



# The Wnt Company – Targeted Regeneration

2021

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# Highlights - Compelling Breakthroughs in Harnessing Wnt Signaling



Global **leaders** in developing antibodies targeting the **Wnt** pathway

- World renowned scientific advisors, founders
- Experienced management team to execute strategy



**Proprietary Wnt therapeutics platform** designed to **selectively** stimulate tissue regeneration

- Surrozen discoveries validate prominent Wnt biology role in normal & diseased tissues
- Two technologies with broad library of receptor specific antibodies to confer selectivity



Advancing **two lead programs** targeting **billion+ dollar markets**

SZN-1326 | Ulcerative Colitis | FIH 2022

SZN-043 | Severe Alcoholic Hepatitis | FIH 2022



**Scientifically** driven **strategy** to **build on leadership** position in **selective Wnt antibodies**

- Target high unmet needs to transform patient outcomes in broad spectrum of diseases
- Leverage our platform to advance product candidates and to expand our patent portfolio (17 applications filed)
- Potential to partner post value generating milestones



**Cash runway** to advance lead programs through **phase 1b** and nominate **additional IND candidates**

# Our Novel Approach Overcomes Previous Challenges

Paving the Way to Targeted Antibody Regeneration

## Integrated, Repeatable Wnt Therapeutics Platform

Potential first synthetic soluble Wnt mimetics

Two antibody technologies: SWAPs & SWEETS

Designed to have desirable drug-like properties & mimic normal physiologic responses

Confer potency & selectivity through multivalent binding targeting - target specific Fzd or cell specific receptors

## Validation of Our Prominent Role in Wnt Biology Breakthroughs

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

**nature**

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

 CellPress

Tissue-targeted R-spondin mimetics for liver regeneration

**SCIENTIFIC  
REPORTS**  
natureresearch

Structural Basis of Wnt Recognition by Frizzled

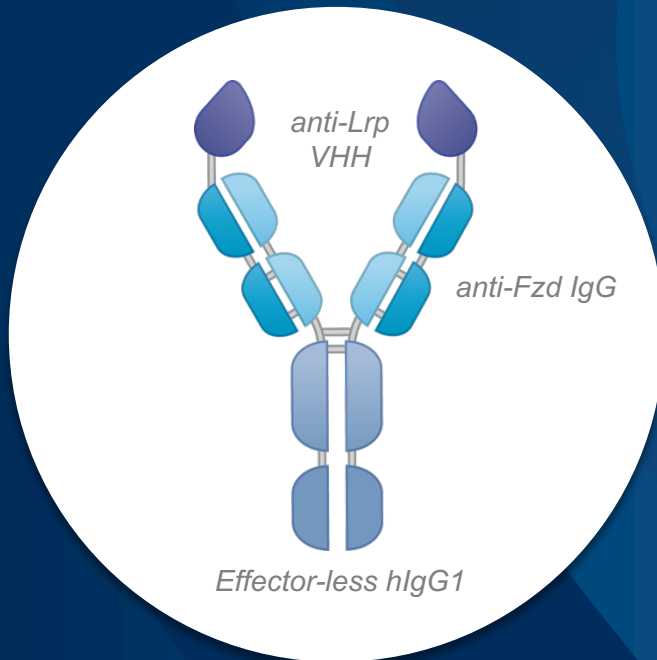
**Science**



# Proprietary Technologies Enable Potent, Selective Wnt Signaling

## SWAPs & SWEETS

### SWAP Technology



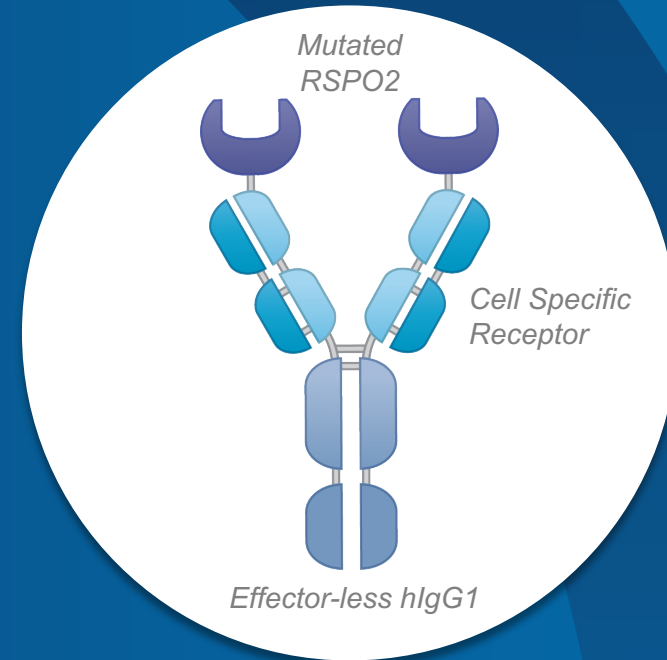
Antibody Based Bi-Specific

Mimics natural Wnt in activating Wnt signaling

Applied in disease states with deficient Wnt ligand

Engineered to be tissue selective targeting with individual Fzd receptor selectivity

### SWEETS Technology



Antibody-based fusion protein

Mimics natural R-Spondin in enhancing Wnt signaling

Applied in diseases with adequate ligand, but deficient Wnt signaling

Engineered to be cell selective with cell specific receptors

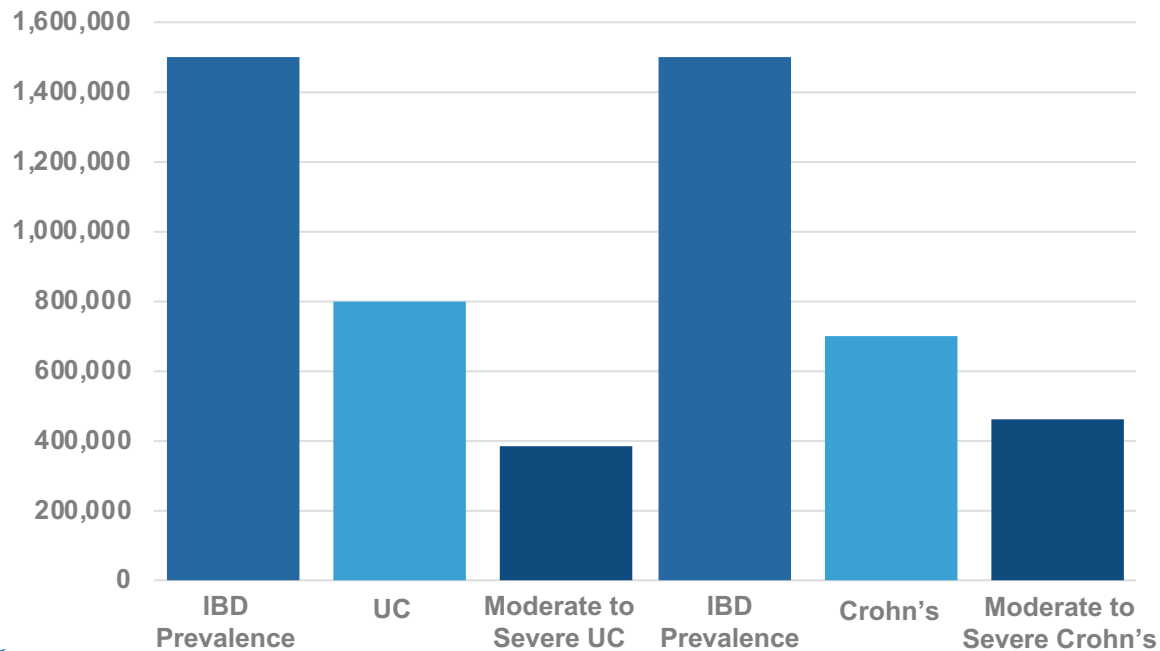
# Deep Wnt Signaling Expertise Supports Productive R&D Pipeline

IND Enabling Studies Ongoing for SZN-1326 and SZN-043; Planned Phase 1 Clinical Trials 2022

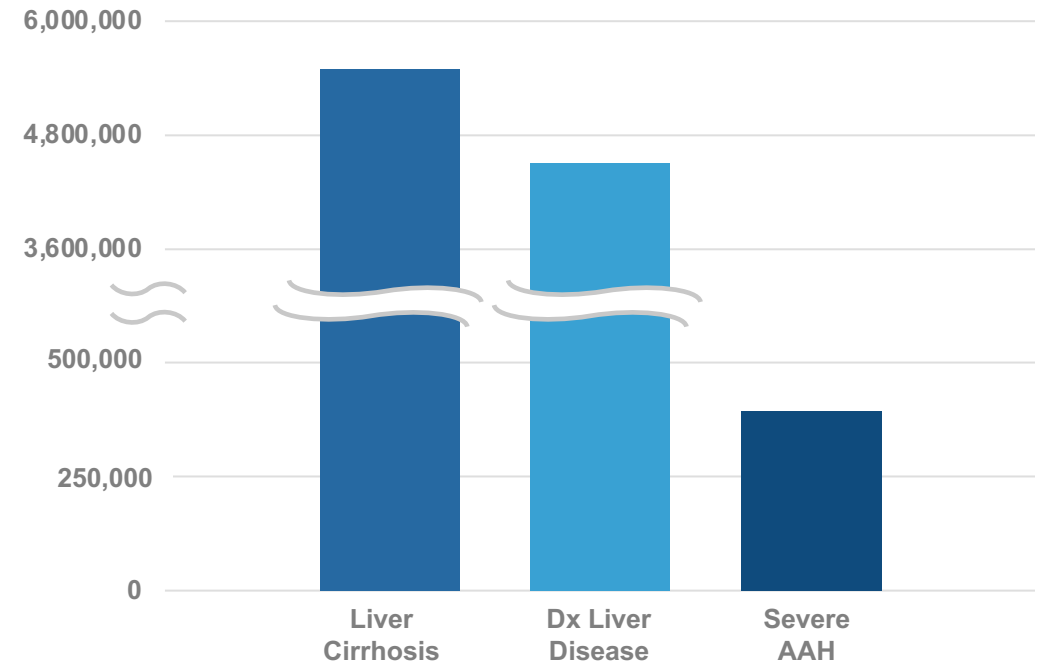
LEAD PROGRAMS	INDICATION/S	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGULATORY	NEXT MILESTONE
SZN-1326	Moderate to Severe IBD	<div></div>						First in Human 2022
SZN-043	Severe Alcoholic Hepatitis	<div></div>						First in Human 2022
RESEARCH PROGRAMS	Tissue	Indications			Discovery	Proof of Concept		Lead Candidate
	Retinal Vasculature	Diabetic Retinopathy, Wet AMD			<div></div>			
	Cornea	Fuch's Dystrophy, Limbal Cell Def			<div></div>			
	RPE	Dry AMD			<div></div>			
	Lacrimal Gland	Dry Eye, Sjögren's			<div></div>			
	Intestine	Short Bowel Syndrome			<div></div>			
	Cochlea	Hearing Loss			<div></div>			
	Lung	IPF, COPD			<div></div>			
	Renal	Polycystic Kidney Disease, FSGS			<div></div>			

