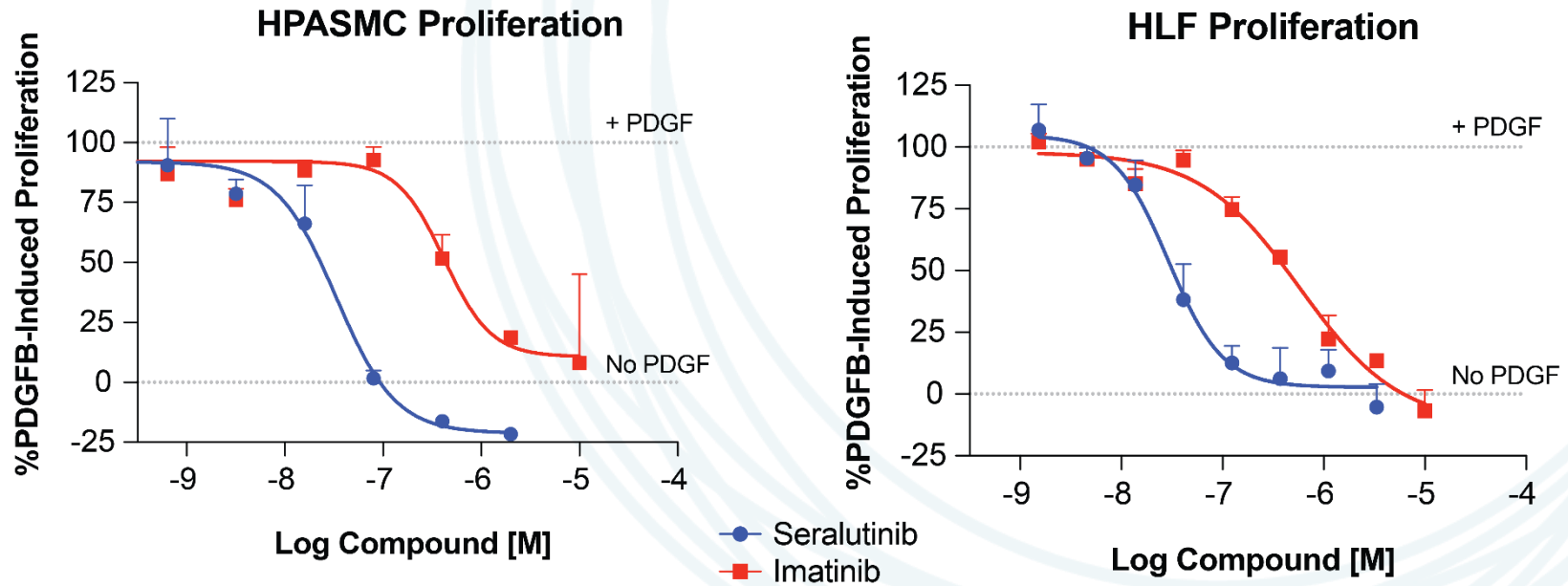
- Seralutinib formulation and administration via dry powder inhaler (DPI) designed to reach areas of the deep lung
- Designed to deposit inhaled seralutinib at site of disease due to proximity of terminal bronchiole and alveolar space to affected pulmonary arteries
- In pre-clinical studies, has resulted in 30x ratio of lung-to-systemic exposure, potentially providing for an improved therapeutic index in the clinic
- DPI device is small, convenient and currently used in commercial products

# Seralutinib In Vitro Profile

Seralutinib is a potent PDGFR, CSF1R and c-KIT inhibitor

Compound	Cell Based IC50 (nM)				
	H1703 PDGFR $\alpha$	HLF PDGFR $\beta > \alpha$	PASMC PDGFR $\alpha = \beta$	CSF1R	c-KIT
Seralutinib	32	29	33	8	14
Imatinib	62	579	419	1032	230

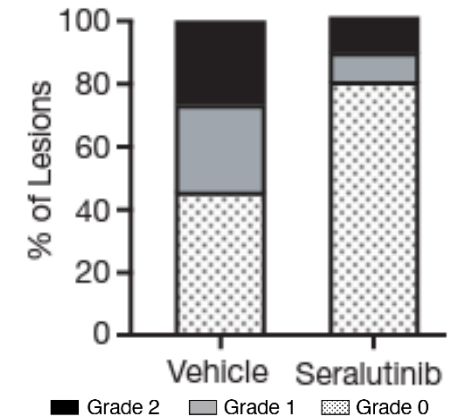
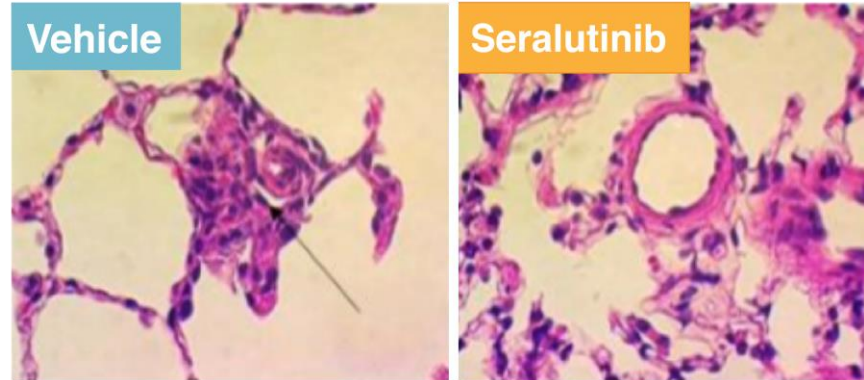
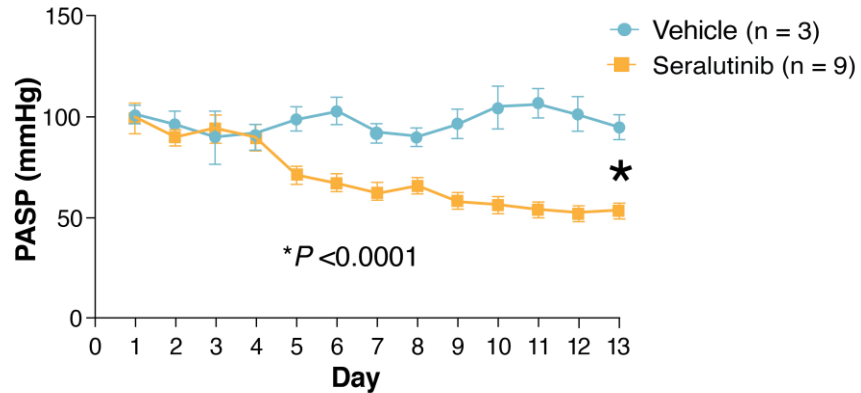
Seralutinib is highly potent in PASMC and HLF proliferation assays



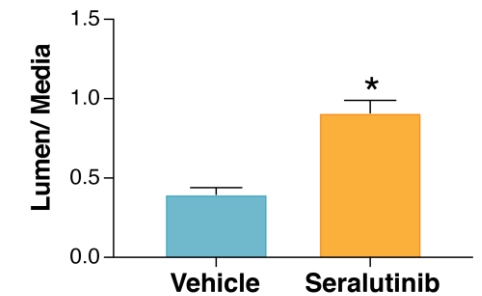
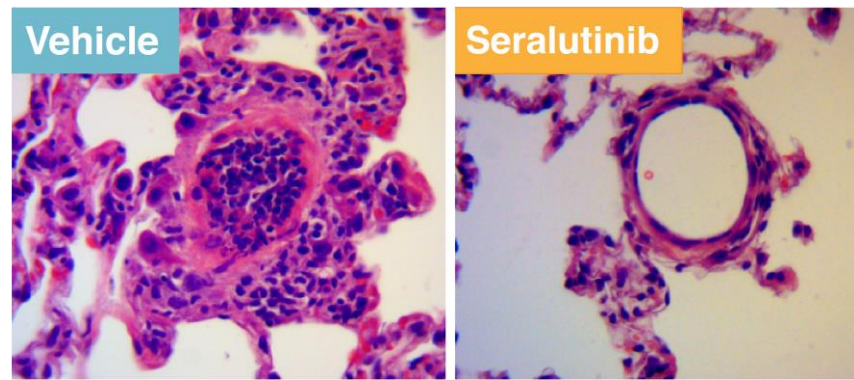
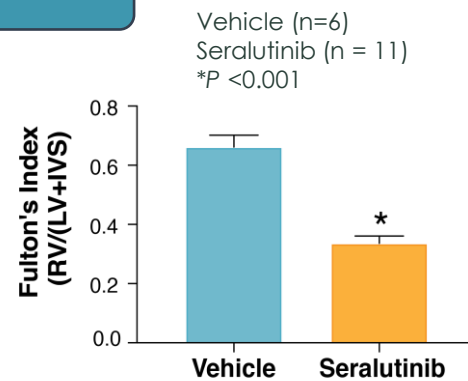
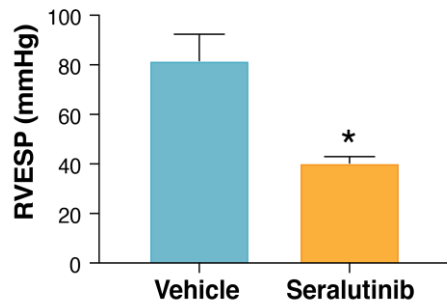
HPASMC: human pulmonary arterial smooth muscle cell; HLF: human lung fibroblast  
Source: Ten Freyhaus, Arterioscler Thromb Vasc Biol 2015, 35(5):1236; Barst, J Clin Invest 2005, 115(10):2691; Gomez-Arroyo, et al, Am J Physiol (2012) 302(10):L1014; Sawada, et al, J Exp Med (2014) 211 (2):263; Talati, et al, PLoS One (2014) 9(4):e94119; Abid, et al, Eur Respir J 2019, 10;54(4):1802308; Savai, et al., Am J Respir Crit Care Med 2012, 186(9):897; Montani, et al., Am J Respir Crit Care Med 2011, 184(1):116

