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# 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**

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# 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
nature research

Structural Basis of Wnt Recognition by Frizzled

Science

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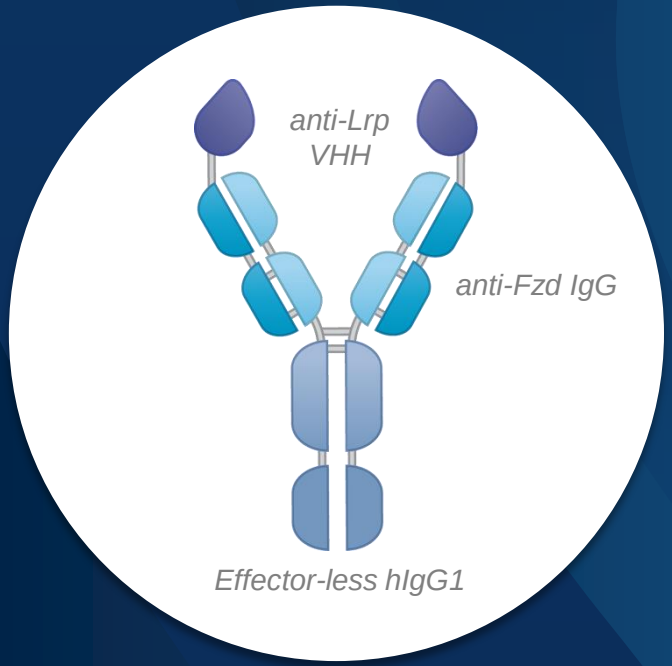
# Proprietary Technologies Enable Potent, Selective Wnt Signaling
## SWAPs & SWEETS

### SWAP Technology



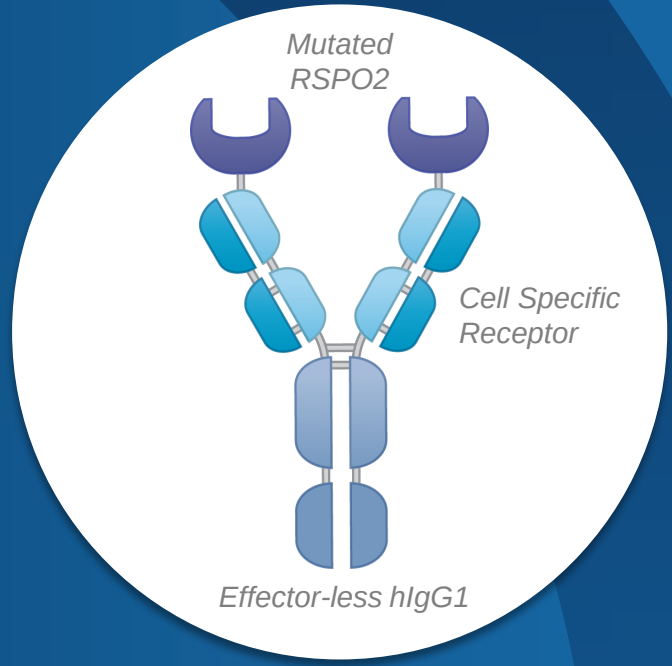

Antibody Based Bi-Specific

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

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# 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 | | | | | | | First in Human 2022 |
| **SZN-043** Severe Alcoholic Hepatitis | | | | | | | First in Human 2022 |

**RESEARCH PROGRAMS**

| Tissue | Indications | Discovery | Proof of Concept | Lead Candidate |
|---|---|---|---|---|
| Retinal Vasculature | Diabetic Retinopathy, Wet AMD | | | |
| Cornea | Fuch's Dystrophy, Limbal Cell Def | | | |
| RPE | Dry AMD | | | |
| Lacrimal Gland | Dry Eye, Sjögren's | | | |
| Intestine | Short Bowel Syndrome | | | |
| Cochlea | Hearing Loss | | | |
| Lung | IPF, COPD | | | |
| Renal | Polycystic Kidney Disease, FSGS | | | |