# SZN-1326 & SZN-043 Represent Significant Market Opportunities

- 2nd line biologics in UC represent a \$4B market in US
- Moderate to severe Crohn's 2nd line market of > \$7B in the US
- Opportunity for combination of SZN-1326 with all biological treatments

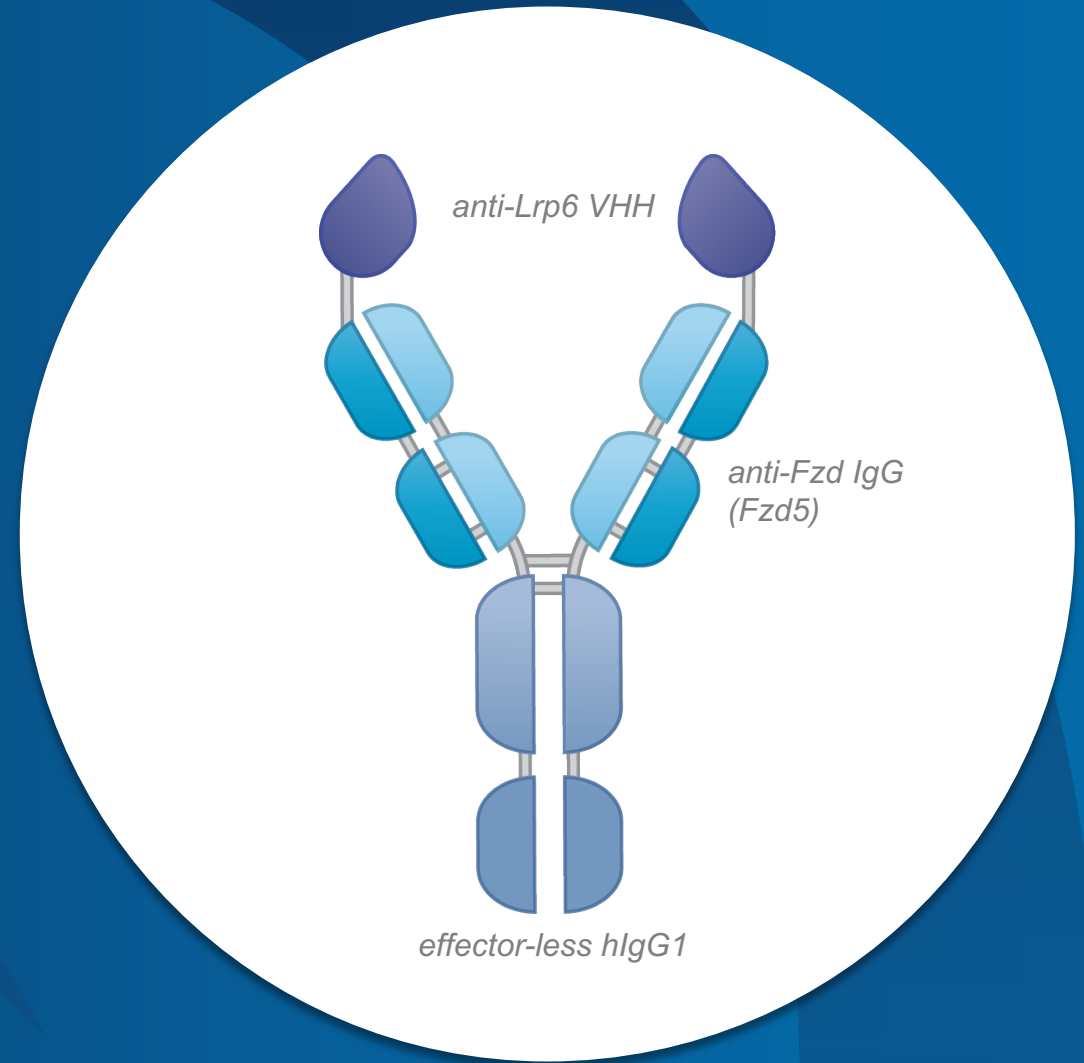


- Estimated 100,000 U.S. hospitalizations due to severe AH
- ~50% of patients covered by commercial insurance
- Potential for expansion to other severe liver diseases



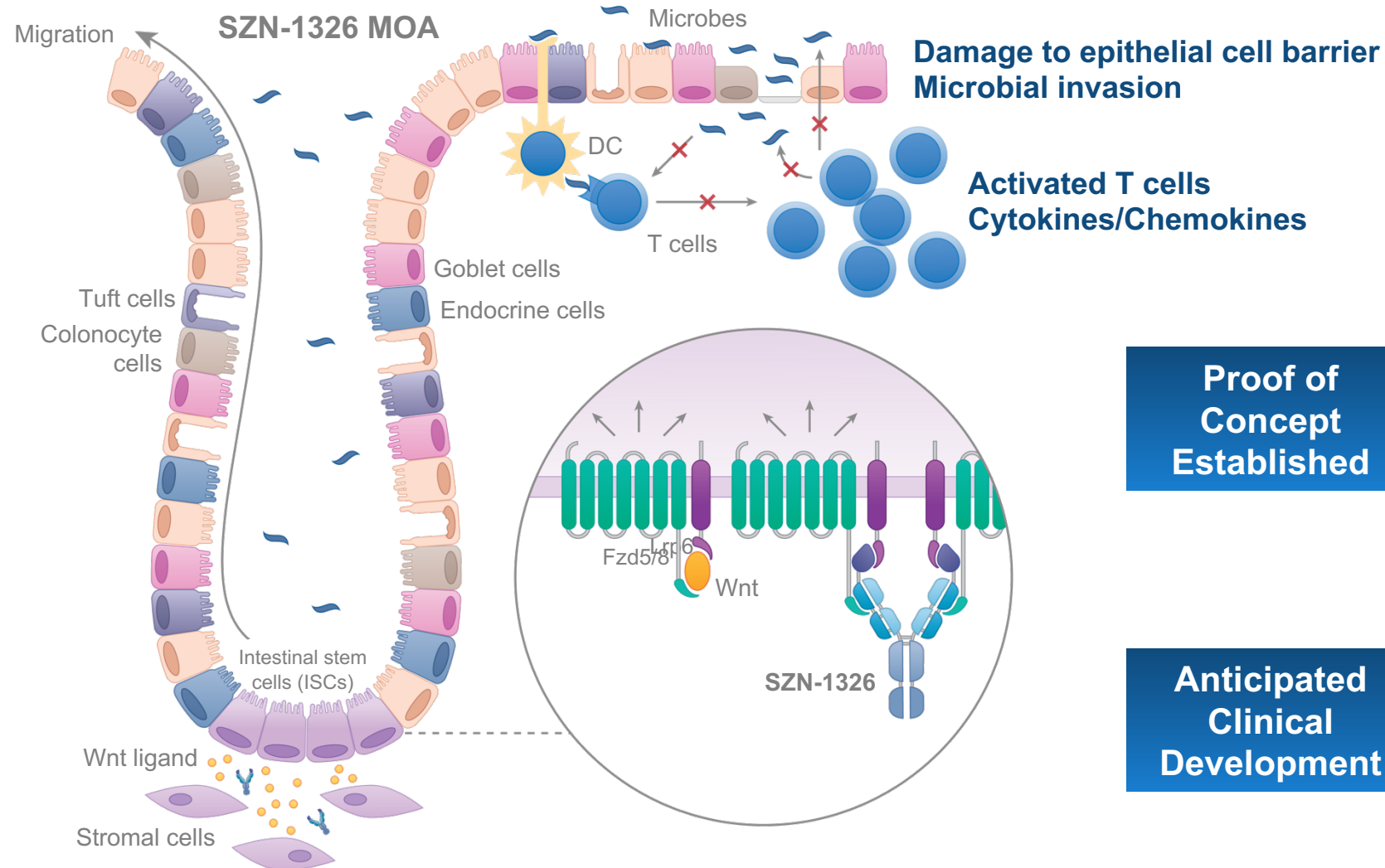
# SZN-1326

## Moderate to Severe IBD



# SZN-1326 – Intestine Targeted Epithelial Restoration

Mechanism Suggests Potential New Treatment Paradigm in Inflammatory Bowel Disease



## Proof of Concept Established

- Selective Wnt activation
- Epithelial repair
- Functional improvement

## Anticipated Clinical Development

- 2022 – First in human
- 2022 – Safety
- 2023 – Phase 1b proof-of-concept in UC

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

## High Unmet Need

Need for rapid induction: SOC takes months to induce remission

Better efficacy, especially mucosal healing: SOC achieve remission in <50% and low rates of mucosal healing (< 20%)

Need for additional MOAs: Patients fail first-line anti-inflammatory biologics and subsequently fail 2<sup>nd</sup> and 3<sup>rd</sup> line therapies

## Differentiated Preclinical Data

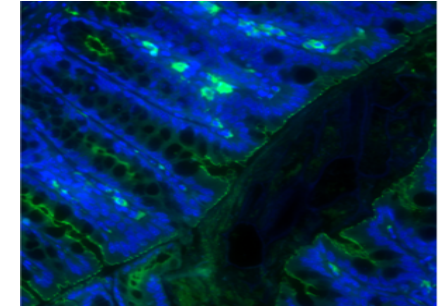
Repairs damaged colon epithelium

Restores colon tissue structure, epithelial tight junctions and improves mucosal healing

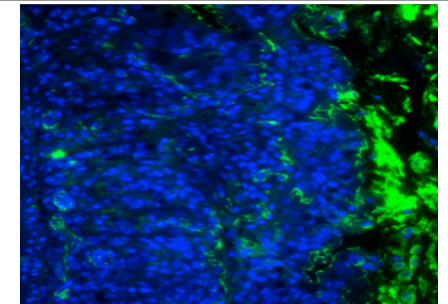
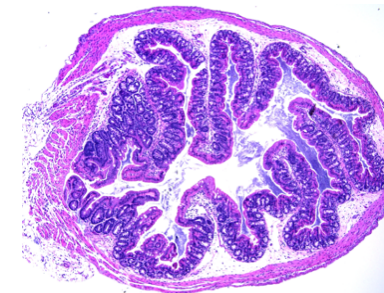
Reduces inflammation and improves disease activity index

Superior to cyclosporin and anti-TNF's

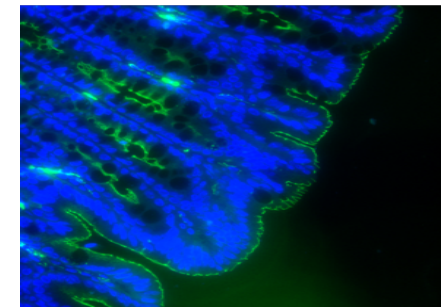
Normal (No DSS Damage)



Damaged (DSS Damage)



Restored (DSS Damage + SZN-1326)



# Initial Clinical Development Focus on Ulcerative Colitis

## Potential to Expand Into Additional IBD Indications

- Phase 1a in healthy volunteers dosed for up to 12 weeks IV and SQ either weekly or biweekly
- Phase 1b placebo controlled in UC patients provides potential to generate clinical proof of concept; endoscopies and biopsies enable blinded central reads of
  - Clinical remission (symptom scores)
  - Histologic remission/mucosal healing (histopathology)