# Seralutinib Demonstrates Efficacy in the SU5416/Hypoxia and MCT/PN Models

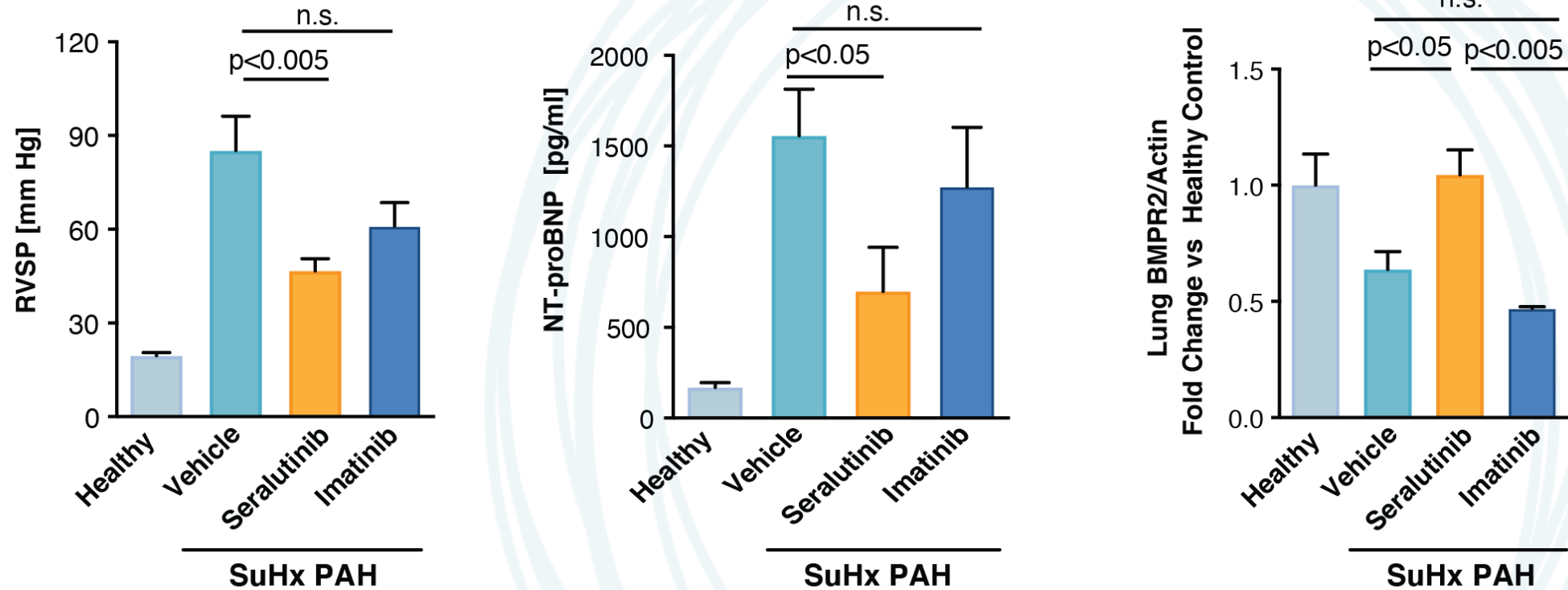
## SU5416/H telemetry study



## MCT/PN study



# Inhaled Seralutinib Outperformed Oral Imatinib in a Head-to-Head Preclinical SuHx PAH Study

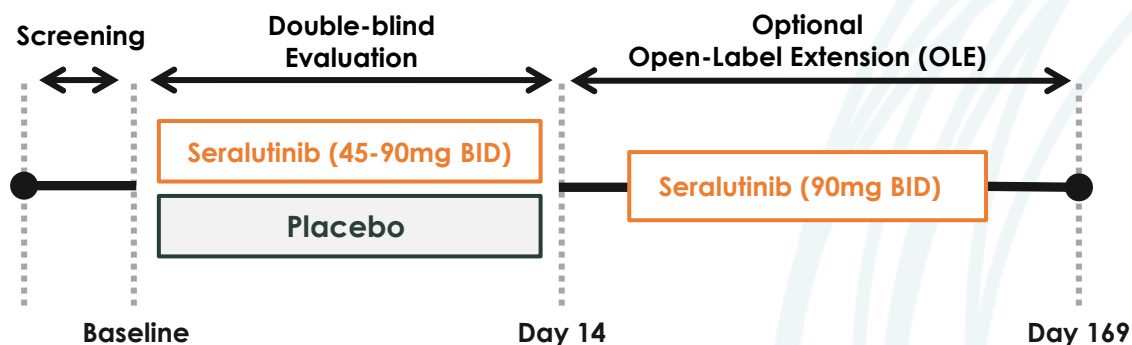


Data presented as Mean +/- SEM. Statistical analysis was performed using one-way ANOVA with Dunnett's multiple comparisons test (Healthy n=8; Vehicle n=7; Seralutinib n=9; Imatinib n=7)

- Seralutinib treatment led to a significant improvement in RVSP
- Seralutinib reduced circulating levels of NT-proBNP and increased lung BMPR2 protein expression



# Overview of Phase 1b Study in Patients with PAH



- First subjects enrolled Q1:20; study interrupted by COVID-19 related site closures in the spring of 2020, limiting ability for patients to continue treatment on OLE
- Site re-openings in the fall of 2020 allowed enrollment of additional subjects, including opportunity for roll-over to the OLE
- A total of 8 subjects enrolled and completed the double-blind period (6 Seralutinib, 2 Placebo) with 2 subjects continuing and completing the OLE

## Study Objectives

### Primary

- To evaluate the safety and tolerability of inhaled seralutinib

### Secondary

- To evaluate the pharmacokinetics (PK) of seralutinib

### Exploratory

- To evaluate pharmacodynamic (PD) biomarker on blood samples

## Inclusion Criteria and Dosing

### Key Inclusion Criteria

- Diagnosis PAH, WHO group 1, FC II-IV
- Prior cardiac catheterization data c/w PAH
- Baseline 6-minute walk >100 m
- On PAH background medications

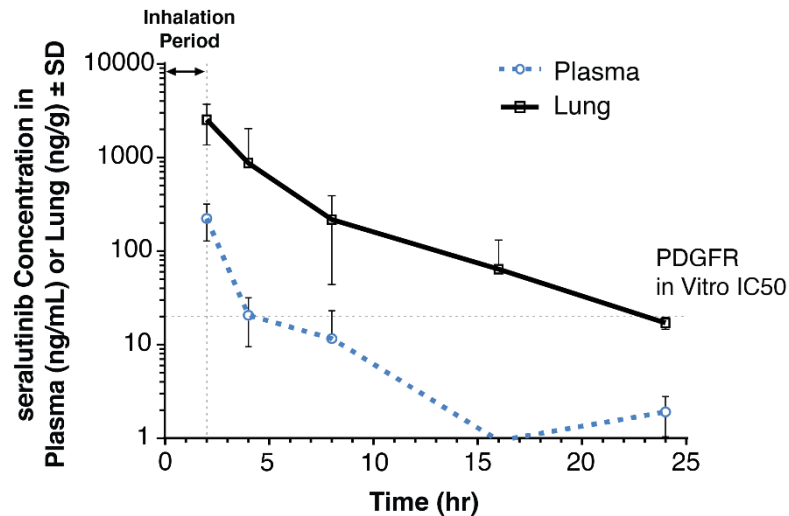
### Dosing

- 45 mg (wk 1) to 90 mg (wk 2) BID dose escalation first 14 days
- 90 mg BID in OLE days 15 - 169



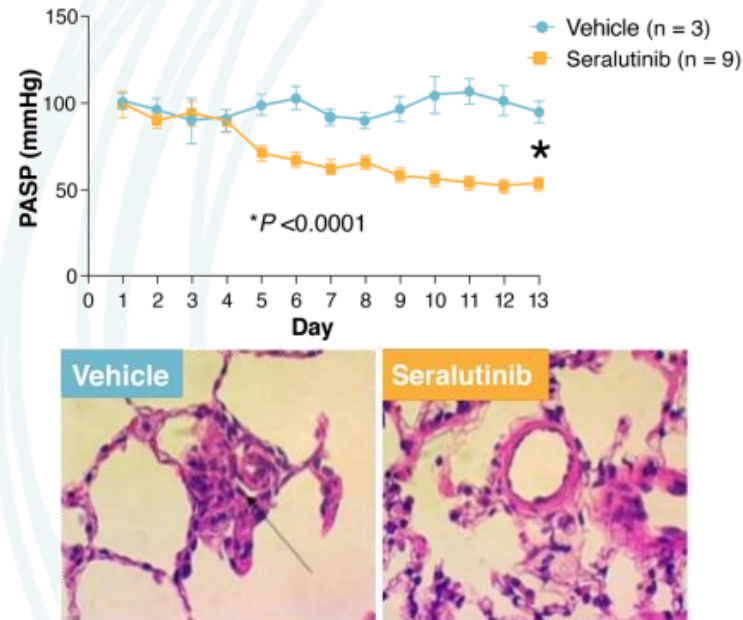
# Gossamer Took A Systematic Approach to Arrive at 45 – 90mg BID Dosing for Seralutinib

## Seralutinib Designed to be an Inhaled Therapeutic



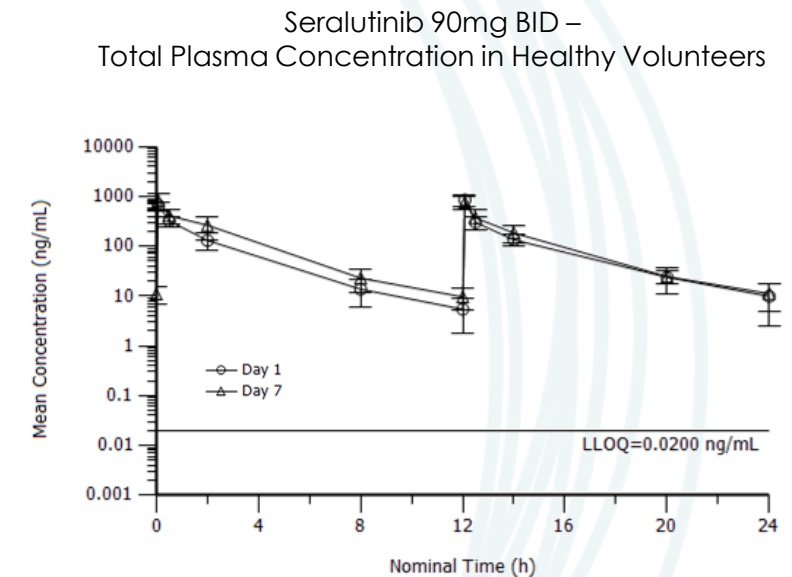
- ✓ Much greater (~30x mean) lung-to-plasma ratio and lung half life (~6 hours vs. 3 hours in plasma) observed in rats

