



## The Wnt Company – Targeted Regeneration

August 15, 2022

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# From Wnt Gene Discovery to the Clinic

## Scientific Discovery

1<sup>st</sup> **Wnt** gene **discovered**  
(Roel Nusse, Harold Varmus)

1982

## Biologic Validation

**Surrozen founded**  
by The Column Group in collaboration with preeminent Wnt biologists

2016

2013

**Breakthrough Prize in Life Sciences**  
awarded to Hans Clevers for  
"describing the role of Wnt signaling in tissue stem cells"

2017

**Breakthrough Prize in Life Sciences**  
awarded to Roel Nusse for  
"pioneering research on the Wnt pathway"

## Therapeutic Transformation

**First Wnt** modulating **antibody approved**, Amgen's Evenity (romosuzumab) for osteoporosis

2019

2020

**Publication** of Surrozen's **SWAP** and **SWEETS** antibody platform discoveries

Surrozen **progresses targeted Wnt therapeutics** platform; **initiated FIH trials Q2'22**; **Published SZN-1326 preclinical data**

2022+

# What is Wnt Biology?

Wnt Signaling Essential to Many Cell and Tissue Types

## Fundamental Signal Transduction Biology

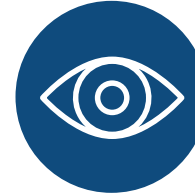
### Wnt pathway central to:

- Regulating stem cell renewal, proliferation & differentiation
- Regenerating tissue

### Wnt proteins generate array of Wnt signaling critical for:

- Shaping tissues during development
- Maintaining tissue architecture
- Repairing injured tissue

## Many Organs and Tissues Require Wnt signaling



Eye



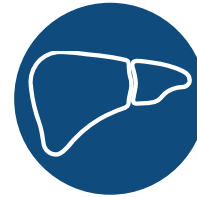
BBB



Lung



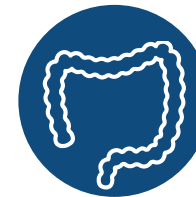
Cochlea



Liver



Pancreas

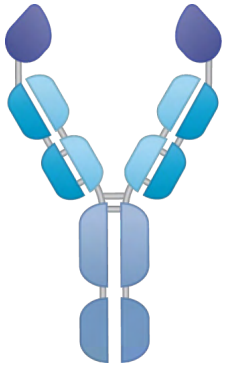


GI



Kidney

# Surrozen – Leaders in Wnt Biology



## Vision

Selectively target Wnt pathway to harness the body's own repair mechanism

## Initial focus

Wnt related severe or acute diseases: GI, Liver, Ophthalmology

## First in class

Proof of mechanism / biology, preclinical proof of safety with clinical trials underway for SZN-1326 and SZN-043

## Lead Product Candidates

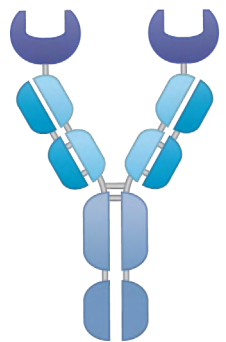
- Earlier than planned initiation of two clinical trials
- ✓ SZN-1326: Inflammatory Bowel Disease (initiated Q2'22)
  - ✓ SZN-043: Severe Liver Disease (Initiated Q2'22)
  - SZN-413: Ophthalmology

## Proprietary platform

Unparalleled capabilities; demonstrated preclinical POC for several programs

## Well positioned

\$93M cash balance



# Our Novel Approach Overcomes Previous Challenges

Paving the Way to Targeted Antibody Regeneration

## Potential first synthetic soluble Wnt mimetics

**Selectivity:** Target specific Fzd or cell surface receptors

**Potency:** Confer potency through multivalent binding

**Safety:** Mimic normal physiologic responses

**Manufacturing:** Easily manufacturable leveraging typical antibody methods with high yields

*Validation of Our Prominent Role in Wnt Biology Breakthroughs*

**nature**

Surrogate Wnt agonists that phenocopy canonical Wnt and  $\beta$ -catenin signaling

 CellPress

Development of Potent, Selective Surrogate Wnt Molecules and Their Application in Defining Frizzled Requirements

**SCIENTIFIC  
REPORTS**

nature research

Tissue-targeted R-spondin mimetics for liver regeneration

**Science**

Structural Basis of Wnt Recognition by Frizzled

# Fully Integrated, Repeatable Discovery Capabilities

Potential to Transform Patient Outcomes

## Internal Capabilities

**Wnt Biology Expertise**

**Wnt Modulating  
Antibody Engineering**

**Wnt Pathway Profiling**

## Scientifically Driven Strategy

Scientifically Driven Strategy

~60 R&D employees

~ 50% PhD, MDs or PhD/MDs

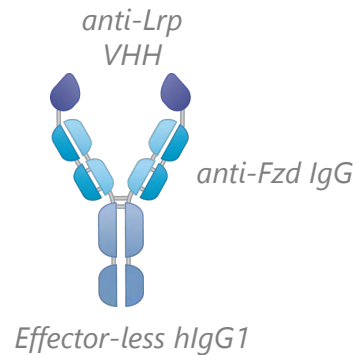
Focus on diseases with compelling Wnt biology