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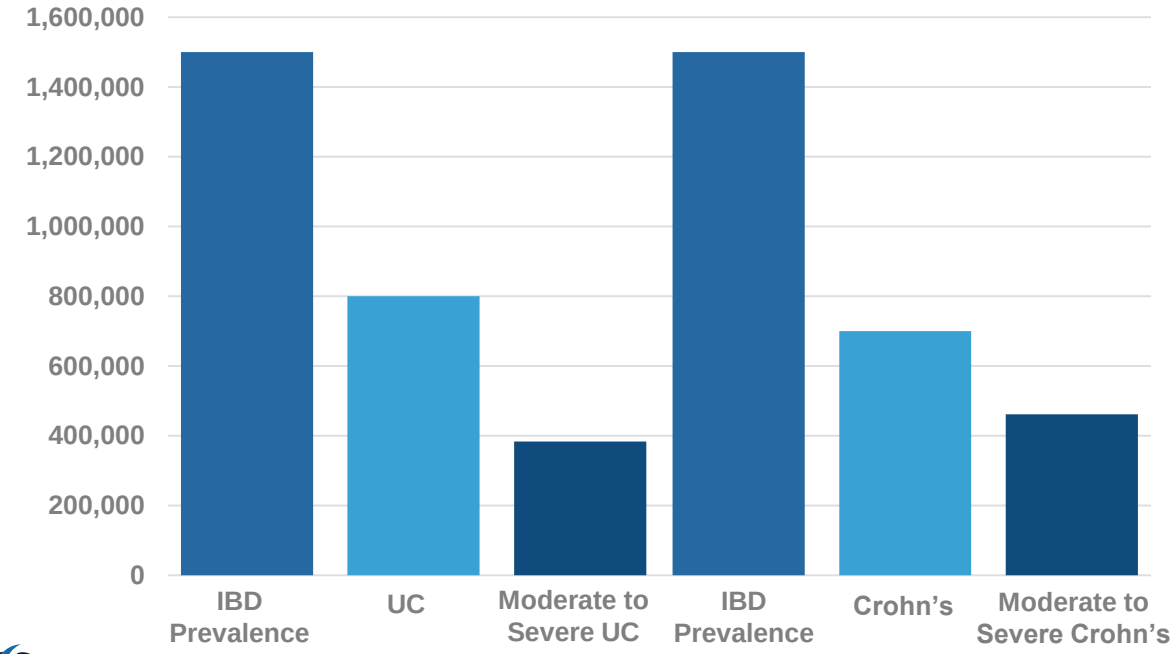
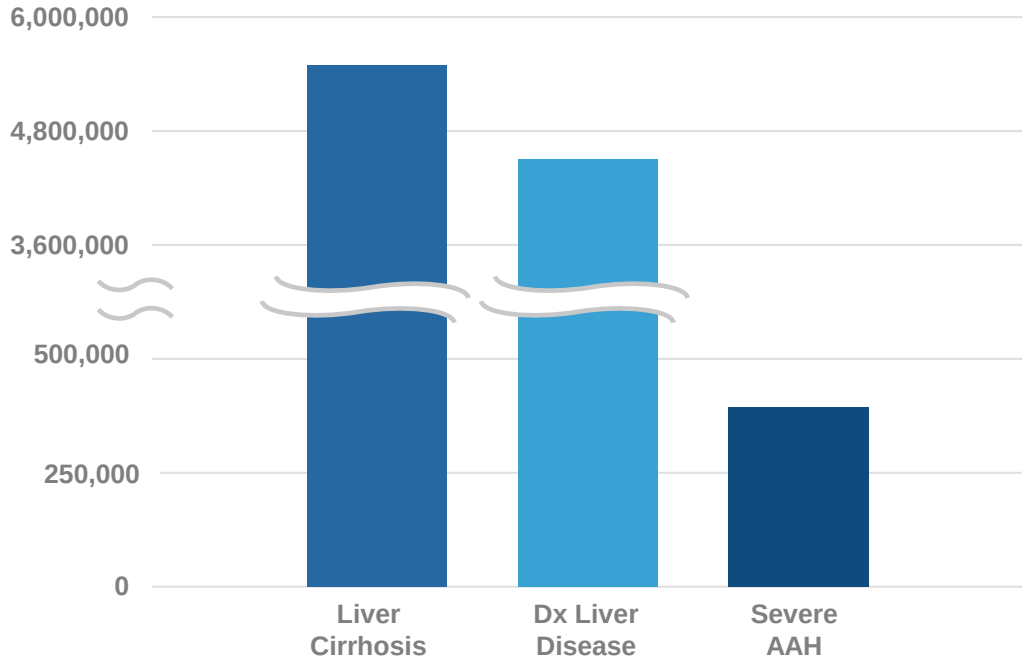
# SZN-1326 & SZN-043 Represent Significant Market Opportunities