## Human Dose Scaled to Efficacious Results in Rats



- ✓ Allometric and direct scaling for inhalation products<sup>†</sup> suggests ~12.8 mg/kg BID dose efficacious in SuHx PAH model translates to ~90 mg BID in humans

## Phase 1 PK Confirms Scaling and IC50 Coverage of Target Kinases

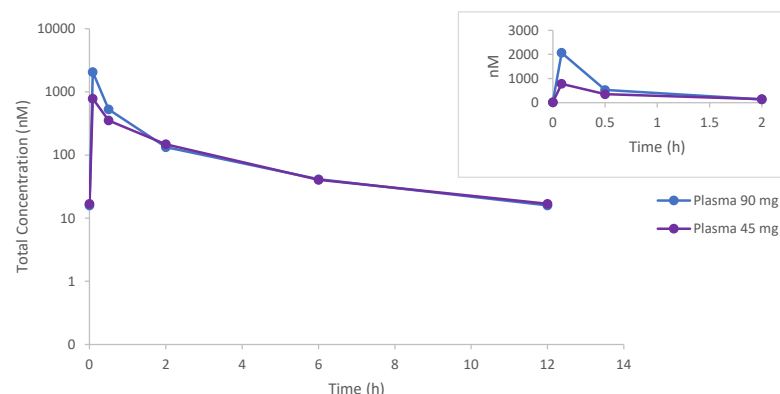


- ✓ 45mg and 90mg BID doses selected to maintain IC50 coverage in the lung above the IC50 values of PDGFR $\alpha$ , PDGFR $\beta$ , c-KIT, and CSF1R based on Phase 1 NHV data

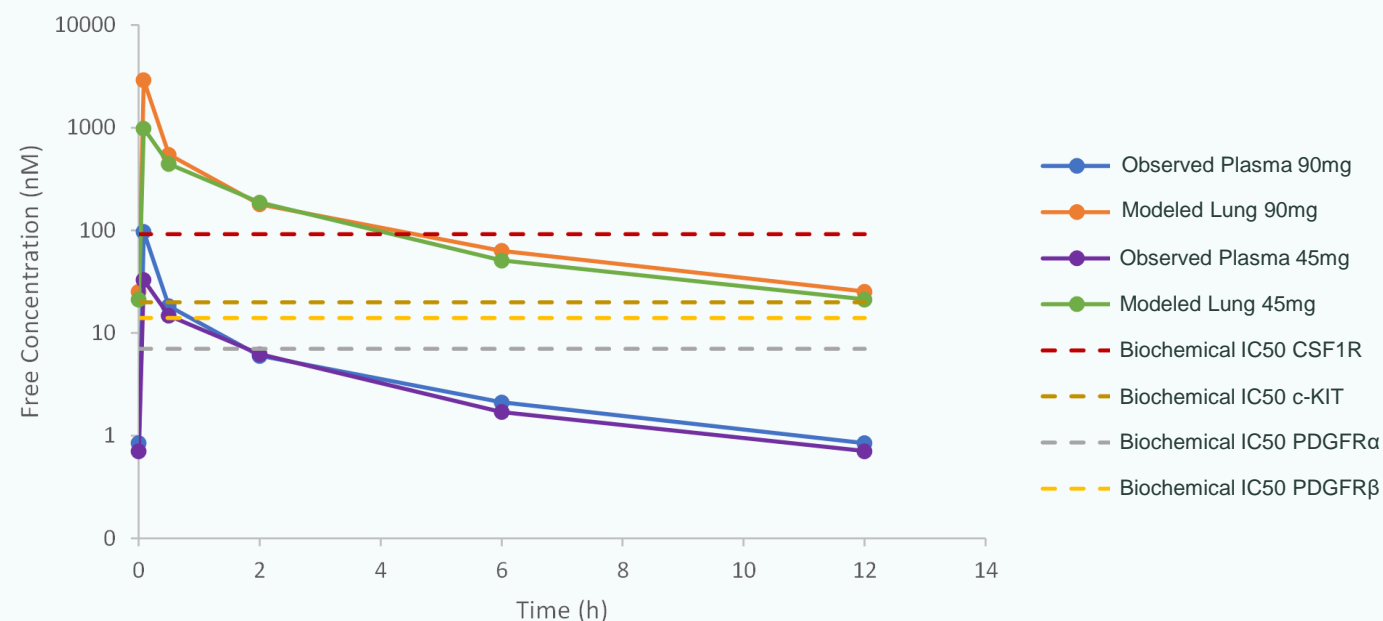
<sup>†</sup>Allometric and direct scaling approaches as described in JE Philips; Pharmacology & Therapeutics, 178 (2017) Theres'e Ericsson et al; Pharm Res, July 2017  
BID: twice daily; SD: standard deviation; PASP: pulmonary arterial systolic pressure; SuHx: sugen hypoxia; NHV: normal healthy volunteers

# Phase 1b PK Profile, Target Engagement Data, and Extrapolated Lung Concentrations Support Target Coverage of Dose Range Predictions

## Systemic Total Drug PK in PAH Patients Matches Normal Healthy Volunteer Experience

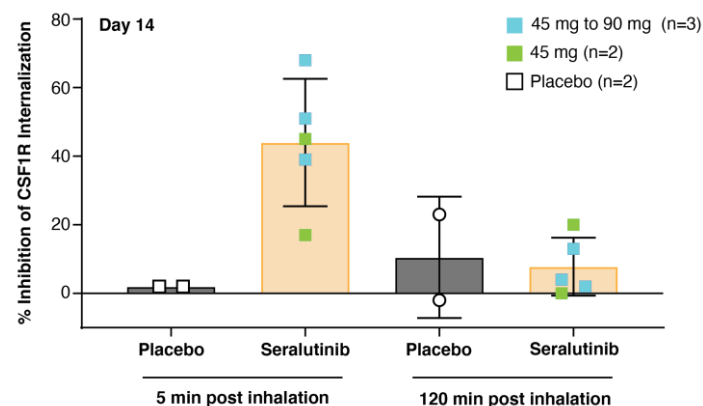


## Observed Phase 1b Free Plasma and Modeled Free Lung Concentrations Support Target Coverage in Lungs and Systemic Sparring



- Seralutinib systemic PK in PAH characterized by  $T_{max}$  of 5-6 min and half-life of ~4 hours following a single inhaled dose
- Blood target engagement biomarker (CSF1R) data consistent with free drug concentration levels considering biochemical IC50 of CSF1R
- With the extrapolated lung exposures of ~30x and in-vitro biochemical IC50's, seralutinib doses of 45-90 mg BID are anticipated to provide target coverage in the lung over 24 hours

## Seralutinib Transiently Inhibits CSF1R in Plasma



# Summary of Key Outcomes From Phase 1b Study in PAH with Seralutinib

## Summary of Outcomes By Section of Study

### Double-blind period

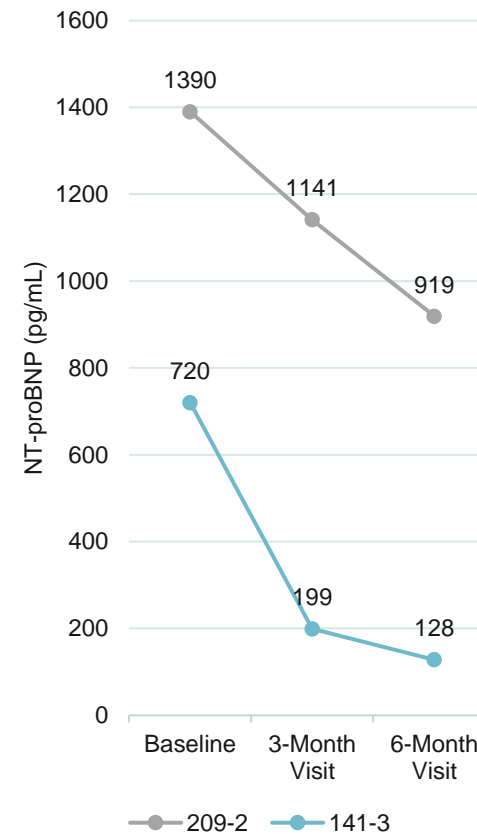
- All 8 subjects completed the 14-day treatment period
- No SAEs reported
- The most frequently reported AEs were:
  - Cough (mild-moderate)
  - Headache (mild)
- There were no clinically significant changes in labs, ECGs, PFTs, or vital signs
- Evidence of peripheral blood target engagement (e.g., CSF1R)

### Open-Label Extension (OLE)

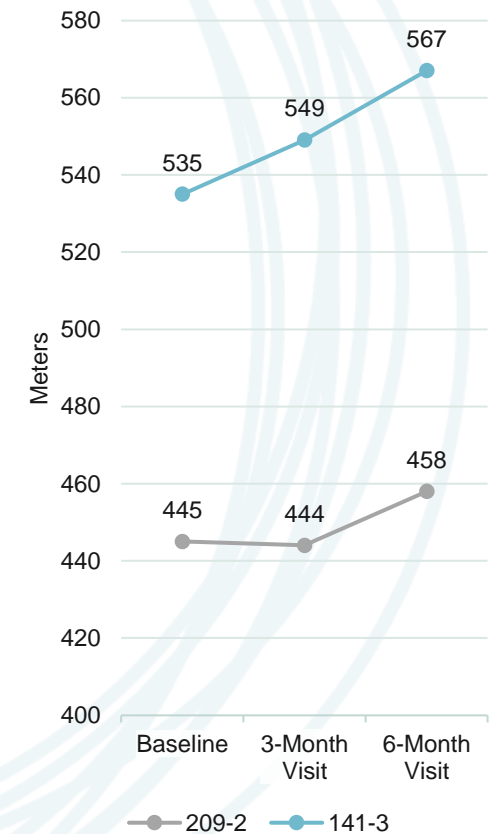
- 2 subjects entered and completed the OLE receiving 90 mg BID
- No SAEs reported and no safety concerns identified with longer term dosing
- NT-ProBNP levels decreased and 6-minute walk distances increased