R&D opportunities for deep/broad pipeline targeting Wnt pathway

Employ models with translatability to human disease

# Proprietary Technologies Enable Selective Wnt Signaling

## SWAP Technology

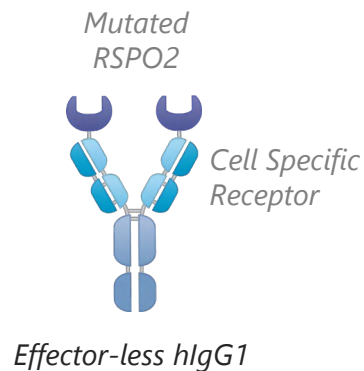


**Mimic normal** physiologic **response** (natural Wnt or natural R-spondin)

**Applied** in diseases with **deficient Wnt ligand** or **Wnt signaling**

**Customized** for each disease state

## SWEETS Technology



**Targeted** with Fzd receptor selectivity or cell specific receptors



# Deep Wnt Signaling Expertise Supports Productive & Expanding R&D Pipeline

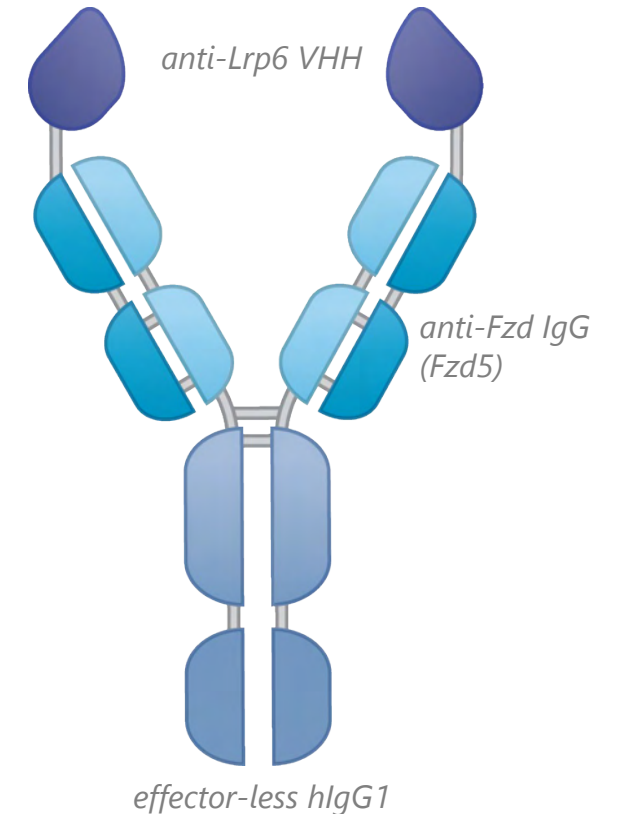
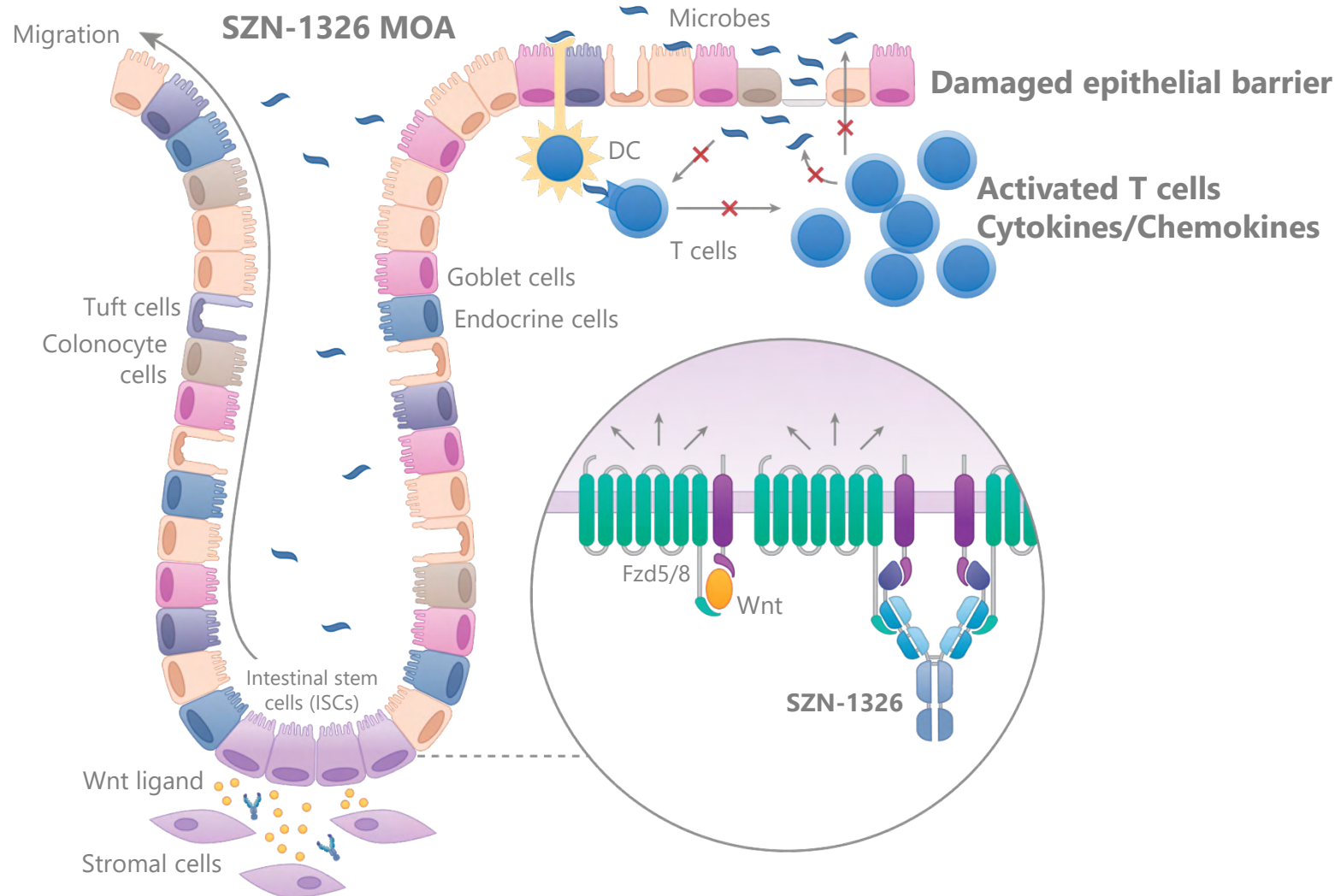
Lead Programs	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Phase 3	Regulatory	Next Milestone
<b>SZN-1326</b>	Moderate to Severe IBD							Initiated clinical trial Q2'22
<b>SZN-043</b>	Severe Alcoholic Hepatitis							Initiated clinical trial Q2'22
<b>SZN-413</b>	Retinopathies							Nominated candidate Q1'22