	PHASE 1a SAD/MAD	PHASE 1b MAD	PHASE 2
<b>Population</b>	Healthy	UC Patients	UC Patients
<b>N</b>	Up to 60	Dose Escalation: Up to 24 Expansion (Mono and Combo): Up to 24	120-150
<b>Key Objectives</b>			
<b>Early Efficacy</b>		○	○
<b>Inform Dose</b>	○	○	○
<b>Proof of Mechanism</b>		○	○
<b>Safety / PK/ ADA</b>	○	○	○
<b>Additional End-Points</b>	PD markers	CRP, FC, cytokines, histology, stool frequency, rectal bleeding, endoscopy subscore, PD markers	UC-100, clinical remission and response, endoscopic remission, endoscopy subscore, histology, histological remission, QOL, PD markers



# SZN-043

## Severe Liver Disease





# Potential for First Approved Treatment for Severe Alcoholic Hepatitis

## Liver Specific Wnt Activation and Regeneration

### SZN-043 MOA



### Proof of Concept Established

- Selective Wnt activation
- Specific hepatocyte proliferation
- Functional improvement

### Anticipated Clinical Development

- 2022 - First in human
- 2023 – Phase 1b in severe AH
- Potential for fast-track designation and fast path to approval
- Potential for expansion to other severe liver diseases

# SZN-043 – Potential to Significantly Improve Patient Outcomes in Severe Alcoholic Hepatitis

## High Unmet Need

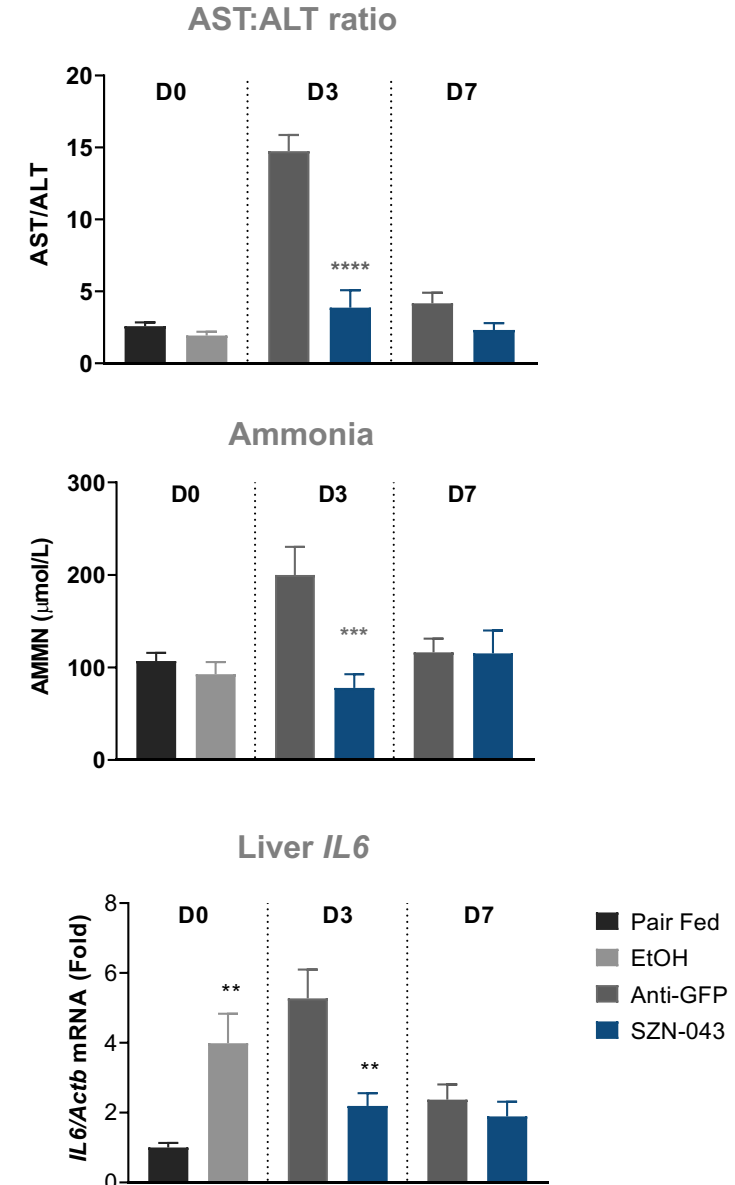
No approved drugs: SOC: steroids

High mortality: 90-day mortality of 30%

Liver transplant denied: Limited availability, costly, denied due to alcoholism

## Differentiated Preclinical Data

- >25 preclinical studies conducted
- SZN-043 addresses underlying pathophysiology
- Activates Wnt Signalling
- Induces mature hepatocyte proliferation and improves clotting time
- Reduces markers of liver injury & inflammation



# Clinical Development Plan Provides Fast Path to POC and Approval

- Phase 1a: Potential to demonstrate clinical activity – methacetin breath test marker for hepatocyte proliferation
- Phase 1b: Endpoints Lille and MELD scores highly correlated with survival; potentially lead to Fast Track Designation
- Phase 2/3: Adaptive design may accelerate development timeline, primary endpoint readout at 90 days

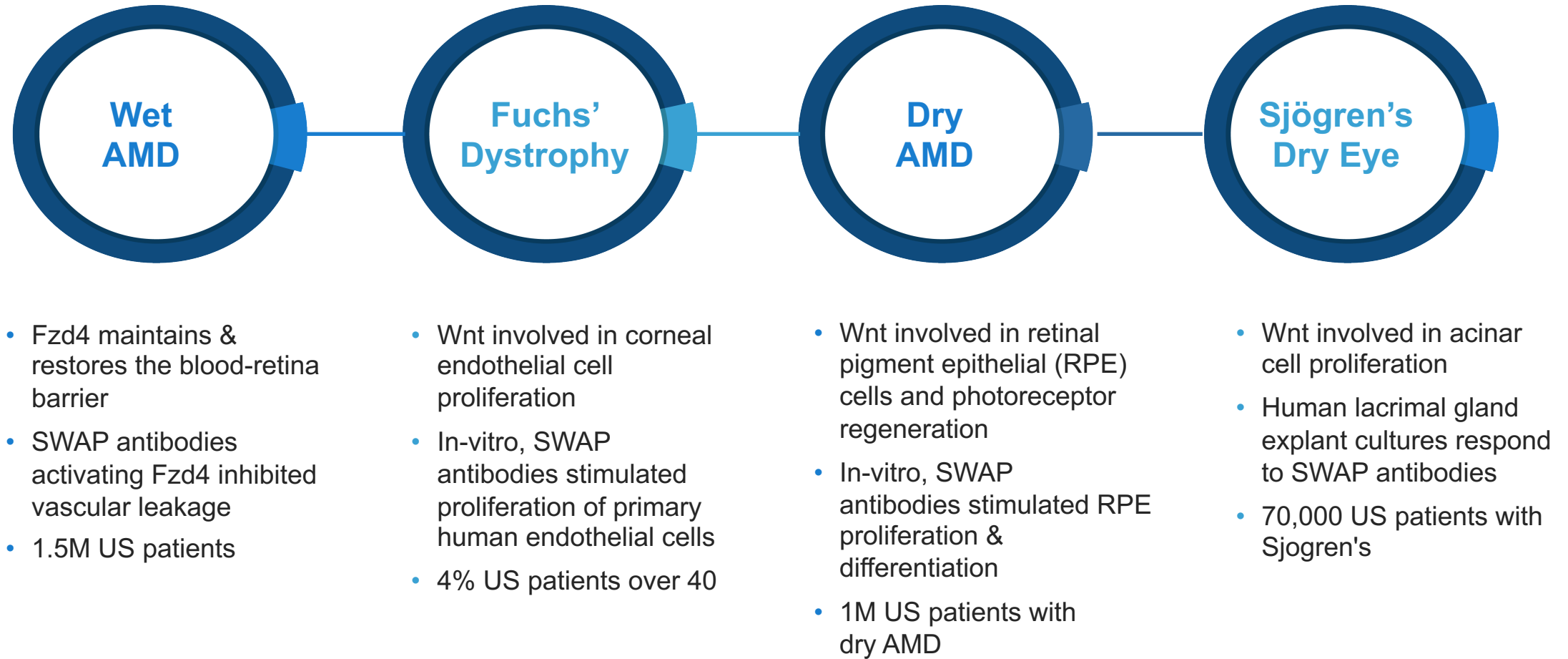
	PHASE 1a SAD	PHASE 1b MAD	PHASE 2/3
<b>Pop</b>	HV/Early cirrhosis	Severe Alcoholic Hepatitis	Severe Alcoholic Hepatitis
<b>N</b>	30-45	Up to 30	300 (placebo controlled)
<b><u>Key Objectives</u></b>			
<b>Early Activity/Clinical Efficacy</b>	○	○	○
<b>Inform Dose</b>	○	○	○
<b>Proof of Mechanism</b>	○	○	○
<b>Safety / PK</b>	○	○	○
<b>Additional End-Points</b>	PD markers (angiogenin, Lect2, Methacetin)	7day Lille score, MELD score PD markers	90-day mortality

# Beyond Intestine and Liver...

Broad Opportunities in Ocular Disease

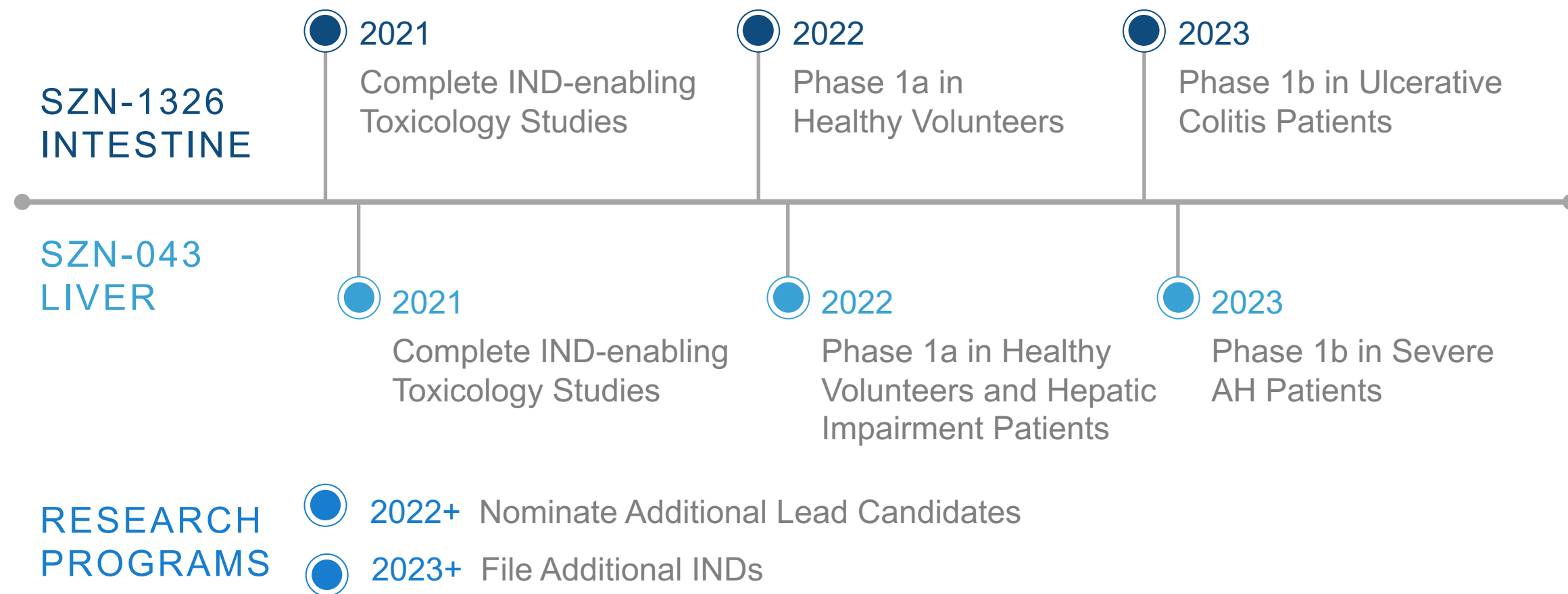
# Preclinical Data Supports Advancement of Ocular Programs