## Biomarker & Functional Outcomes for OLE Patients

### Δ in NT-proBNP from Baseline



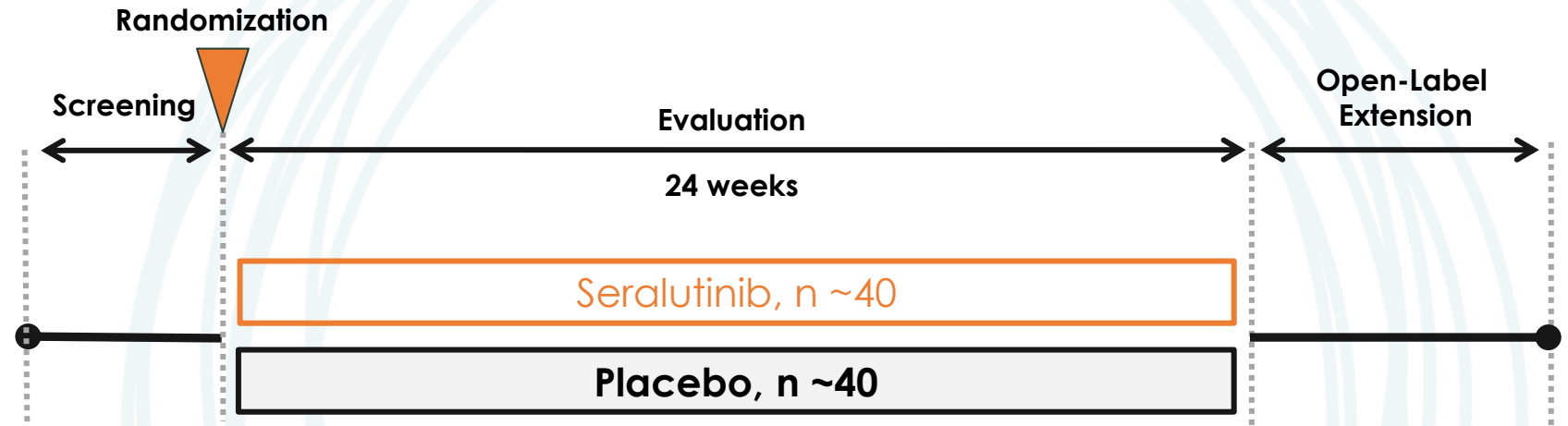
### Δ in 6MWD from Baseline



# TORREY: Phase 2 Study of Seralutinib in Patients With Functional Class II and III PAH

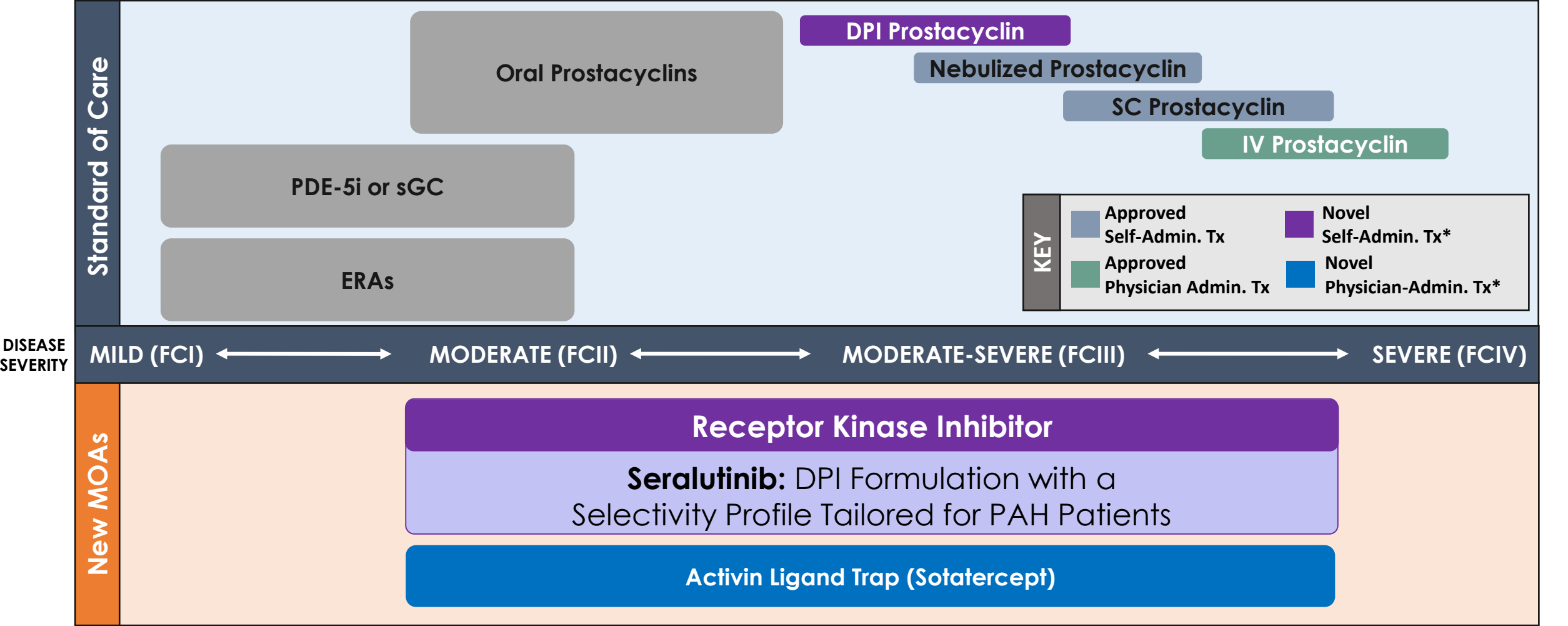


**TORREY  
STUDY**



<b>Patient Population</b>	Functional Class II and III PAH patients on standard background therapy (including triple therapy); PVR $\geq 400$ dyne*s/cm <sup>5</sup>
<b>Endpoints</b>	<b>Primary:</b> PVR Change from Baseline at Week 24 <b>Key Secondary:</b> 6MWD Change from Baseline at Week 24
<b>Dosing Regimen</b>	Dose-titrated in range of 45 to 90mg BID

# Seralutinib Offers a New, Multifaceted Approach to Treating PAH, Differentiating it From the Competitive Landscape



*Seralutinib is being evaluated on-top of background therapy (≥1 therapy)*



# GB004

Gut-Targeted,  
Hypoxia Inducible Factor 1-Alpha  
(HIF-1 $\alpha$ ) Stabilizer

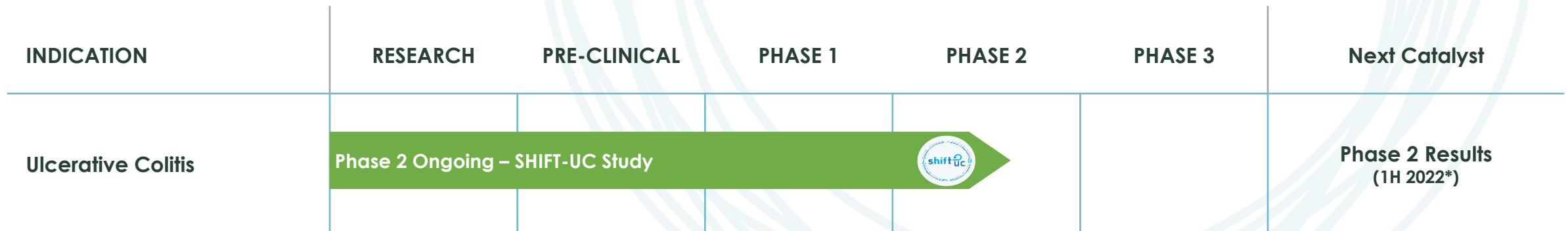
Inflammatory Bowel Disease (IBD),  
including Ulcerative Colitis (UC) and  
Crohn's Disease (CD)



# GB004: Gut-targeted, HIF Stabilizer in Development for the Treatment of IBD

## Product Candidate Description

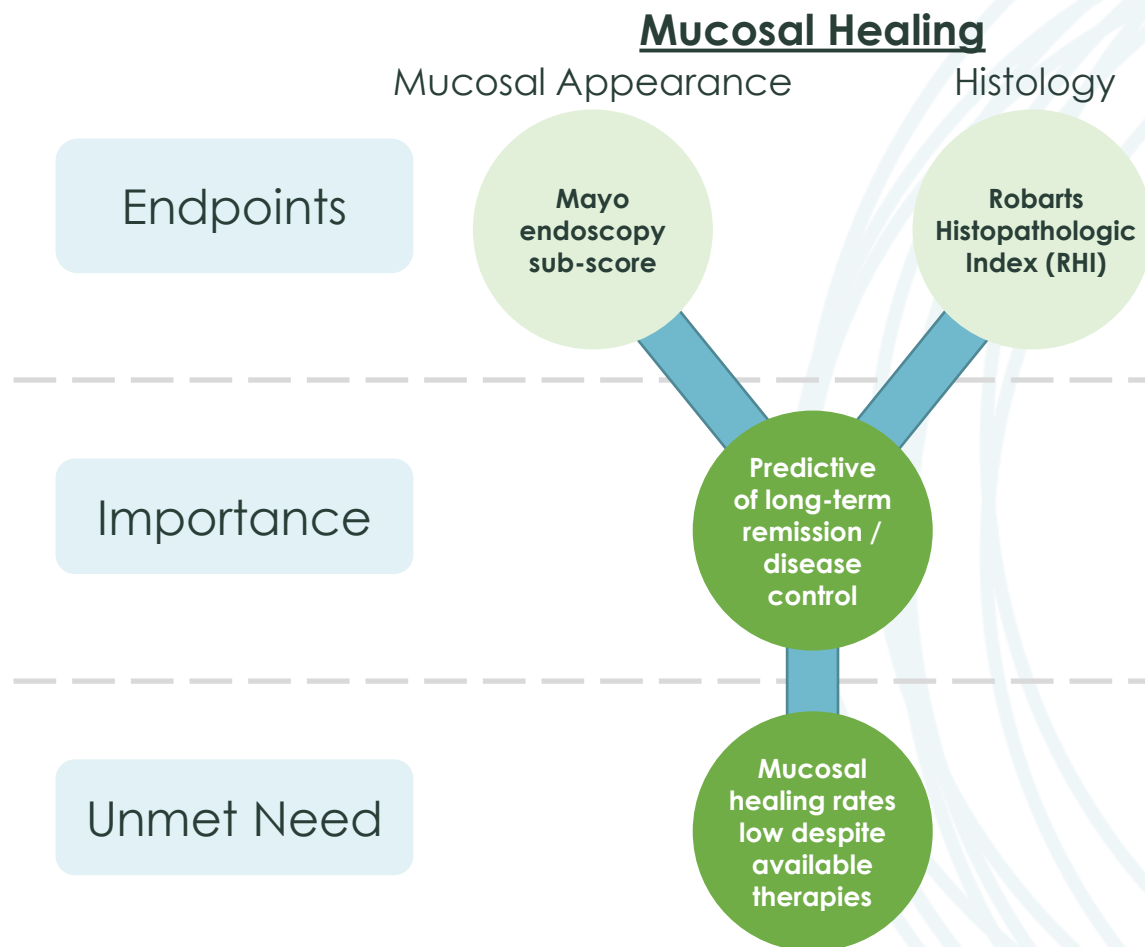
- Oral, small molecule, gut-targeted, prolyl hydroxylase inhibitor that is designed to stabilize HIF-1α for the treatment of inflammatory bowel disease (IBD)
- HIF-1α stabilization restores epithelial barrier function and exerts innate immunomodulatory effects, which is expected to reduce inflammation and enhance mucosal healing in human IBD
- Potential for use as mono or combo therapy for IBD
- Promising results from 4-week Phase 1b study announced in Q2:20
- Patent protection to 2035<sup>(1)</sup>



1) Includes assumption of maximum 5 years of patent term extension. Corresponding patent(s) and patent application(s) with compound-specific claims.