## Research Programs

Tissue	Indications	Discovery	Proof of Concept	Lead Candidate/s
Lung	IPF			
Lacrimal Gland	Severe Dry Eye (Sjögren's)			
Cornea	Fuchs' Dystrophy			
Lung	COPD			
Pancreas	Type 1 Diabetes			
Skin	Wound Healing			

# SZN-1326 – Intestine Targeted Epithelial Restoration

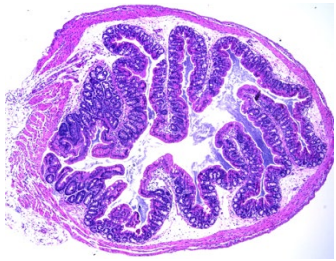
Mechanism Suggests Potential New Treatment Paradigm in Inflammatory Bowel Disease



# SZN-1326 – Potential to Transform Treatment Paradigm in UC

Targeted antibody designed to repair epithelial barrier; induce mucosal healing

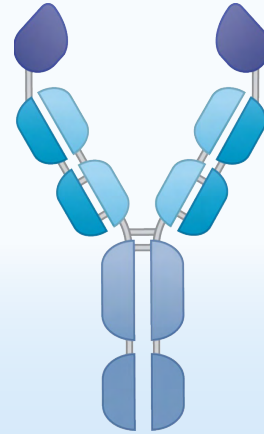
## Background



### Moderate to Severe Ulcerative Colitis

- Characterized by large intestine inflammation and ulcers
- Debilitating: frequent diarrhea, bloody stools, weight loss, dehydration, and anemia
- Complications from severe and chronic inflammation can become life-threatening
- SOC: Treated with anti-inflammatory agents
  - Takes months to induce remission
  - Achieve remission in < 50% and mucosal healing in < 20%
  - Fail multiple therapies

## Our Solution



### MOA: Designed to repair epithelial barrier & induce mucosal healing

- Dysregulation of Wnt signaling may play a role in abnormal epithelial healing in IBD
- Mucosal healing associated with better patient outcomes

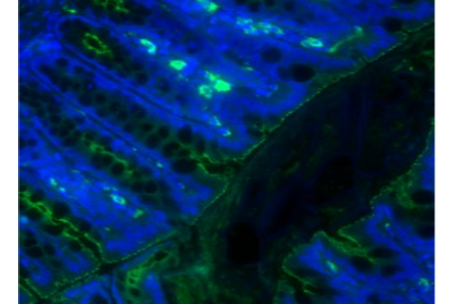
**Targeted: Selectively targets Fzd5 abundant in intestinal epithelium**

# Intestine-Targeted Regeneration and Functional Improvement

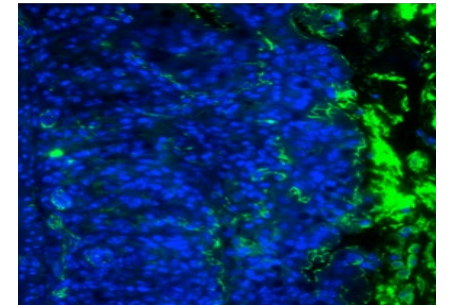
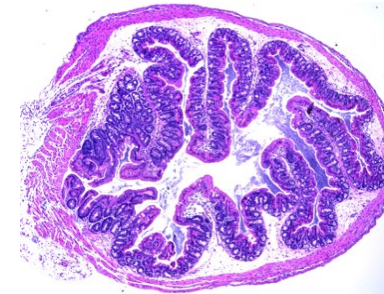
## Differentiated Preclinical Data