## Broad Set of Opportunities in Ocular Diseases



# Near Term Outlook and Potential Milestones

Multiple Clinical Milestones with Potential for Early Proof of Concept





# The Wnt Company - Targeted Regeneration

2021



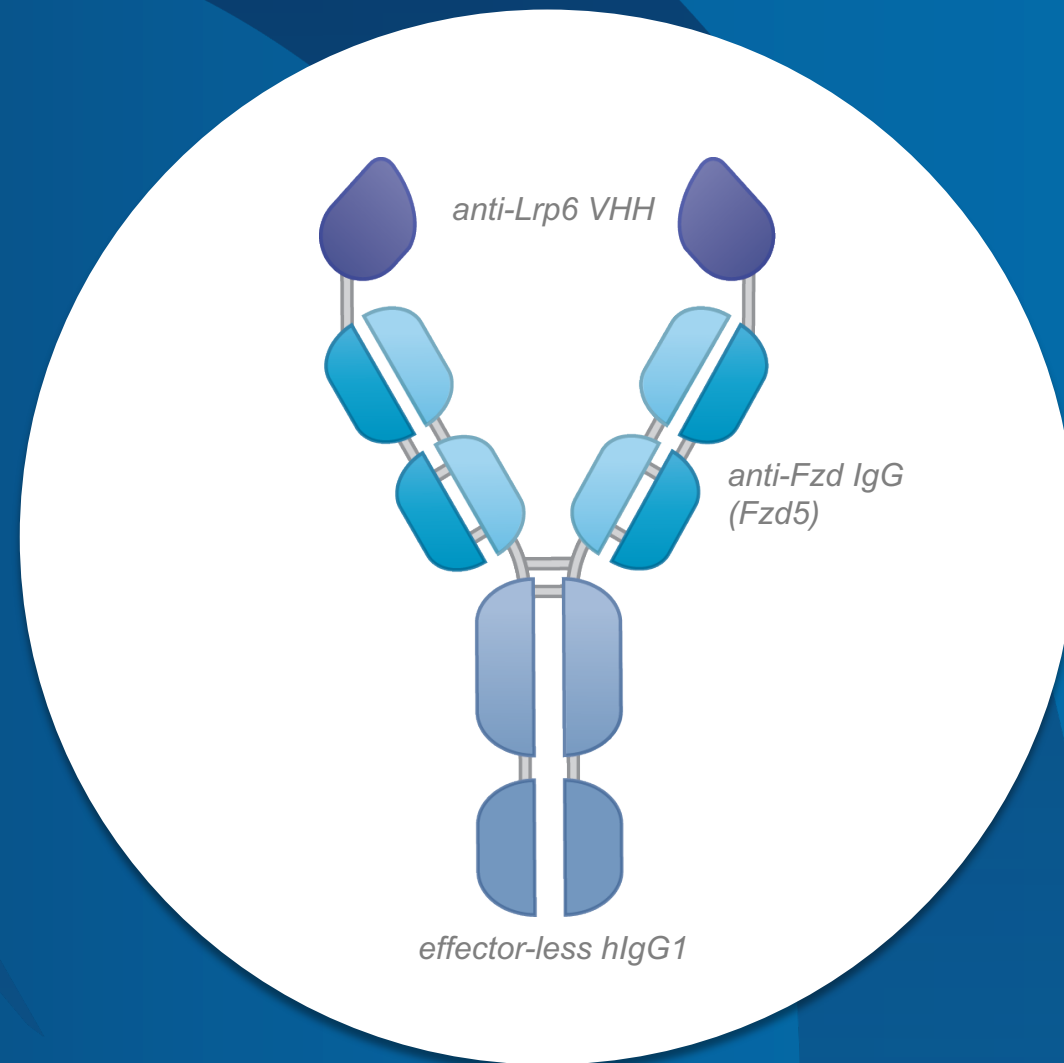
# Appendix

2021



# SZN-1326

## Preclinical Data



# SZN-1326 – Restores Wnt Signaling in Damaged Intestine

## Selective Binding Profile

☒ Selective Wnt activation



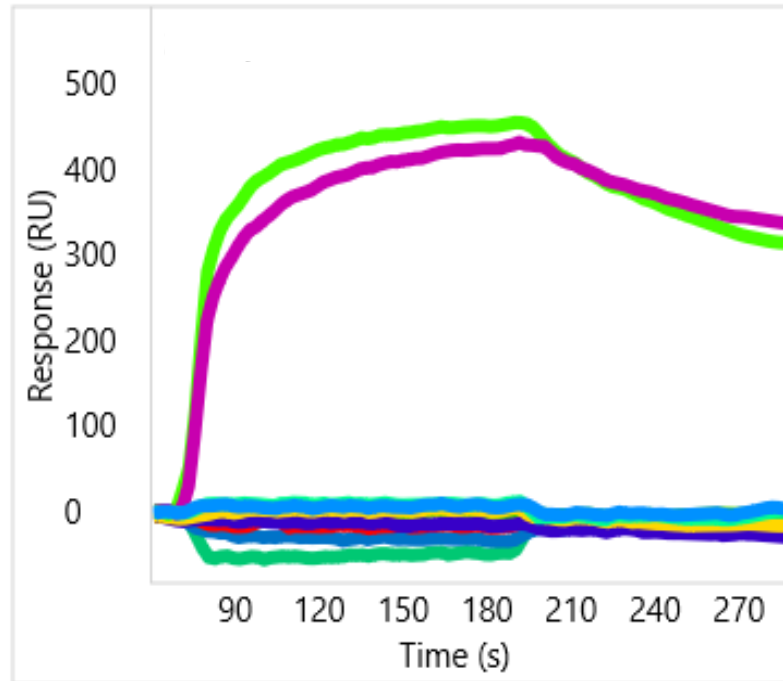
☐ Epithelial repair



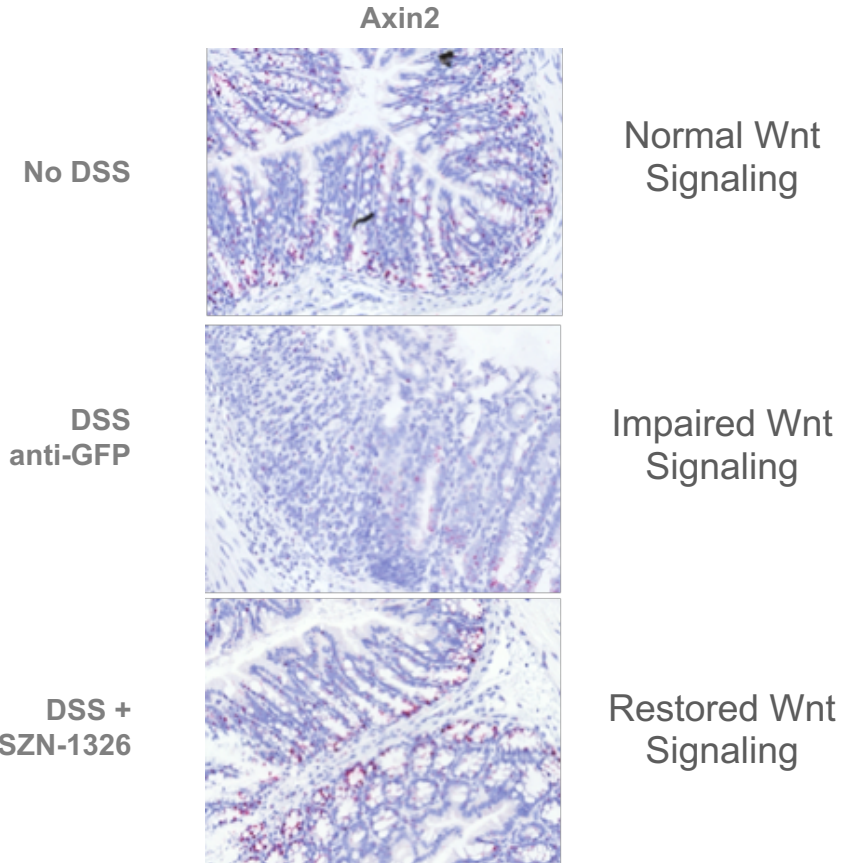
☐ Inflammation reduction



☐ Functional improvement



## Restores Wnt Signaling in Damaged Intestinal Epithelium



# SZN-1326 – Repairs Damaged Colon Epithelium

☒ Selective Wnt activation



☒ **Epithelial repair**

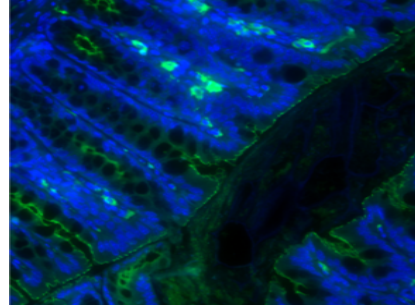
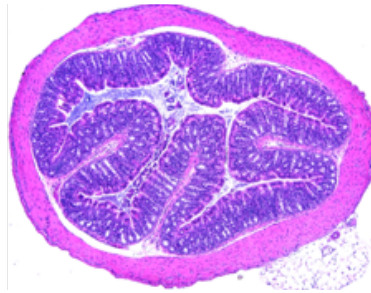


☐ Inflammation reduction

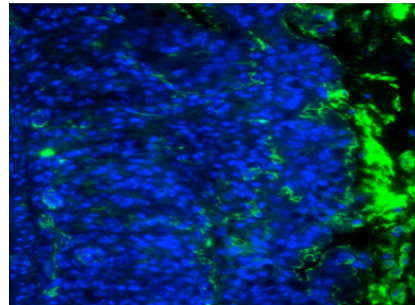
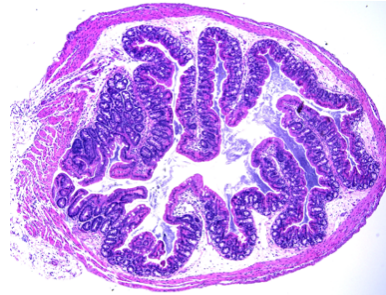