\*Subject to further developments in the ongoing COVID-19 pandemic.

# Improved Mucosal Healing is a High Unmet Need in UC

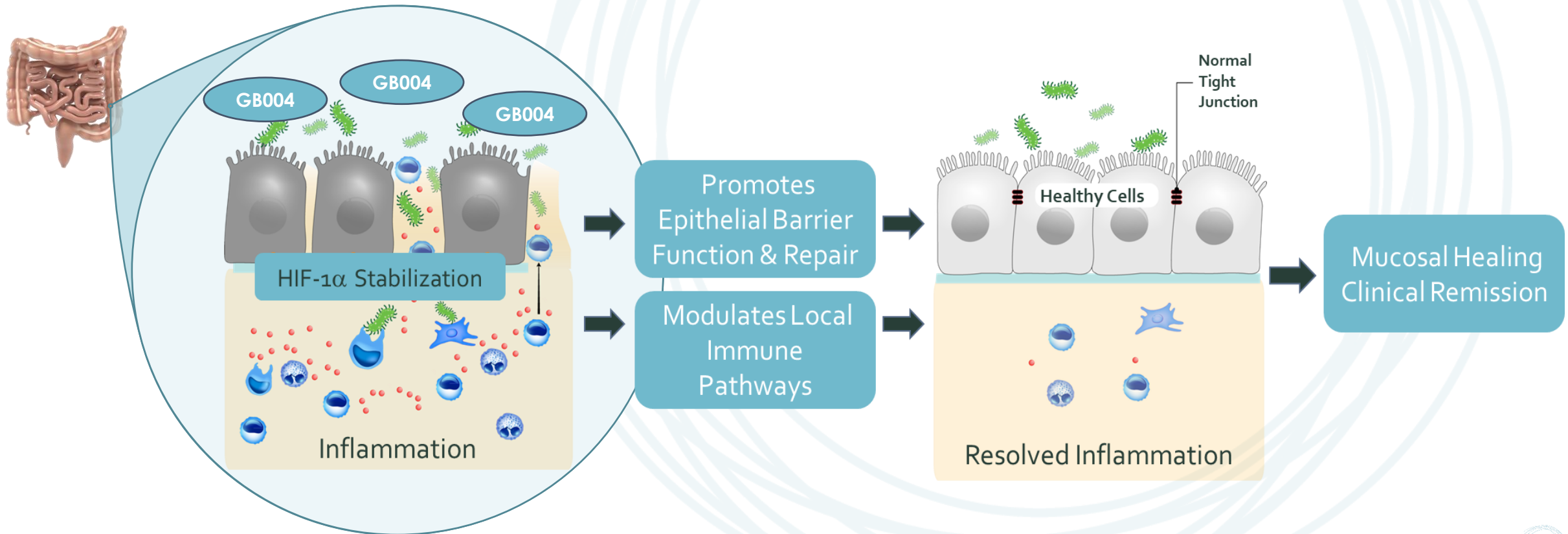


- Historically, endoscopy alone had been used to evaluate “mucosal healing”
- Following data and guidance from KOLs, the FDA, and the EMA, histology has emerged as an important third therapeutic target and second component of mucosal healing
- Histology has been shown to be a better predictor of long-term rates of disease relapse, hospitalizations, colectomy, and corticosteroid use than endoscopy
- While endoscopy assesses mucosal improvement at the tissue level, histology magnifies to the cellular level
- Current therapies do not adequately achieve mucosal healing

Patients in Gossamer's Phase 1b study of GB004 in UC were required to have active disease as evaluated by RHI

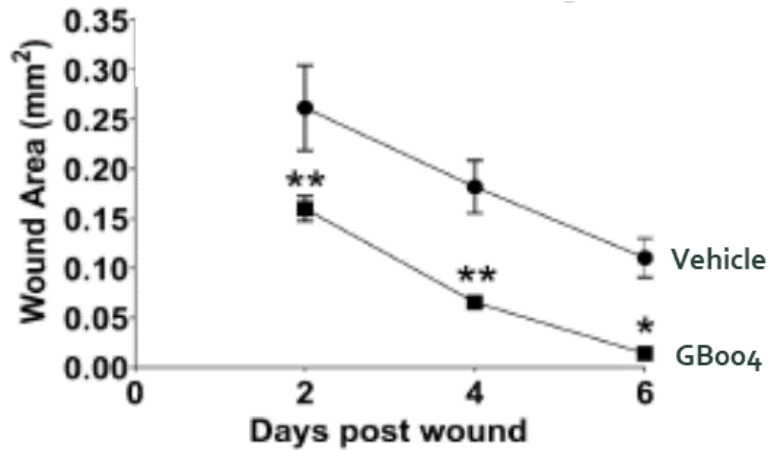
# GB004 Targets the HIF-1 $\alpha$ Pathway, Demonstrating a Unique Mechanism for Mucosal Healing in Ulcerative Colitis

- GB004 stabilizes HIF-1 $\alpha$  specifically in gut tissue and sustains HIF-1-driven gene expression
- HIF-1 $\alpha$  plays a crucial role in the maintenance of epithelial barrier integrity and function
- GB004 facilitates local immune homeostasis in intestinal epithelial cells and promotes mucosal healing



# Treatment with GB004 Leads to Accelerated Barrier Repair and Intestinal Wound Healing in Mouse Model

## In Vivo Wound Healing Assay



## Key Takeaway

GB004 leads to accelerated re-epithelialization and crypt reformation of disrupted intestinal epithelial tissue

## Day 2 Endoscopy

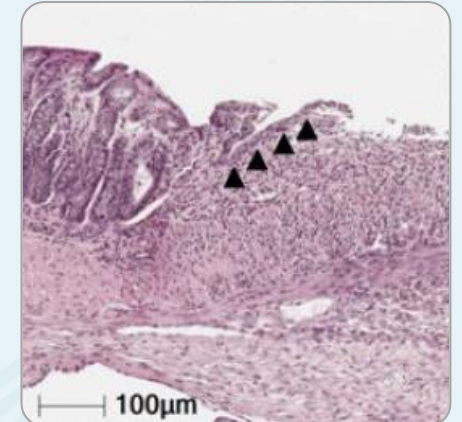
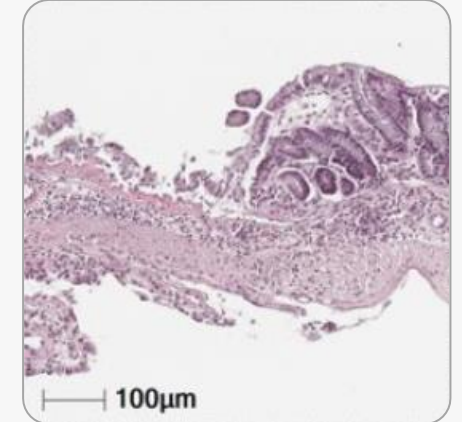
Vehicle



GB004



## Day 2 Histology



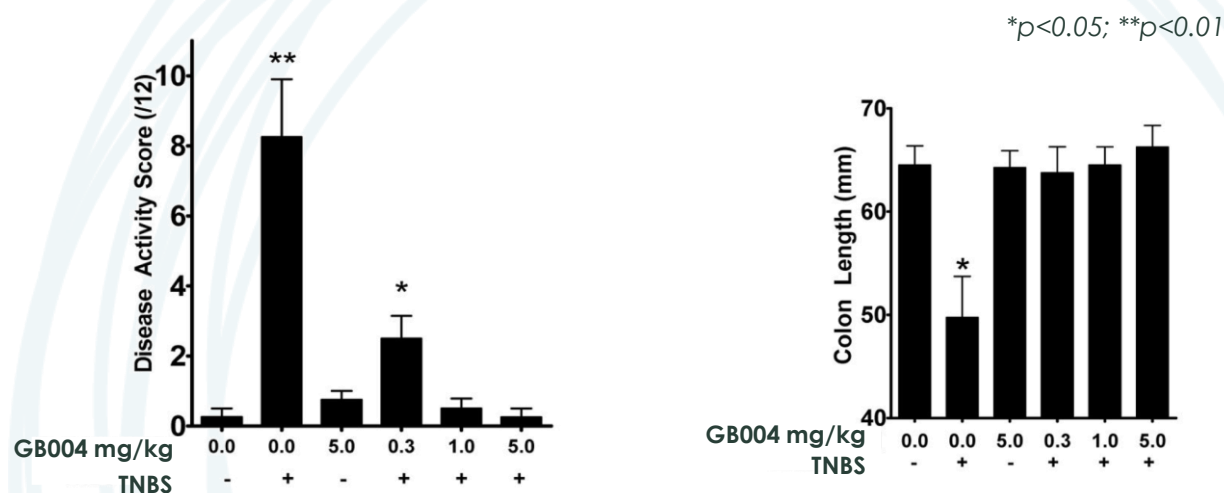
▲ Areas of pathological healing, incl. re-epithelialization and crypt reformation