- Repairs damaged colon epithelium
- Induces mucosal healing
- Reduces inflammation
- Improves disease activity index
- Better activity than other anti-inflammatory agents including biologics
- No adverse findings in GLP tox studies

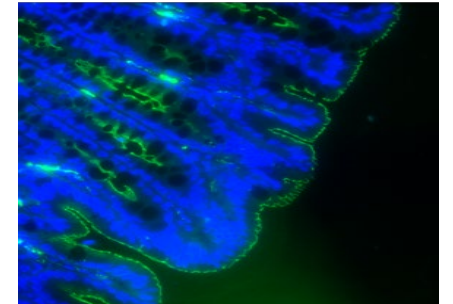
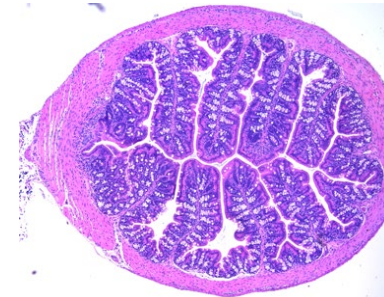
**Normal**  
(No DSS Damage)



**Damaged**  
(DSS Damage)



**Restored**  
(DSS Damage + SZN-1326)



# SZN-1326 Phase 1 Trial Overview

Focus - Proof of Clinical Concept in Ph 1b Ulcerative Colitis  
Phase 1 Trial Ongoing

## Three-Part Ph 1 Randomized Trial Design

### Ph 1a – SAD

Healthy volunteers

N = up to 44

Up to 5 randomized IV cohorts, and 2 SC cohorts

### Ph 1a – MAD

Healthy volunteers

N = up to 24

Up to 3 randomized cohorts (IV)  
Dosing for 4 doses

### Ph 1b – MAD

Moderate-severe patients with UC

N= up to 24

*Proof of clinical concept*

Up to 3 randomized cohorts dosed IV weekly or biweekly for 12 wks. Follow-up - 24 weeks

## Key Endpoints

### Ph 1a SAD/MAD

- Safety
- PK/PD
- ADA

### Ph 1b UC MAD

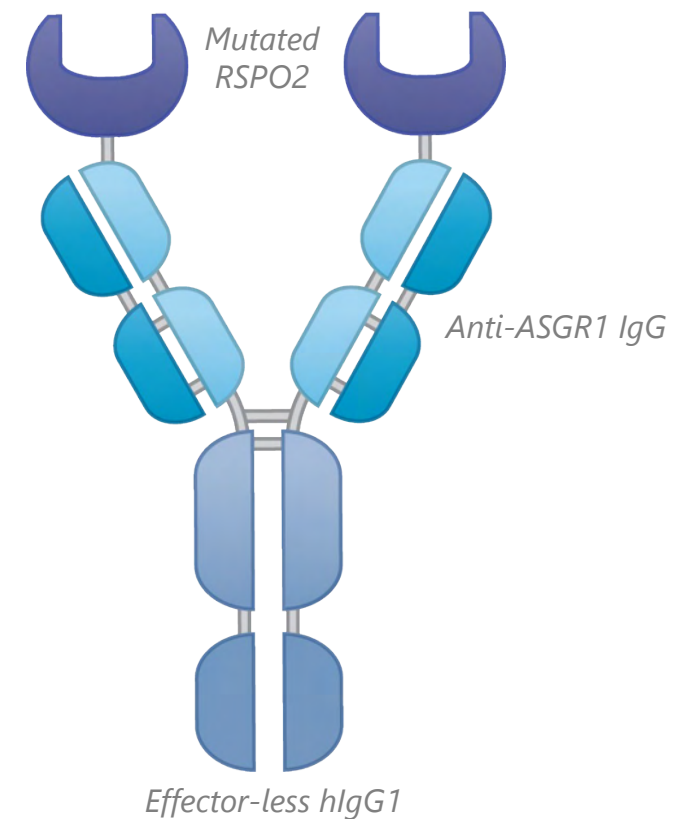
- Clinical remission and response
- Endoscopic remission
- Histologic remission
- UC-100
- PD markers



# Potential for First Approved Treatment for Severe Alcoholic Hepatitis

## Liver Specific Wnt Activation and Regeneration

### SZN-043 MOA

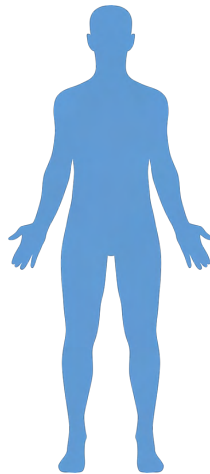


# SZN-043 Potential to Transform Patient Outcomes in Severe AH

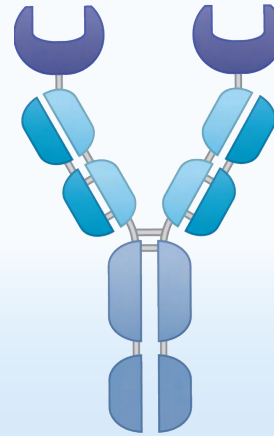
Targeted antibody designed to induce hepatocyte proliferation and improve liver function