☐ Functional improvement

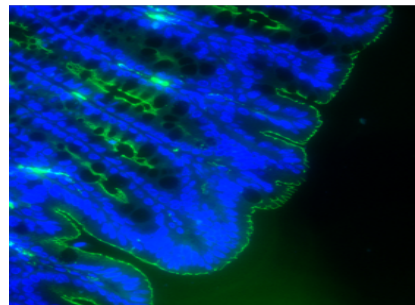
Normal (No DSS Damage)



Damaged (DSS Damage)



Restored (DSS Damage + SZN-1326)



## Effects of SZN-1326 Administration

- Repairs damaged colon epithelium in acute and chronic colon injury models
- Restores key cell lineages including colonocytes, goblet cells, and tuft cells
- Restores epithelial tight junctions, which are critical for normal barrier function

**Surrozen *in vivo* study (SRZ-279):** Administered 4% DSS in mice for 7 days resulting in intestinal epithelial injury. SZN-1326 10mpk on days 4 and 7. 1% DSS on days 8-10. Readout on day 10

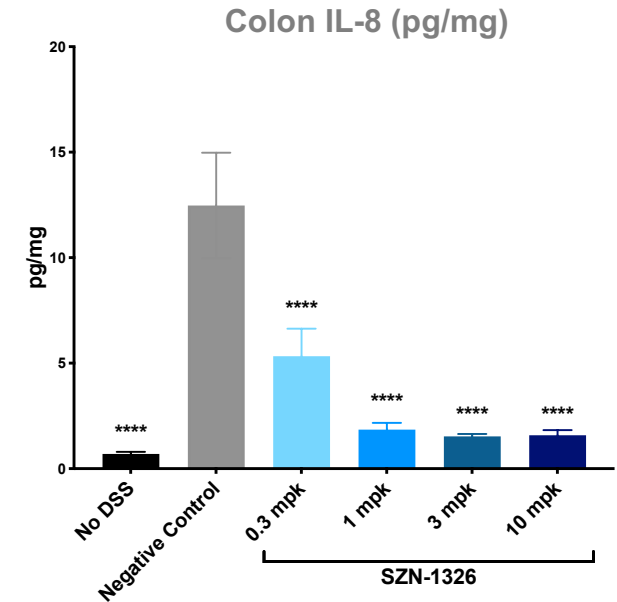
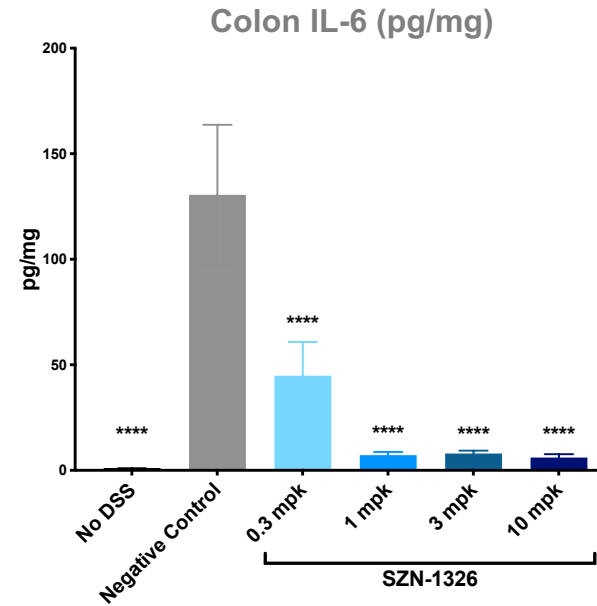
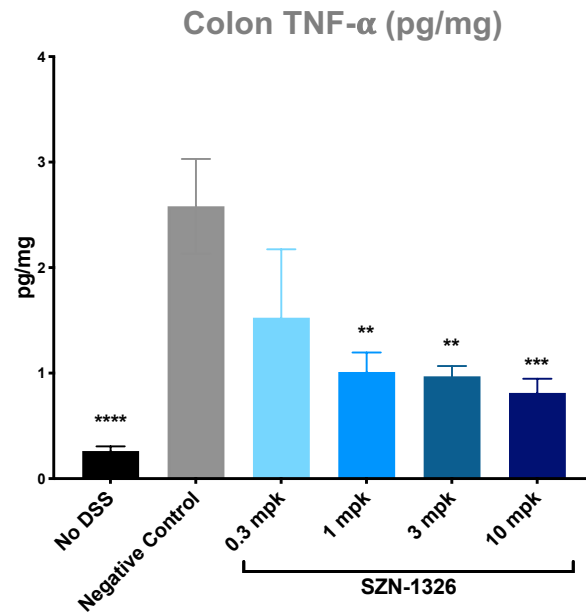
# SZN-1326 – Reduces Inflammatory Cytokines

☒ Selective Wnt activation

☒ Epithelial repair

☒ Inflammation reduction

☐ Functional improvement



- Reduces key inflammatory cytokines induced by DSS and implicated in human IBD
- Results reproducible in both localized colon tissue and systemic serum samples

Statistical Analyses: One-way ANOVA, Holm-Sidak test (GraphPad Prism). All comparisons made with the anti-GFP group. Error bars: Mean with SD.  
\* p<0.05, \*\* p<0.01, \*\*\* p<0.001, \*\*\*\* p<0.0001

**Surrozen in vivo study (SRZ-299):** Administered 4% DSS in mice for 7 days resulting in intestinal epithelial injury. SZN-1326 treatment on days 4 and 7. 1% DSS on days 8-10. Readout on day 10.

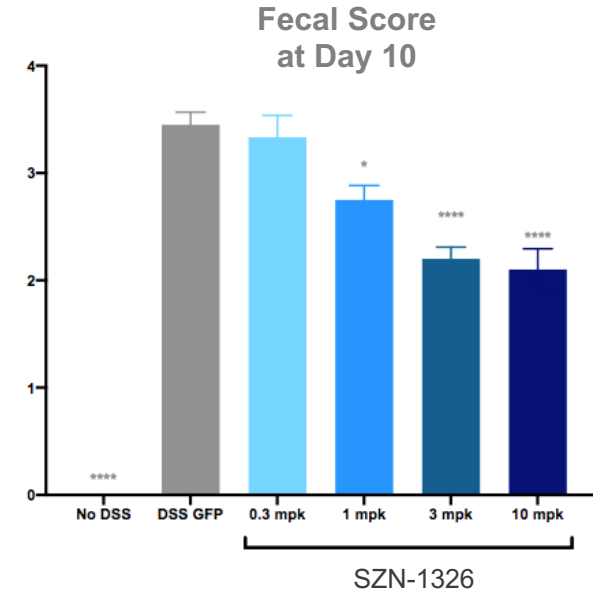
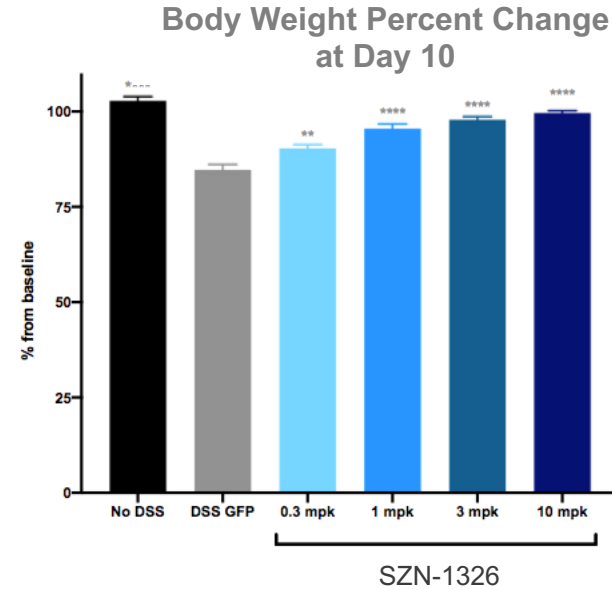
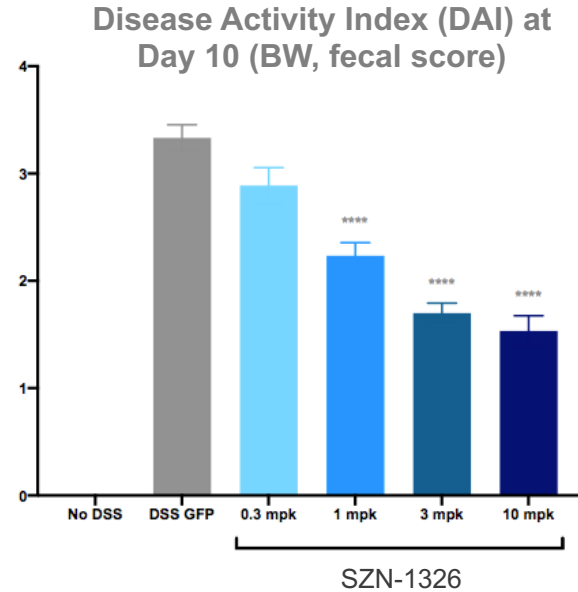
# SZN-1326 – Reduces Disease Activity

☒ Selective Wnt activation

☒ Epithelial repair

☒ Inflammation reduction

☒ Functional improvement



SZN-1326 decreases disease activity scores in acute and chronic DSS mouse models:

- Reverses DSS-induced weight loss
- Restores normal bowel function

Statistical Analyses: One-way ANOVA, Holm-Sidak test (GraphPad Prism). All comparisons made with the anti-GFP group. Error bars: Mean with SD.  
\* p<0.05, \*\* p<0.01, \*\*\* p<0.001, \*\*\*\* p<0.0001

**Surrozen in vivo study (SRZ-299):** Administered 4% DSS in mice for 7 days resulting in intestinal epithelial injury. SZN-1326 treatment on days 4 and 7. 1% DSS on days 8-10. Readout on day 10.