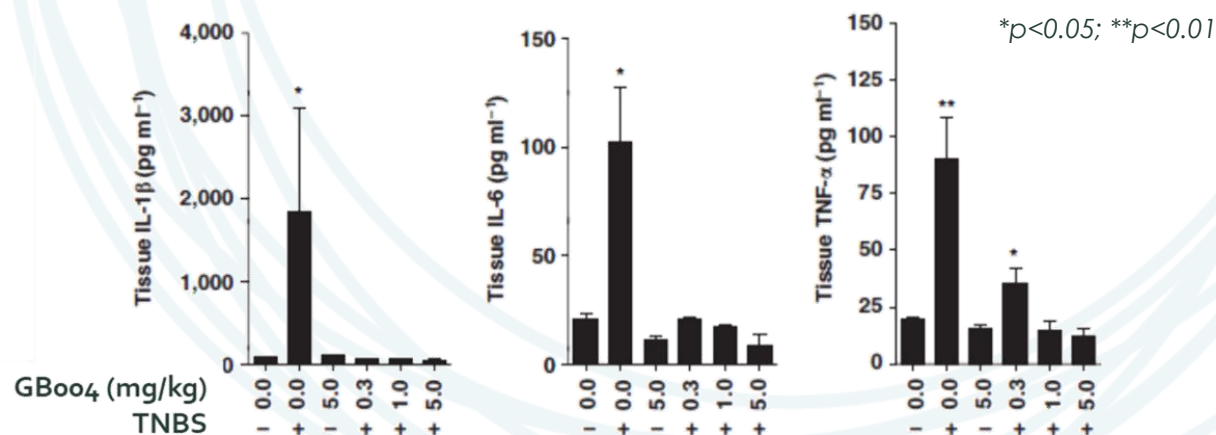
# GB004 Leads to Epithelial Reconstitution and Disease Activity Improvement in TNBS Colitis Mouse Models



## Disease Activity Score and Colon Length

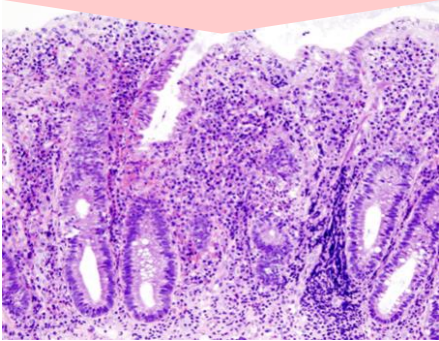


## Colon Inflammatory Cytokines

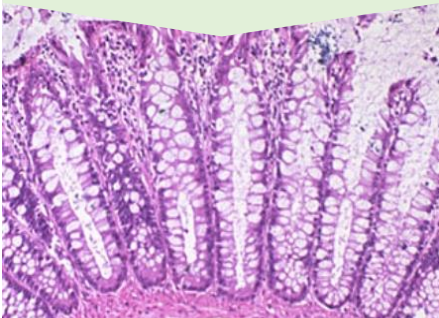


# Histologic Healing is Predictive of Favorable Patient Outcomes

**Severe Histologic Activity**



**Histologic Remission**



**Histological Remission and Healing in UC is Predictive of...**

☑ Steroid free clinical remission

☑ Reduction in disease relapse

☑ Reduction in hospitalizations

☑ Reduction in corticosteroid use

**Long-term clinical, endoscopic, & histological remission**

**More favorable disease course**

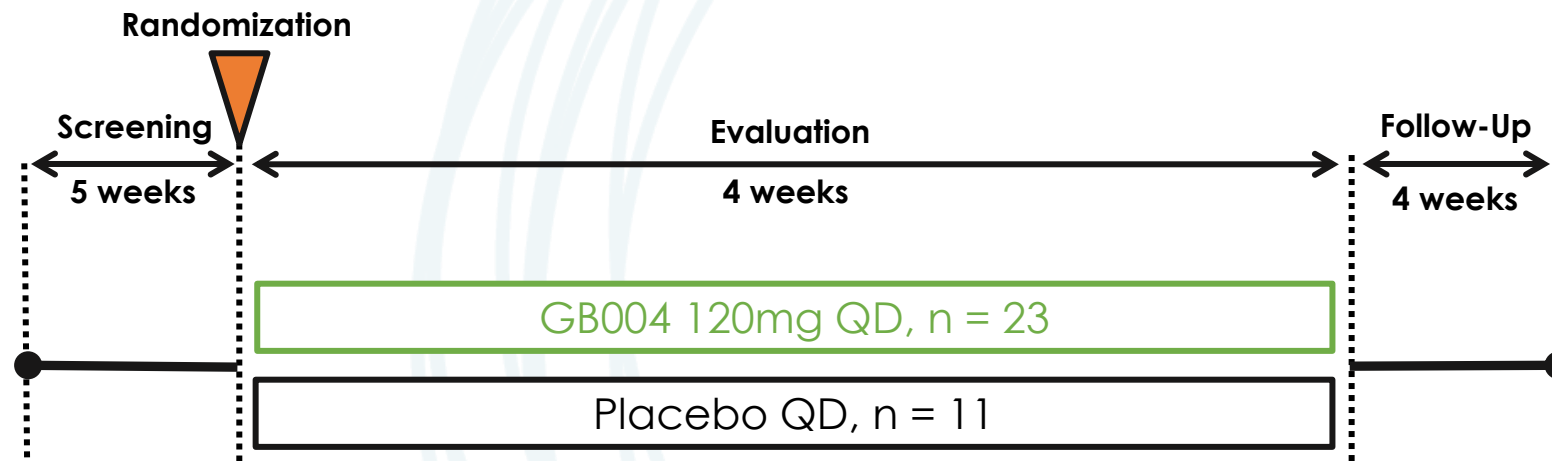
# Phase 1b Utilized the Roberts Histopathology Index

- Entry criteria for GB004 Phase 1b **required active histology as assessed by RHI**
- RHI developed using **4 most reliable indices of Geboes Score**
- Emphasizes presence of **active neutrophils**, the defining histologic hallmark of ulcerative colitis
- Scored 0-33
- Achievement of **histological remission** in the GB004 Phase 1b required:
  - 1) Total score less than or equal to 3, and;
  - 2) Zero on both neutrophil scores

Calculation of Roberts Histopathology Index (RHI) <sup>(1)</sup>	
<b>Chronic inflammatory infiltrate</b> (1 x score [0-3])	0 = No increase
	1 = Mild but unequivocal increase
	2 = Moderate increase
	3 = Marked increase
+	
<b>Lamina propria neutrophils</b> (2 x score [0-3])	0 = No increase
	1 = Mild but unequivocal increase
	2 = Moderate increase
	3 = Marked increase
+	
<b>Neutrophils in epithelium</b> (3 x score [0-3])	0 = None
	1 = <5% of crypts involved
	2 = <50% of crypts involved
	3 = >50% of crypts involved
+	
<b>Erosions or ulcerations</b> (5 x score [0-3])	0 = No erosion, ulceration, or granulation tissue
	1 = Recovering epithelium + adjacent inflammation
	2 = Probable erosion – focally stripped
	3 = Ulcer or granulation tissue

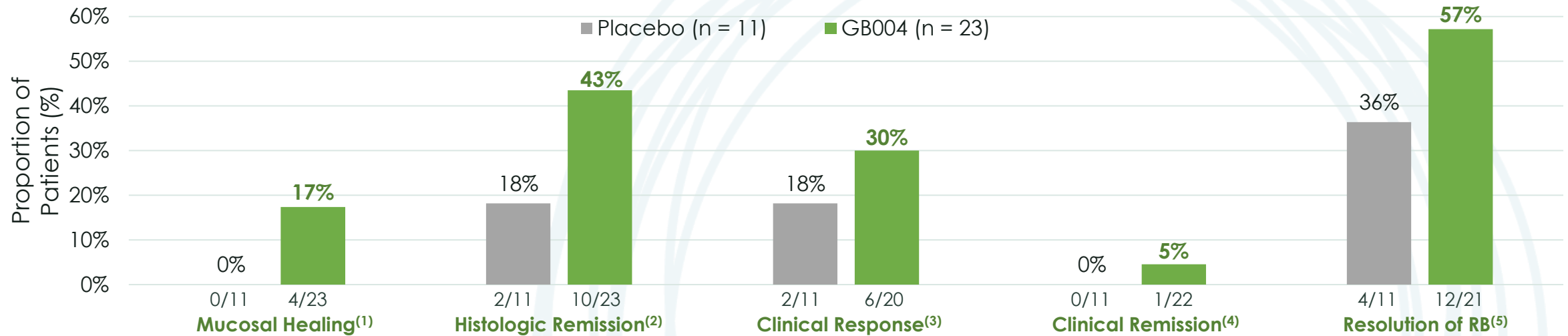
# Completed GB004 Phase 1b Study Design

**A Phase 1b, signal seeking, placebo-controlled study to evaluate the safety and pharmacokinetic profile of GB004 in adult patients with UC**



<b>Patient Population</b>	Adult patients with active (mild disease or greater) UC, with inadequate response or intolerance to 5-ASA or steroids and evidence of active inflammation by histology
<b>Endpoints</b>	<b>Primary:</b> Safety, tolerability <b>Secondary:</b> PK <b>Exploratory:</b> biomarker analysis, and histologic, endoscopic, and clinical indices to evaluate biological effect

## 28-Day Phase 1b Results: Promising Trends in Exploratory Efficacy Outcomes Observed, Especially Related to Epithelial Lining Healing and Repair



Evidence of Clinical Activity with 120mg QD Dose

- **Mucosal healing** (histologic remission + endoscopic improvement) and **clinical remission** reported in GB004 arm; none reported in placebo arm
- Higher rates of **histologic remission**, **clinical response**, and improvement in **rectal bleeding** in GB004 arm compared to placebo

**Full results presented at UEGW Virtual 2020**

Histology, endoscopic improvement, and mucosal healing were evaluated individually in two segments of the large intestine: the sigmoid colon and rectum; RB = rectal bleeding

1) Mucosal healing: achievement of both histologic remission and endoscopic improvement in the same segment. Analysis of patients with mucosal healing in sigmoid or rectum.

2) Analysis of patients with histologic remission in sigmoid or rectum.

3) Three patients on the GB004 arm were unevaluable for clinical response (2 w/baseline rectal bleeding scores of 0, 1 w/baseline sigmoid endoscopic score of 0).