## Background

- Serious form of acute decompensated alcoholic liver disease caused by heavy alcohol use
- Leads to liver cell death, damage and subsequent inflammation
- 90-day mortality of 30%
- ~130K hospitalizations per year
- No approved treatments
  - Steroids: contra-indicated in > 50% of patients; no benefit at 3 months+
  - Liver transplants: limited supply, costly and often denied



## Our Solution



### MOA: SZN-043 designed to address underlying pathophysiology

- Hepatocyte proliferation correlated with increased survival
- Upregulation of Wnt signaling implicated in improved liver function

**Targeted: Selectivity achieved through inclusion of ASGR1**

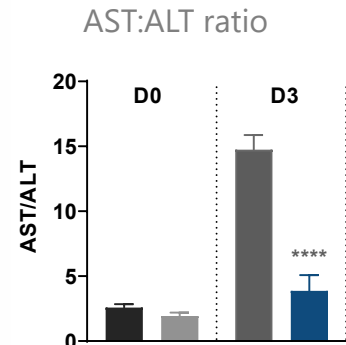
# SZN-043 In Vivo Effects

Liver Specific Proliferation, Functional Improvement, Fibrosis Regression

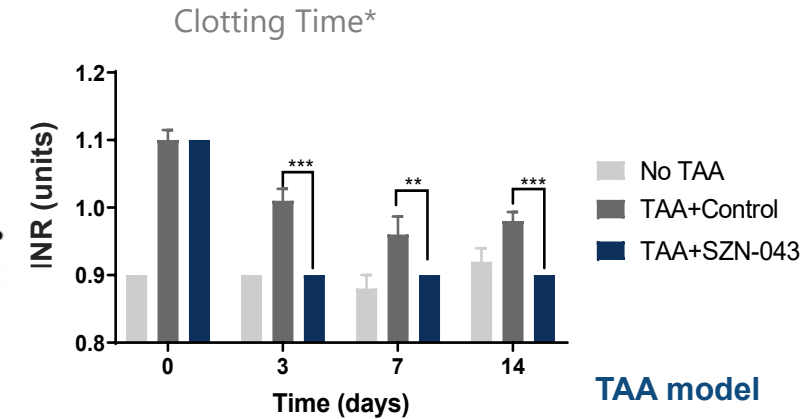
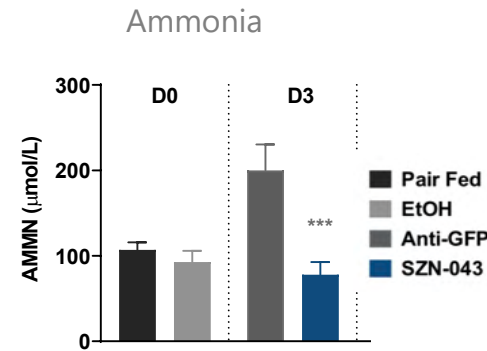
## Compelling Preclinical Data

- >25 preclinical studies conducted
- Selectively activates Wnt Signaling
- Induces hepatocyte proliferation
- Rapidly improves liver function
- Reduces markers of liver injury & inflammation
- No adverse findings in GLP tox studies

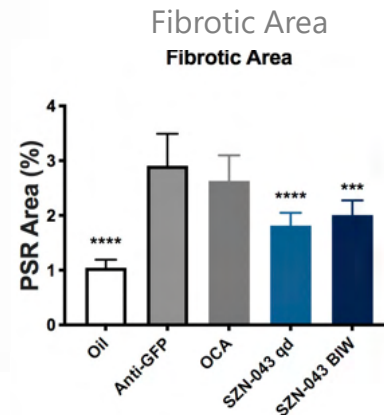
## Improvement in Liver Function



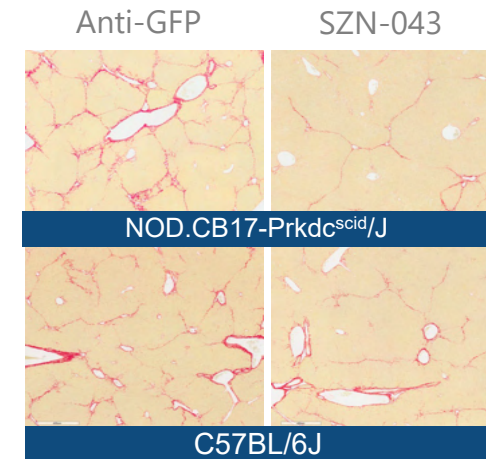
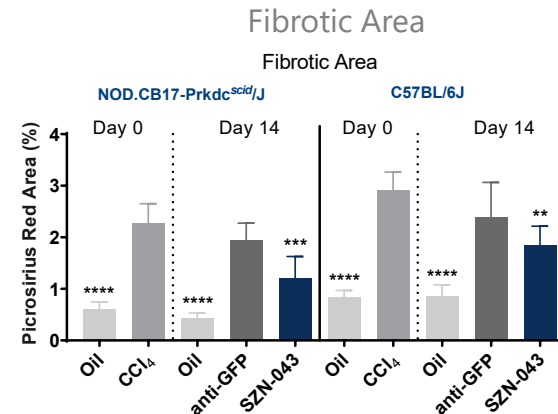
Alcohol liver injury model