# SZN-1326 – Repairs Colon Epithelium *In Vivo* More Than Cyclosporine

## Cross Section of Transverse Colon: H&E Staining

☒ Selective Wnt activation



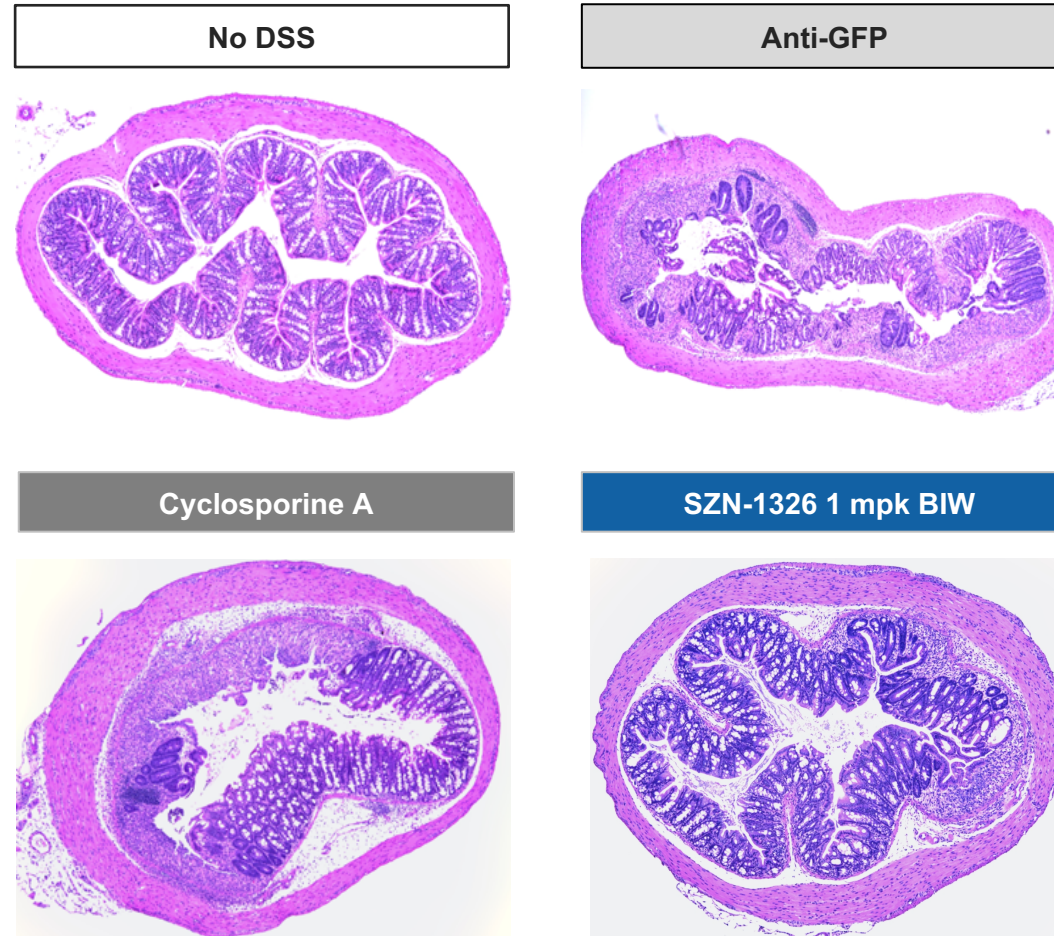
☒ **Epithelial repair**



☐ Inflammation reduction



☐ Functional improvement



**Surrozen *in vivo* study (SRZ-363):** Administered 4% DSS in mice for 7 days followed by 1% DSS for 3 days resulting in intestinal epithelial injury. SZN-1326 treatment on days 4 and 7. Readout on day 10.

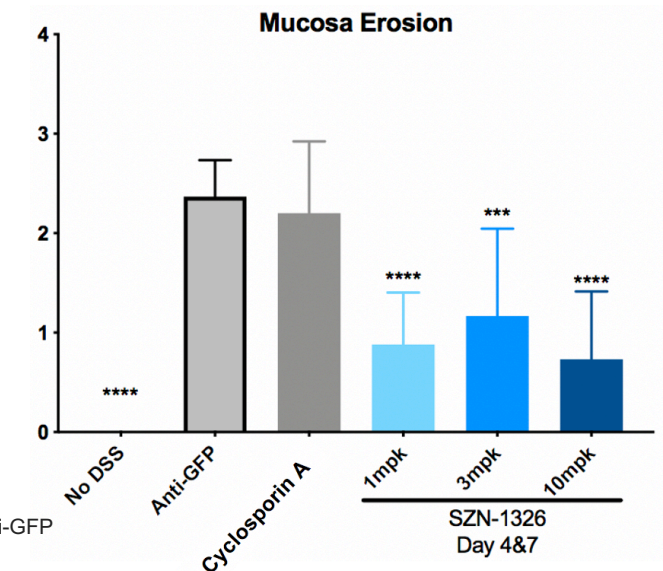
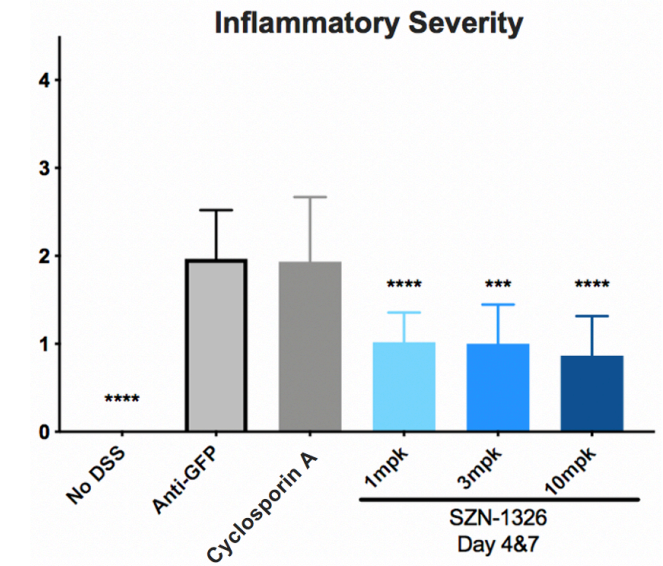
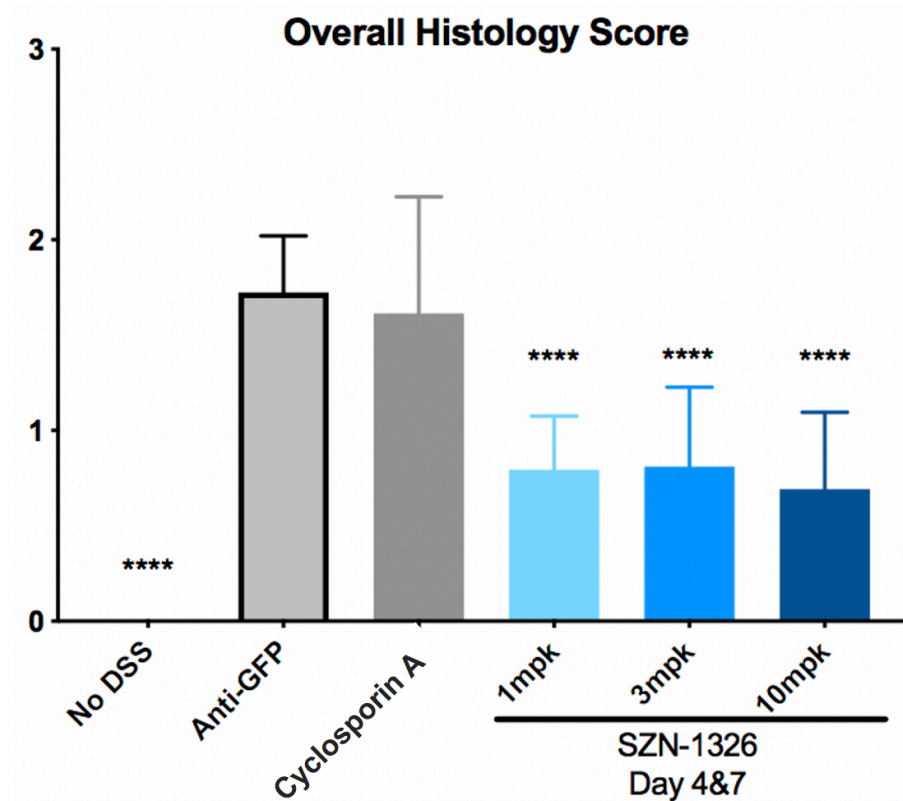
# SZN-1326 – Improves Colon Histology Score *In Vivo* More Than Cyclosporine

☒ Selective Wnt activation

☒ Epithelial repair

☒ Inflammation reduction

☐ Functional improvement



Statistical Analyses: One-way ANOVA, Holm-Sidak test (GraphPad Prism). All comparisons made with the anti-GFP group. Error bars: Mean with SD.

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$

**Surrozen *in vivo* study (SRZ-363):** Administered 4% DSS in mice for 7 days followed by 1% DSS for 3 days resulting in intestinal epithelial injury. SZN-1326 treatment on days 4 and 7. Readout on day 10.



# SZN-1326 – Improves Disease Activity *In Vivo* More Than Cyclosporine

☒ Selective Wnt activation



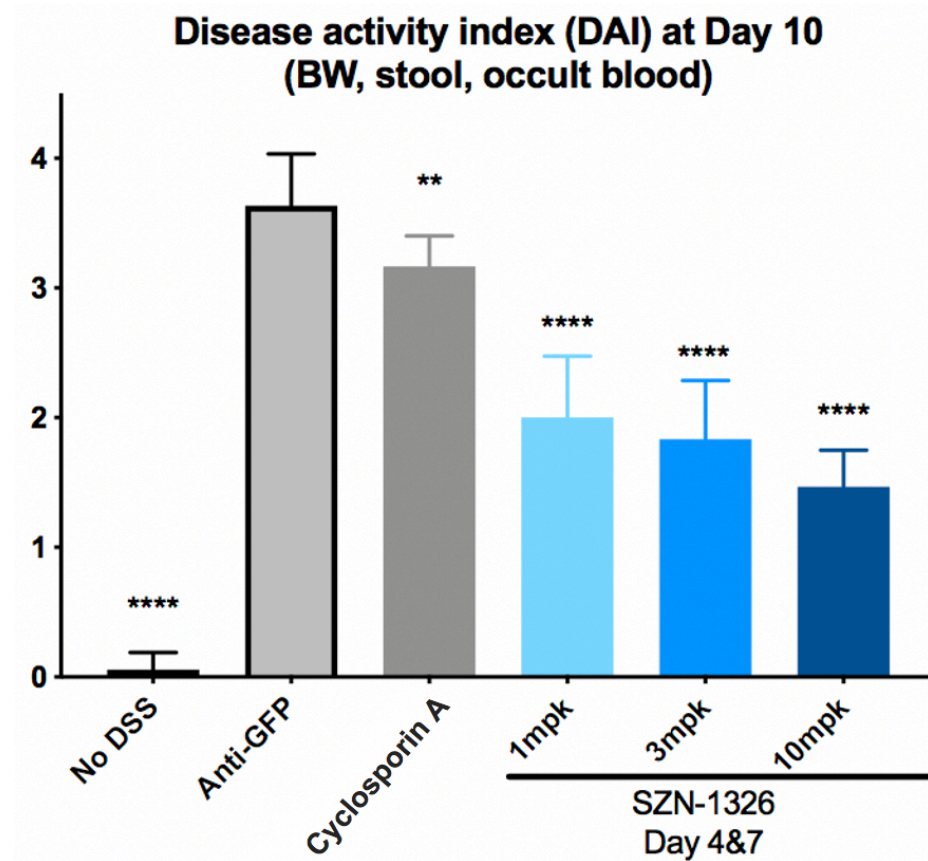
☒ Epithelial repair



☒ Inflammation reduction



☒ Functional improvement



Statistical Analyses: One-way ANOVA, Holm-Sidak test (GraphPad Prism). All comparisons made with the anti-GFP group. Error bars: Mean with SD.  
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# SZN-1326 – Repairs Colon Epithelium Better Than Anti-TNF in Chronic *In Vivo* Model