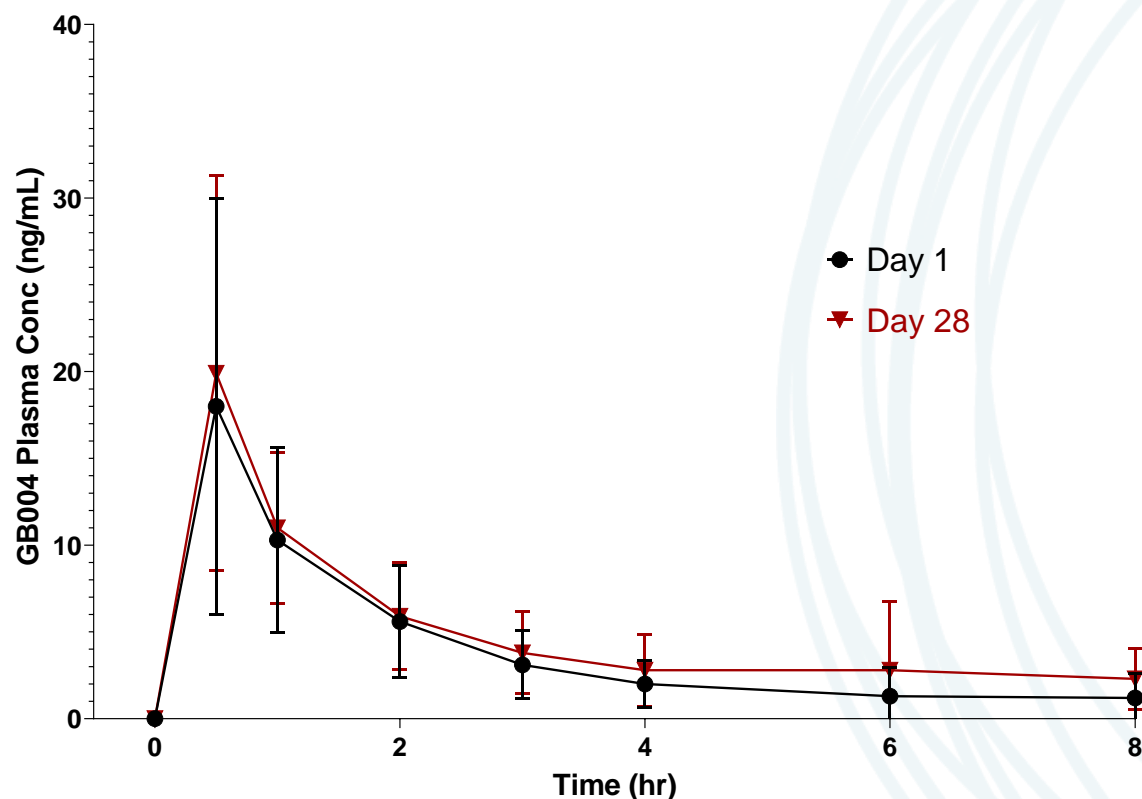
4) One patient on the GB004 arm was unevaluable for clinical remission (baseline sigmoid endoscopic score of 0).

5) Two patients on the GB004 arm were unevaluable for RB resolution (baseline RBS of 0).

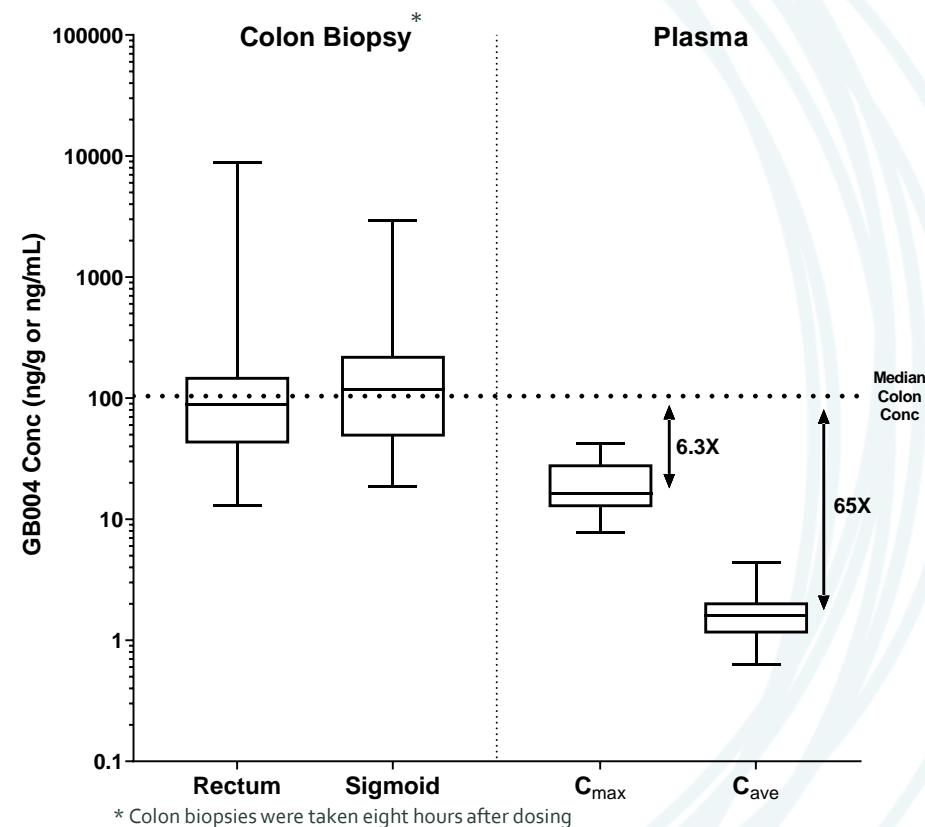


# Phase 1b Results Consistent with Expectations: Gut-Targeted PK

## Rapid Clearance and Minimal Accumulation Observed



## Multi-fold Higher Concentrations Observed in the Gut



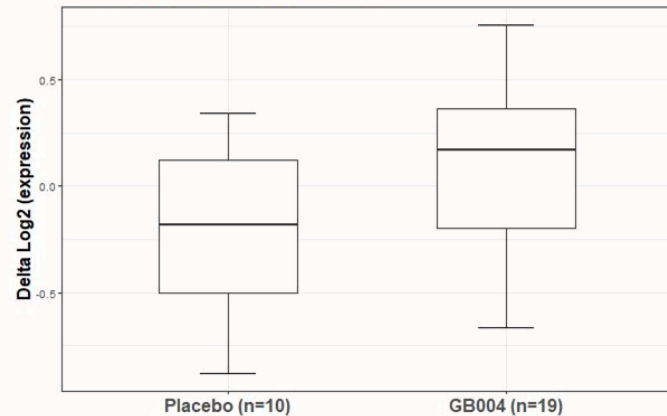
## Gut-Targeted PK Profile

- Minimal to no accumulation of GB004 after 28 days QD dosing
- Colon tissue concentrations exceed plasma concentrations
  - ~6 times  $C_{max}$  and ~65 times  $C_{average}$

# Increased Expression of Genes Associated with Barrier Restitution and Integrity Observed in GB004 Arm Compared to Placebo

## Epithelial Restitution

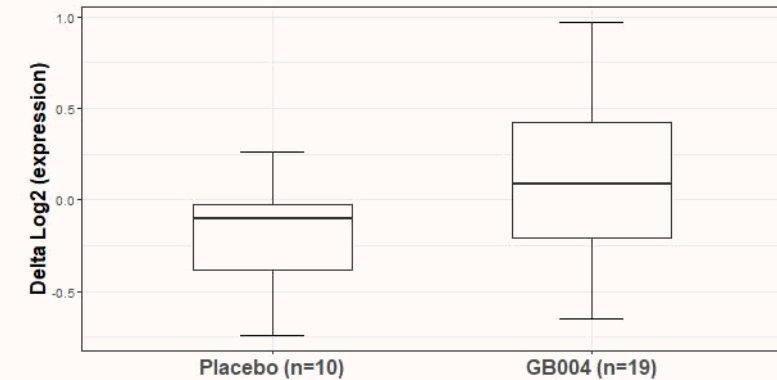
### Integrin- $\alpha 6$ (ITGA6)



- Increase in ITGA6 consistent with increased barrier restitution and migration

## Barrier Integrity

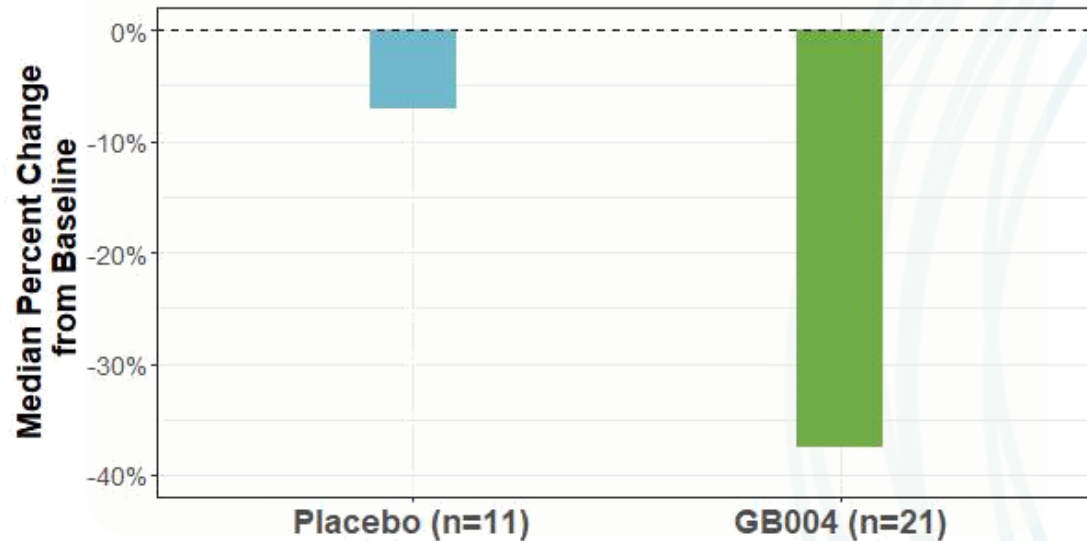
### Tight Junction Protein-1 (TJP1)