## Regression of Fibrosis



\*SZN-043 V.2 in TAA Model





# SZN-043 Phase 1 Clinical Trial Overview

Focus – Proof of Concept in Early Cirrhosis; Potential Expedited Regulatory Pathway  
Phase 1 Trial Ongoing

## Multi-Part Ph 1 Randomized Trial Design

### Ph 1a – SAD

Healthy volunteers

N = up to 24

Up to 4 randomized cohorts (IV)

### Ph 1b – SAD/MAD

Early cirrhosis

N = Up to 16

Up to 2 randomized cohorts (IV)

PD markers indicative of liver proliferation and function improvement

### Ph 1b

Severe Alcoholic Hepatitis (AH)

N = up to 30

Early read on LILLE score and MELD scores – high survival correlation

Further *proof of clinical activity*; potential for Fast Track and Breakthrough Designation



## Key Endpoints

### Ph 1a SAD:

- Safety, ADA
- PK/PD (including methacetin breath test)

### Ph 1b SAD/ MAD - (early cirrhosis)

- Safety
- PK/PD (including methacetin breath test, Hepquant)
- ADA

### Ph 1b Severe AH MAD

- Lille and MELD scores
- Mortality

# Platform Broadly Applicable Across Wide Spectrum of Diseases

## Current Focus Current Technology



### Gastrointestinal/Liver

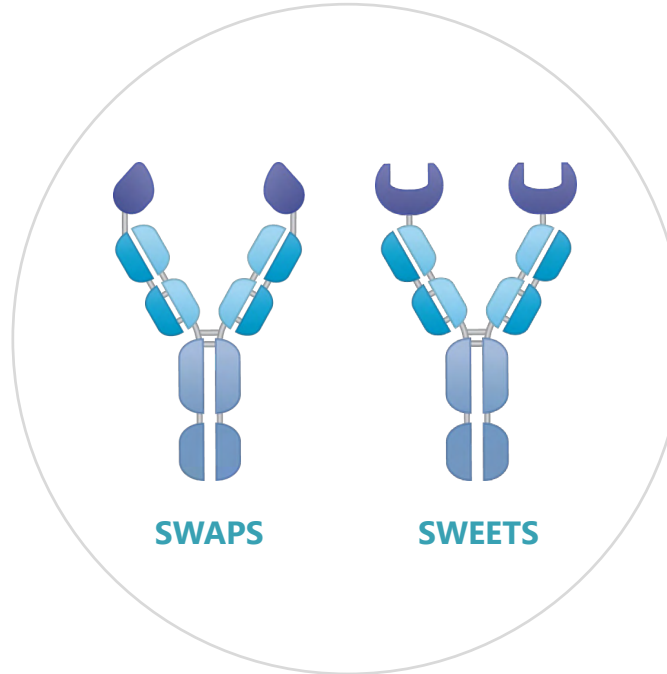


UC, Crohn's, SAH, ACLF



### Ophthalmology

Wet AMD, Diabetic Retinopathy, DME, Severe Dry Eye (Sjögren's)



SWAPS

SWEETS

## Future Opportunities Current Technology

### Kidney

FSGS, PKD



### Lung

IPF, COPD



### Neurology

MS, Stroke



## Current Focus Future Technology

## Future Opportunities Future Technology

# Robust Activity in Multiple Preclinical Ophthalmology Models

## SZN-413 (mono Fzd 4) lead candidate for retinopathy – addresses retinal non-perfusion and vascular leakage simultaneously

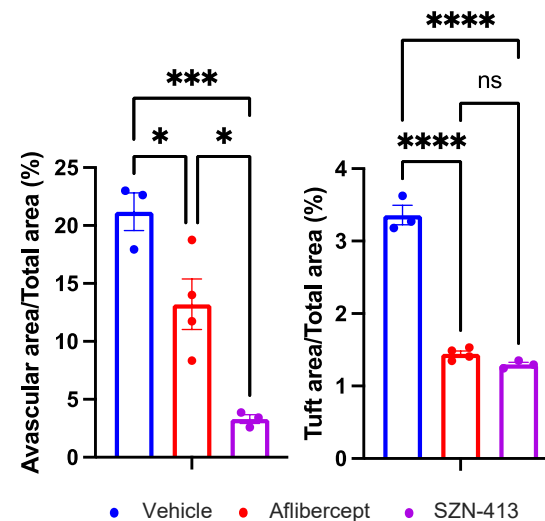
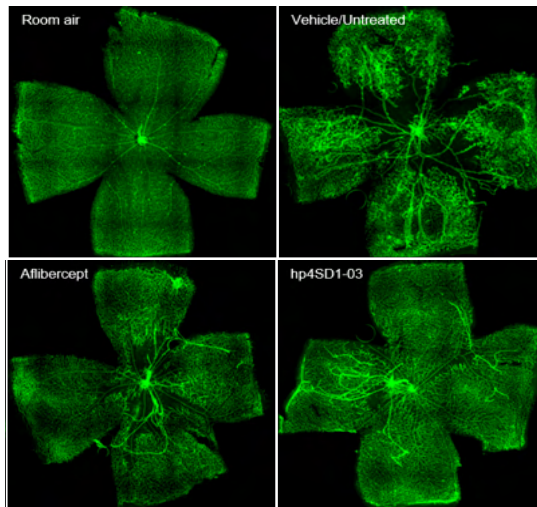
*Fzd4 signaling plays critical role in retinal vasculature integrity*