☒ Selective Wnt activation



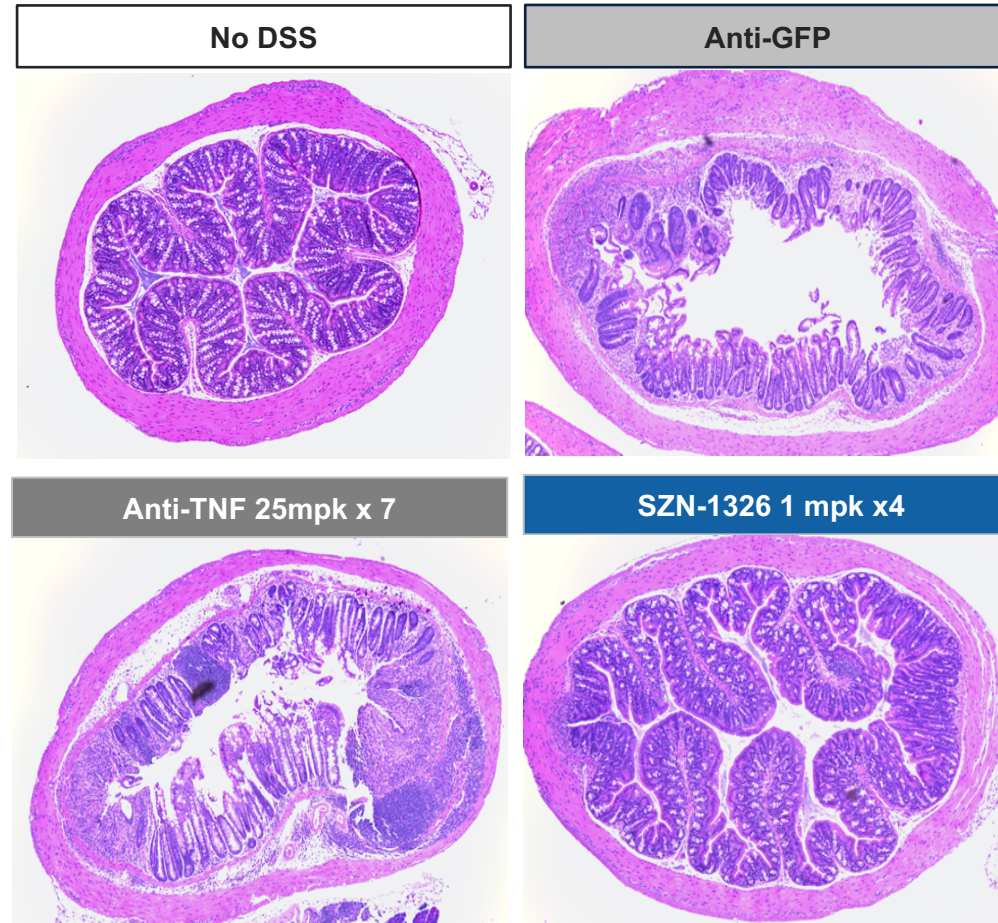
☒ **Epithelial repair**



☐ Inflammation reduction



☐ Functional improvement



**Surrozen *in vivo* study (SRZ-0371):** Administered 3% DSS in mice for three 7-day cycles separated by 7 days off, then a 3-day 1% DSS wash-out period, resulting in chronic intestinal epithelial injury. SZN-1326 treatment administered at 1, 3, or 10 mpk for 2, 4, or 6 days. Anti-TNF administered at 5 or 25 mpk for 4 or 7 days. Readout on day 38.

# SZN-1326 – Improves Colon Histology Score More Than Anti-TNF in Chronic *In Vivo* Model

☒ Selective Wnt activation



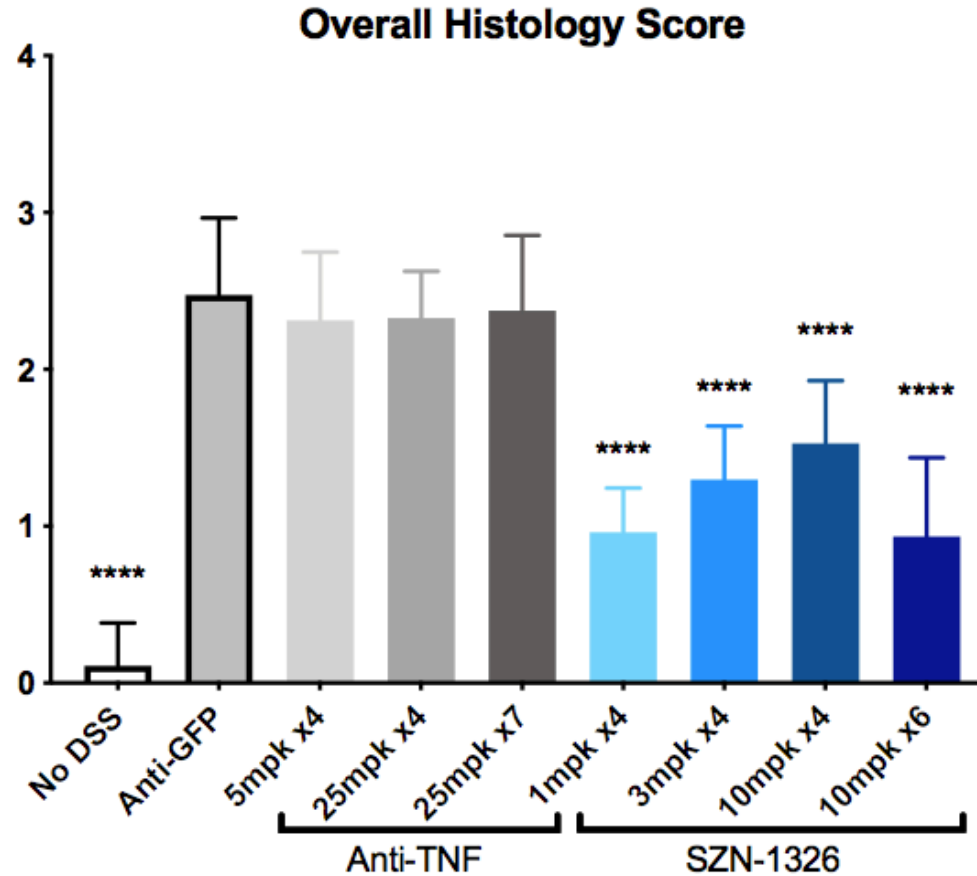
☒ Epithelial repair



☒ Inflammation reduction

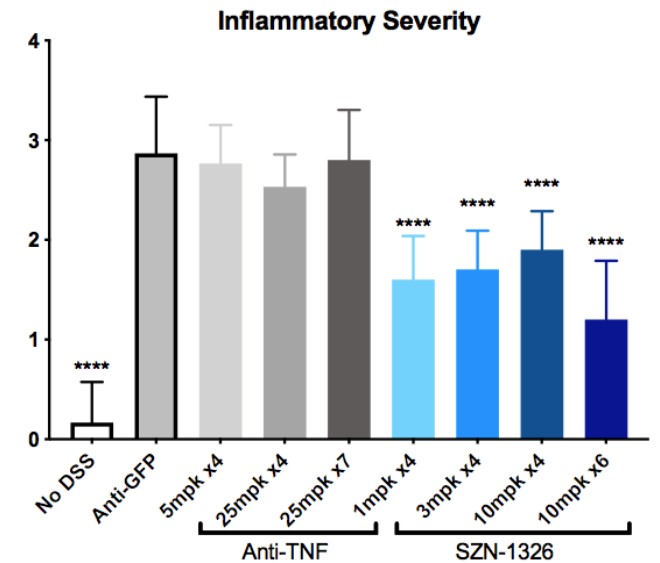
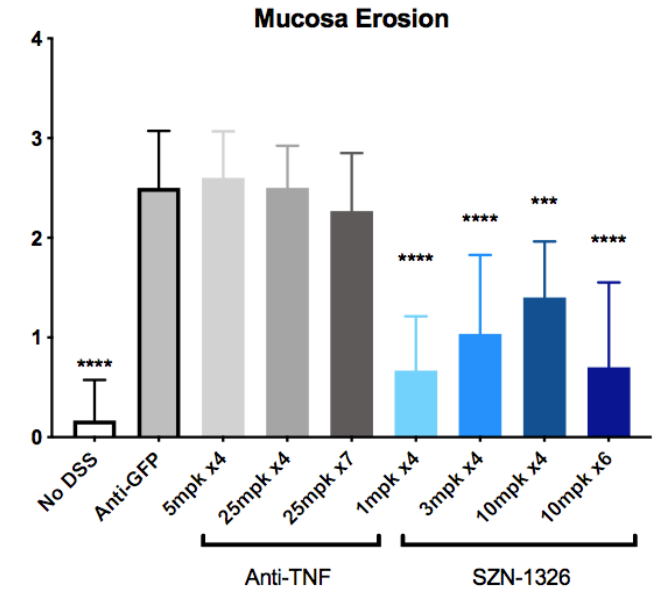


☐ Functional improvement



Statistical Analyses: One-way ANOVA, Holm-Sidak test (GraphPad Prism). All comparisons made with the anti-GFP group. Error bars: Mean with SD. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , \*\*\*\*  $p < 0.0001$

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# SZN-1326 – Improves Disease Activity More Than Anti-TNF in Chronic *In Vivo* Model