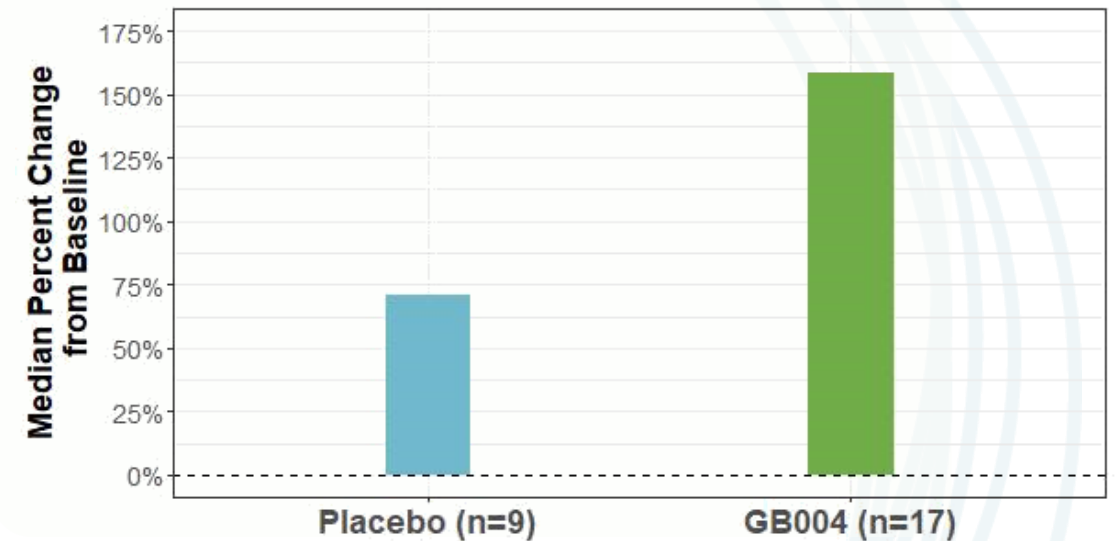
- Increases in TJP1 consistent with restoring the integrity of the gut mucosal barrier

# Stool Biomarkers in GB004 Group Indicate Decreased Inflammation and Improved Epithelial Integrity

↓ Decrease in Fecal Calprotectin

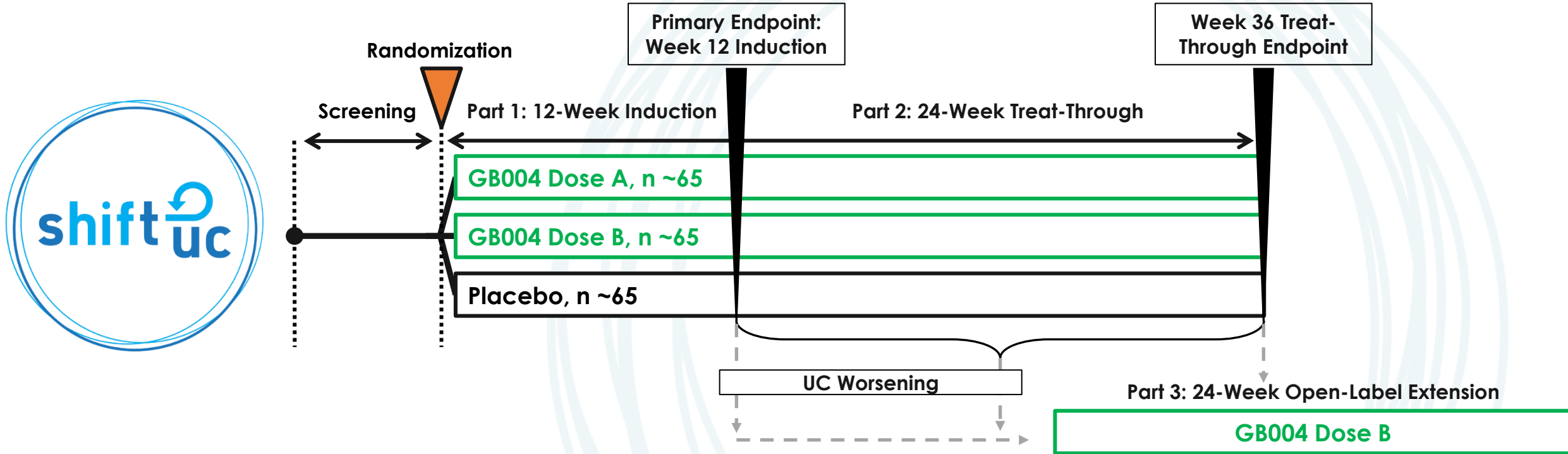


↑ Increase in Secretory IgA (sIgA)



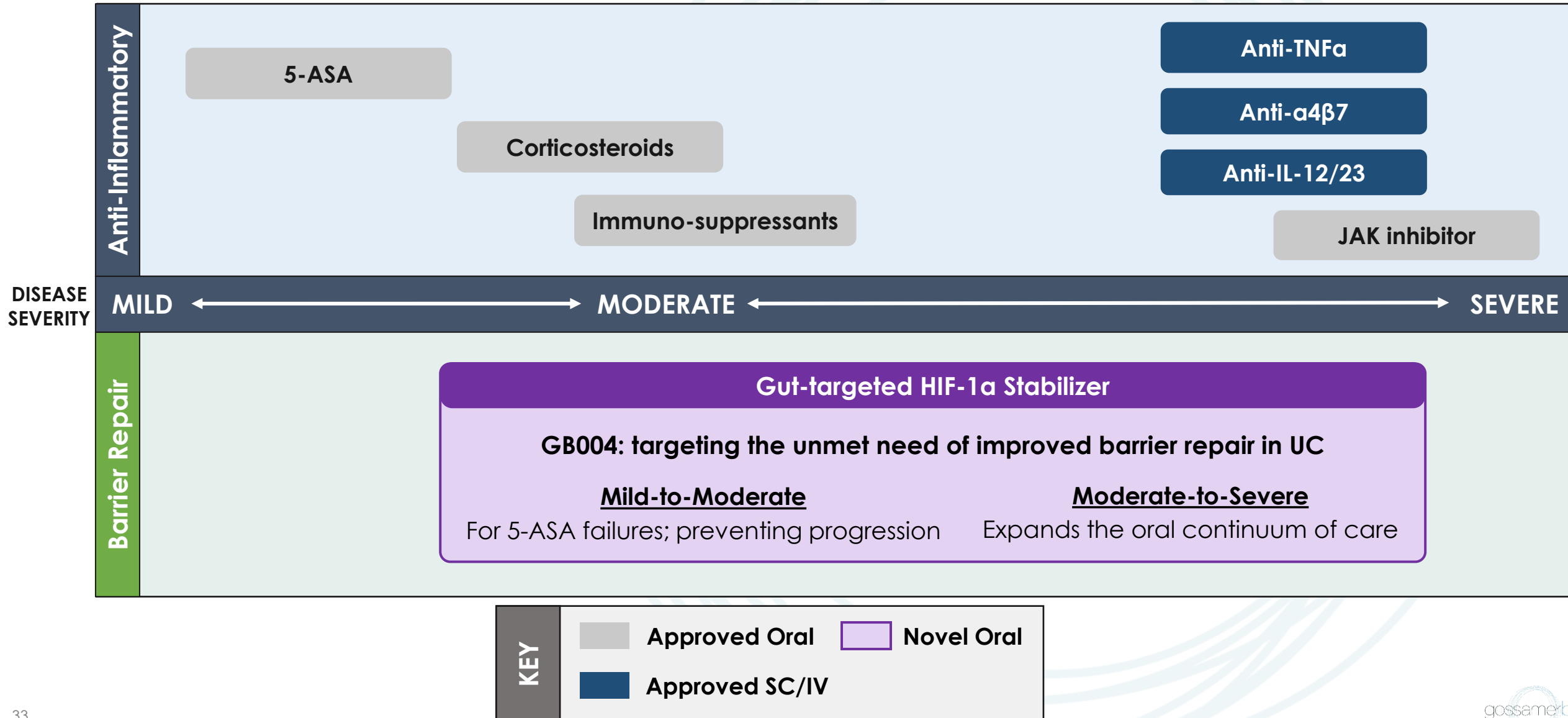
- Decrease in fecal calprotectin is consistent with decreased bowel inflammation
- sIgA increase is consistent with improved gut epithelium and local immune defense

# SHIFT-UC Phase 2 Study In Active UC: Measuring Short- and Long-Term Results of Therapy



<b>Patient Population:</b>	<ul style="list-style-type: none"> <li>Adult UC patients with mild-to-moderate UC, Mayo 5-10, Endoscopic score (MES) <math>\geq 2</math>, RBS <math>\geq 1</math>, Stool Freq <math>\geq 1</math></li> </ul>
<b>Objectives:</b>	<ul style="list-style-type: none"> <li>Assess efficacy and safety of tablet formulation in UC</li> <li>Demonstrate proof of concept for GB004 MoA</li> </ul>
<b>Endpoints:</b>	<ul style="list-style-type: none"> <li><b>Primary:</b> Clinical Remission at 12 weeks</li> <li><b>Secondary:</b> Clinical Response, Mucosal Healing, Endoscopic Improvement, Histologic Remission</li> <li><b>Other:</b> Safety and tolerability, Disease Clearance, serum, fecal, tissue biomarkers</li> </ul>

# GB004 Has the Potential to Address Unmet Needs Across the Severity Spectrum





# Corporate Overview and Milestones



# Financial Overview

Cash, Cash Equivalents and Marketable Securities ~\$406mm  
(As of 6/30/21)

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Debt, *Related to Line of Credit* ~\$30mm  
(As of 6/30/21; initial tranche of \$150 million debt facility, announced 5/2/19)

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Additional Debt Capacity, *Related to Line of Credit* ~\$120mm  
(As of 6/30/21; remaining capacity of \$150 million debt facility, announced 5/2/19)<sup>(1)</sup>

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Principal of Convertible Notes Outstanding ~\$200mm  
(As of 6/30/21)

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Common Shares Outstanding ~75.9mm  
(As of 8/5/21)

mm = millions.

1) Accessible subject to the achievement of certain clinical development milestones and other customary conditions.

# Upcoming Milestones for Clinical Programs

Indication	Milestone	Timing
Seralutinib (Pulmonary Arterial Hypertension)		
PAH	Phase 2 TORREY Study Topline Results	1H 2022*
GB004 (Inflammatory Bowel Disease)		
UC	Phase 2 <b>SHIFT</b> -UC Study Topline Results	1H 2022*
Internal Research Programs		
Autoimmune, Oncology, Inflammation	Initiate Clinical Trial for One Additional Product Candidate	Within 12 months