Stimulated Wnt signaling

Increased tight junction protein expression in endothelial cells

Restored norrin function in Ndp KO mice

Reduced avascular area & pathologic NV tuft formation in OIR model; reduced vascular leakage in VEGF-induced retinal model



## Lacrimal Gland (LG) Program

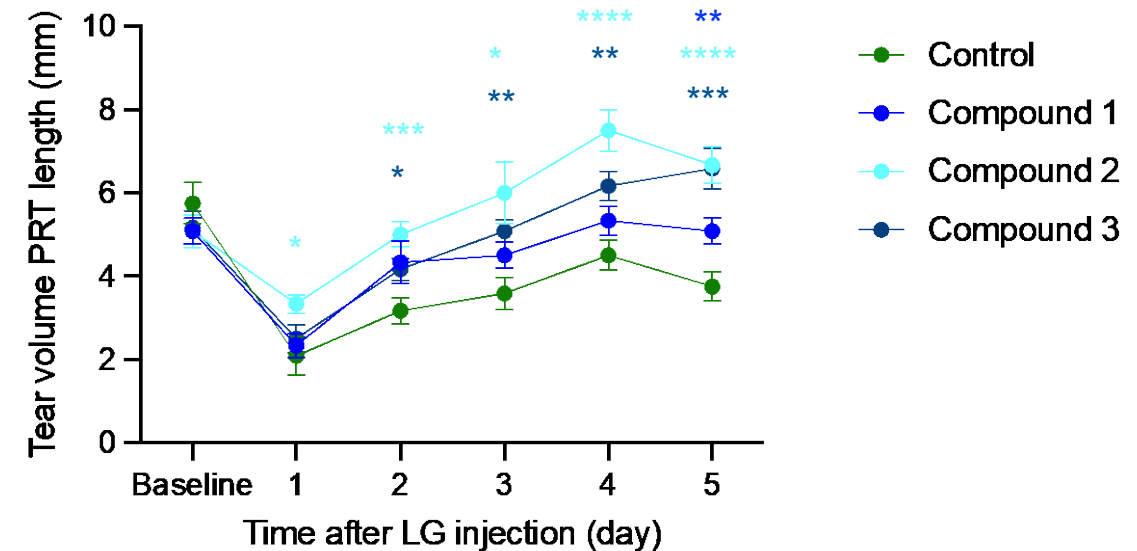
*Tear-producing glands rely on Wnt signaling for function*

Stimulated Wnt signaling

Effect observed in lacrimal and meibomian gland

Increased tear production within 2 days in IL-1a lacrimal gland model

### Tear secreted by ipsilateral eye



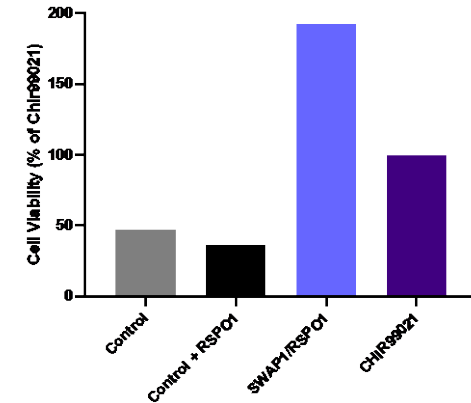
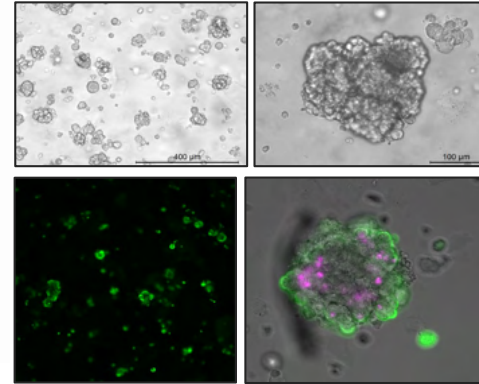
# Lung Regeneration Program

Recent Discoveries Suggest Potential Role for Wnt in Treatment of IPF and COPD

## Compelling Preclinical Data

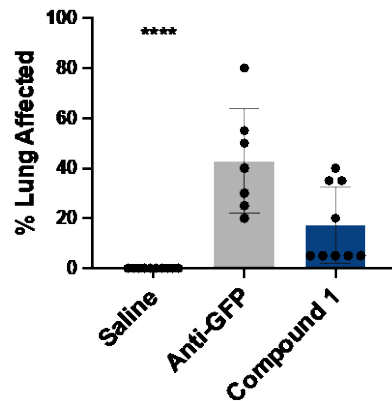
- Activates Wnt Signaling
- Expands alveolar AT2 cell organoids
- Reduced injury and improved fibrosis in the acute bleomycin model