☒ Selective Wnt activation



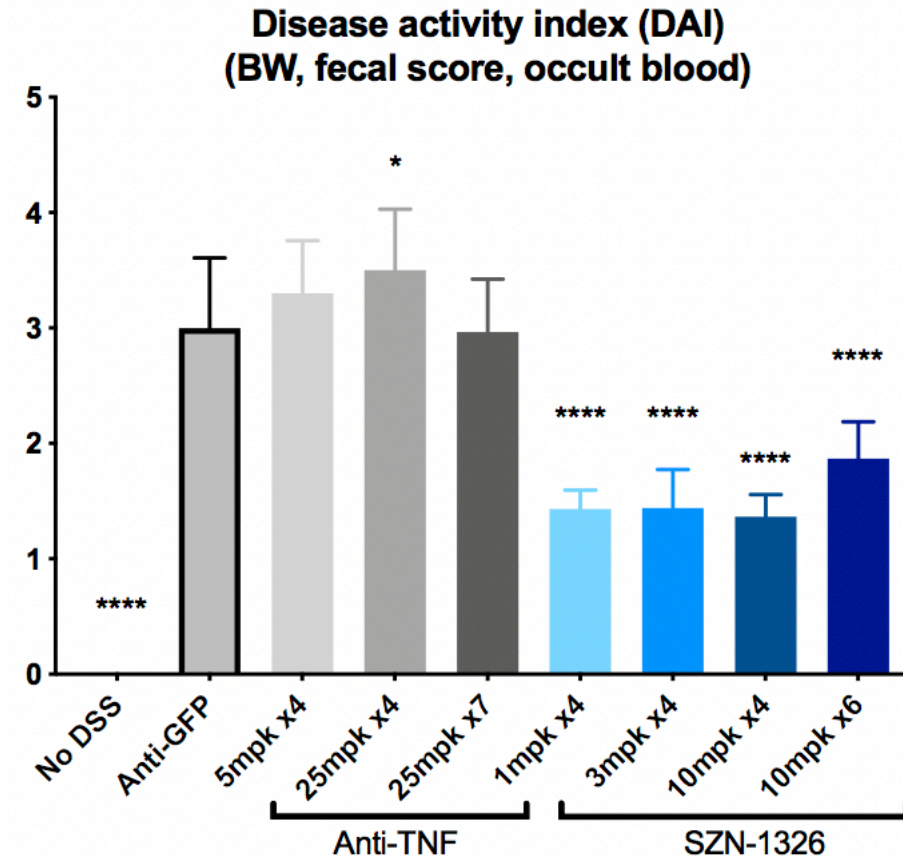
☒ Epithelial repair



☒ Inflammation reduction



☒ Functional improvement

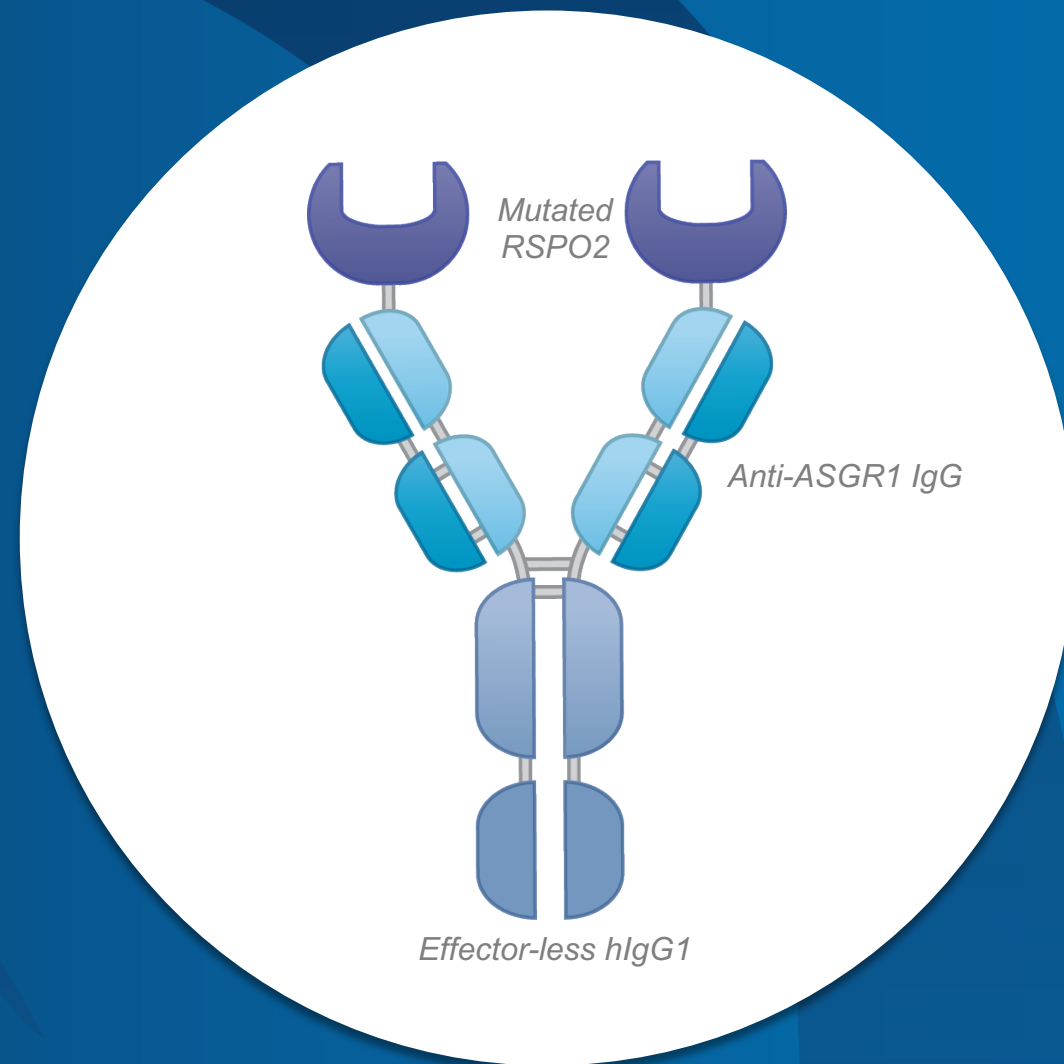


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# SZN-043

## Preclinical Data



# SZN-043 Selectively Stimulates Hepatocyte Proliferation

## Hepatocyte Proliferation Results in Rapid Improvement in Liver Function

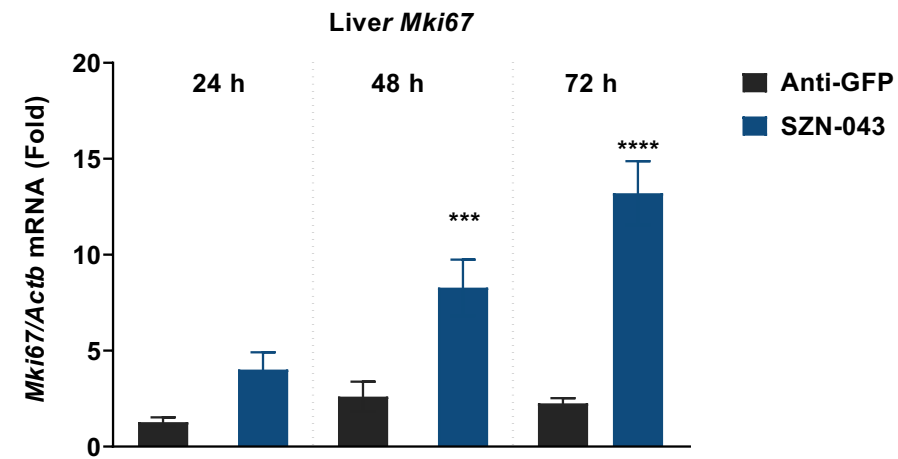
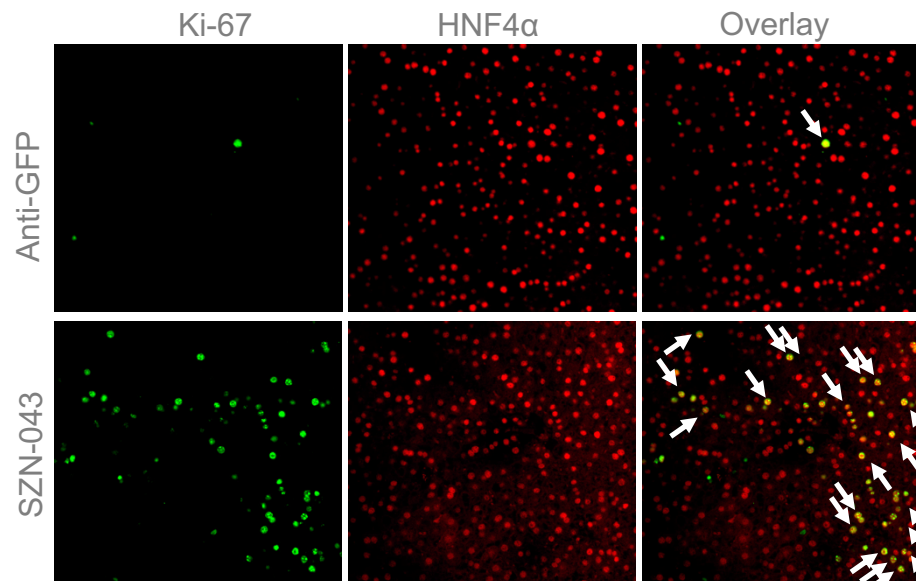
☒ Selective Wnt activation



☒ Hepatocyte Proliferation



☐ Functional Improvement



- SZN-043 induces Axin-2 expression selectively in the liver in normal mice
- Induces mature hepatocyte proliferation in alcoholic hepatitis mouse model and TAA mouse model
- SZN-043 treatment restores normal clotting function in TAA liver injury model by day 3

### Surrozen *in vivo* study (SRZ-347):

Mice were preconditioned with 5% EtOH liquid diet for 10 days followed by a 20% EtOH p.o. binge to establish alcoholic-induced liver injury. Treatment followed with 1 dose of SZN-043 at 30 mpk or 1 equivalent dose of anti-GFP as a negative control. All images from 72 h after SZN-043 treatment.

# SZN-043 Reduces Markers of Liver Injury and Inflammation

Activity in Alcohol Injury Model Support Clinical Development Path

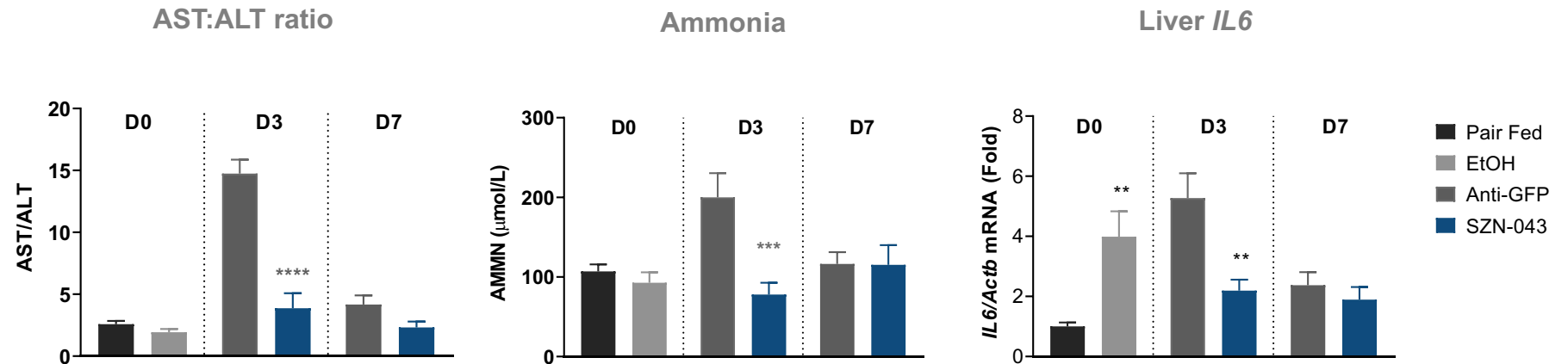
☐ Selective Wnt activation



☐ Hepatocyte Proliferation



☒ **Functional Improvement**



- Surrozen established a rodent model of alcohol-induced liver injury
- Alcohol injury in the model leads to characteristics of severe alcoholic hepatitis in humans, e.g. hepatocyte injury, increased ammonia, elevated cytokines
- SZN-043 treatment reduces ammonia
- SZN-043 treatment reduces the AST:ALT ratio, IL1 $\beta$ , and IL6



## Additional Information

2021



# Glossary

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

DSS – Dextran sodium sulfate

EtOH – Ethyl alcohol

FSGS – Focal segmental glomerulosclerosis

Fzd – Frizzled

GFP – Green fluorescence protein

GI – Gastrointestinal

HNF alpha - Hepatocyte nuclear factor 4 alpha

IBD – inflammatory Bowel Disease

IgG – Immunoglobulin G

IPF – Idiopathic pulmonary fibrosis

IND – Investigational new Drug

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

PIPE – Private investment in public equity

PK – Pharmacokinetic

SAD – Single ascending dose

MAD – Multiple ascending dose

RPE – Retinal pigment epithelium

SOC – Standard of care

SWAP – Surrozen Wnt signal activating proteins

SWEETS – Surrozen Wnt enhancer engineered for tissue specificity

TAA – Thioacetamide

UC – Ulcerative colitis

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