## Expands AT2 Cell Alveolar Organoids

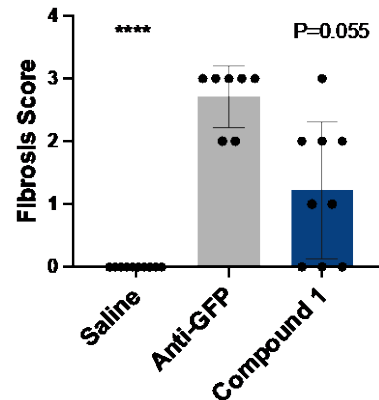


## Reduction of Fibrosis

% Lung affected  
(mice excluded with <5% BW change)

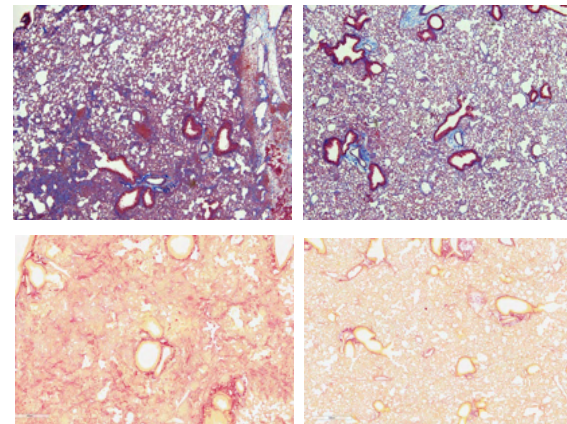


Fibrosis score  
(mice excluded with <5% BW change)

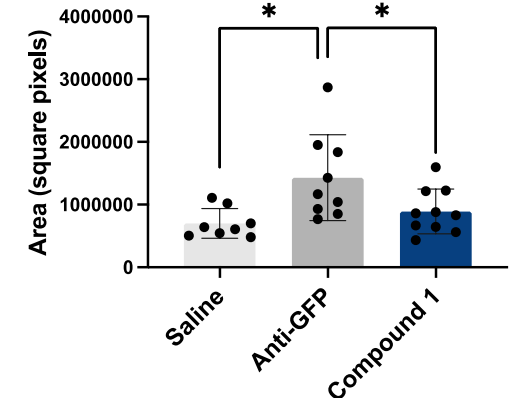


Anti-GFP

Surrozen



ACTA2 quantification



# Near Term Outlook and Potential Milestones

Multiple Clinical Milestones with Potential for Early Proof of Concept

<b>SZN-1326</b> Intestine	<b>2021</b> Completed IND-enabling Toxicology Studies	<b>Q2' 2022</b> Initiated Phase 1a in Healthy Volunteers [HV] (Q2'2022)	<b>2023</b> Phase 1b in Ulcerative Colitis Patients
<b>SZN-043</b> Liver	<b>2021</b> Completed IND-enabling Toxicology Studies	<b>2022</b> Initiated Phase 1a in HV (Q2'2022) Initiate Phase 1b in Early Cirrhosis	<b>2023</b> Phase 1b in Severe AH Patients
<b>SZN-413</b> Retinopathies		<b>Q1'2022</b> Lead Candidate	
<b>Research Programs</b>		<b>2022</b> Nominated Lead Candidate (SZN-413)	<b>2023+</b> Nominate Additional Lead Candidate(s) and File INDs

REPAIR. RESTORE. RENEW.™



# The Wnt Company – Targeted Regeneration

2022



# Glossary

ACLF – Acute-on-chronic liver failure–

ACTA2 – actin protein

ADA – Anti-drug antibodies

AH – Alcoholic hepatitis

ALT – Alanine Aminotransferase

AMD – Age-related macular degeneration

ASGR1 – Asiaglycoprotein receptor 1

AST – Aspartate aminotransferase

AT1/AT2 – Alveolar type epithelial cells

BW – Body weight

COPD – Chronic Obstructive Pulmonary Disease

DC – Dendritic cell

DME – Diabetic macular edema

DSS – Dextran sodium sulfate

EtOH – Ethyl alcohol

FSGS – Focal segmental glomerulosclerosis

Fzd – Frizzled

GFP – Green fluorescence protein

GI – Gastrointestinal

GLP – Good laboratory practice

HNF alpha - Hepatocyte nuclear factor 4 alpha

IBD – inflammatory Bowel Disease

IgG – Immunoglobulin G

IPF – Idiopathic pulmonary fibrosis

IND – Investigational new Drug

INR – International normalized ratio

IV – Intravenous

KO – Knock-out model

LG – Lacrimal gland

Lille – Modeling tool for predicting mortality in patients with alcoholic hepatitis who are not responding to steroid therapy

Lrp Lipoprotein receptor-related protein

MELD – Model for end-stage liver disease score

MOA – Mechanism of action

PD – Pharmacodynamics

Pg – Picogram

Mg – Milligrams

MS – Multiple sclerosis

PIPE – Private investment in public equity

PK – Pharmacokinetic

SAD – Single ascending dose

SC – Subcutaneous

MAD – Multiple ascending dose

RPE – Retinal pigment epithelium

SAH – severe alcoholic hepatitis

SOC – Standard of care

SWAP – Surrozen Wnt signal activating proteins

SWEETS – Surrozen Wnt enhancer engineered for tissue specificity

TAA – Thioacetamide

UC – Ulcerative colitis; Mod-Sev UC – Moderate to Severe UC

UC-100 – A score of a composite disease activity index for drug development in UC

VHH – Single variable domain on a heavy chain (VHH) antibodies