- 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

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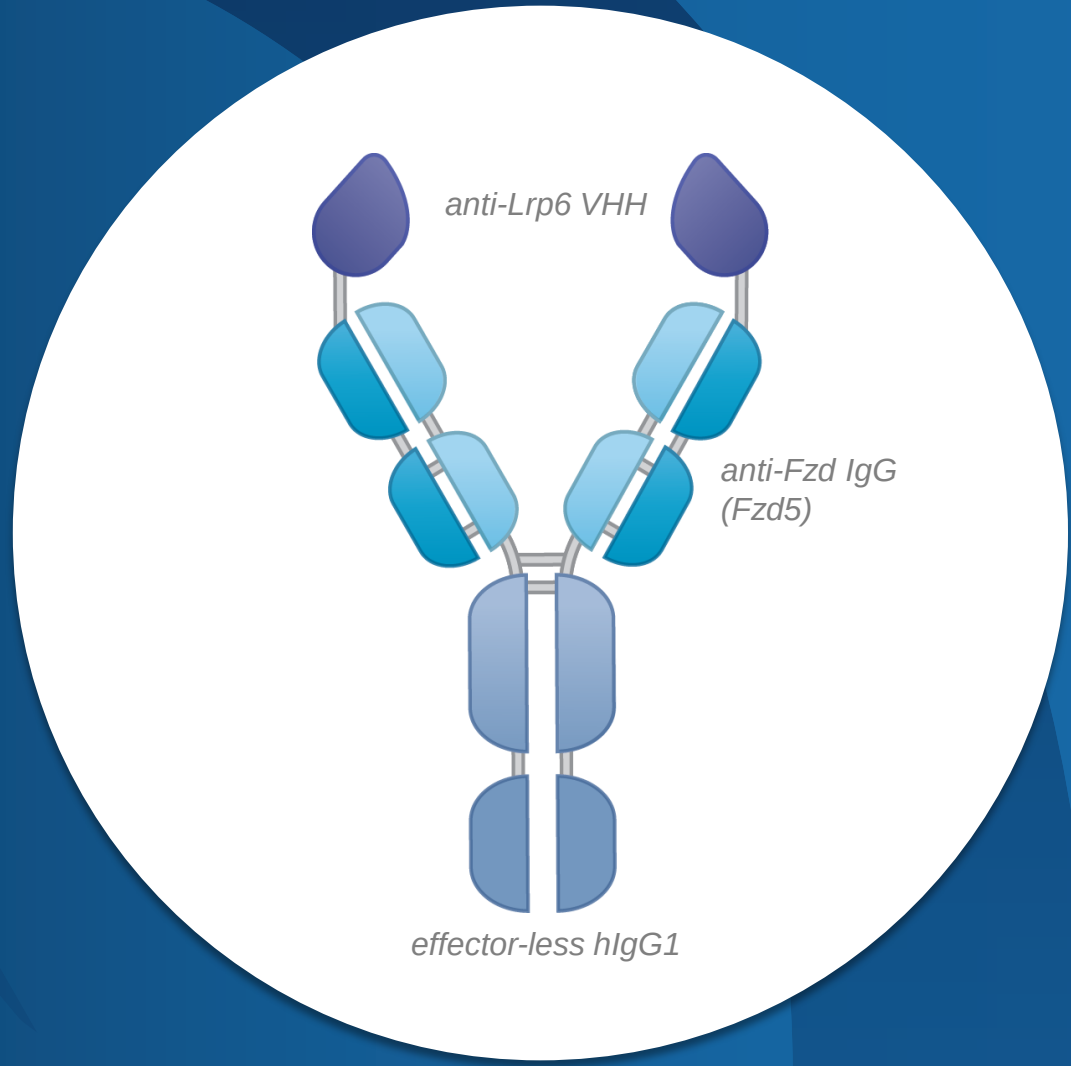
# SZN-1326

## Moderate to Severe IBD

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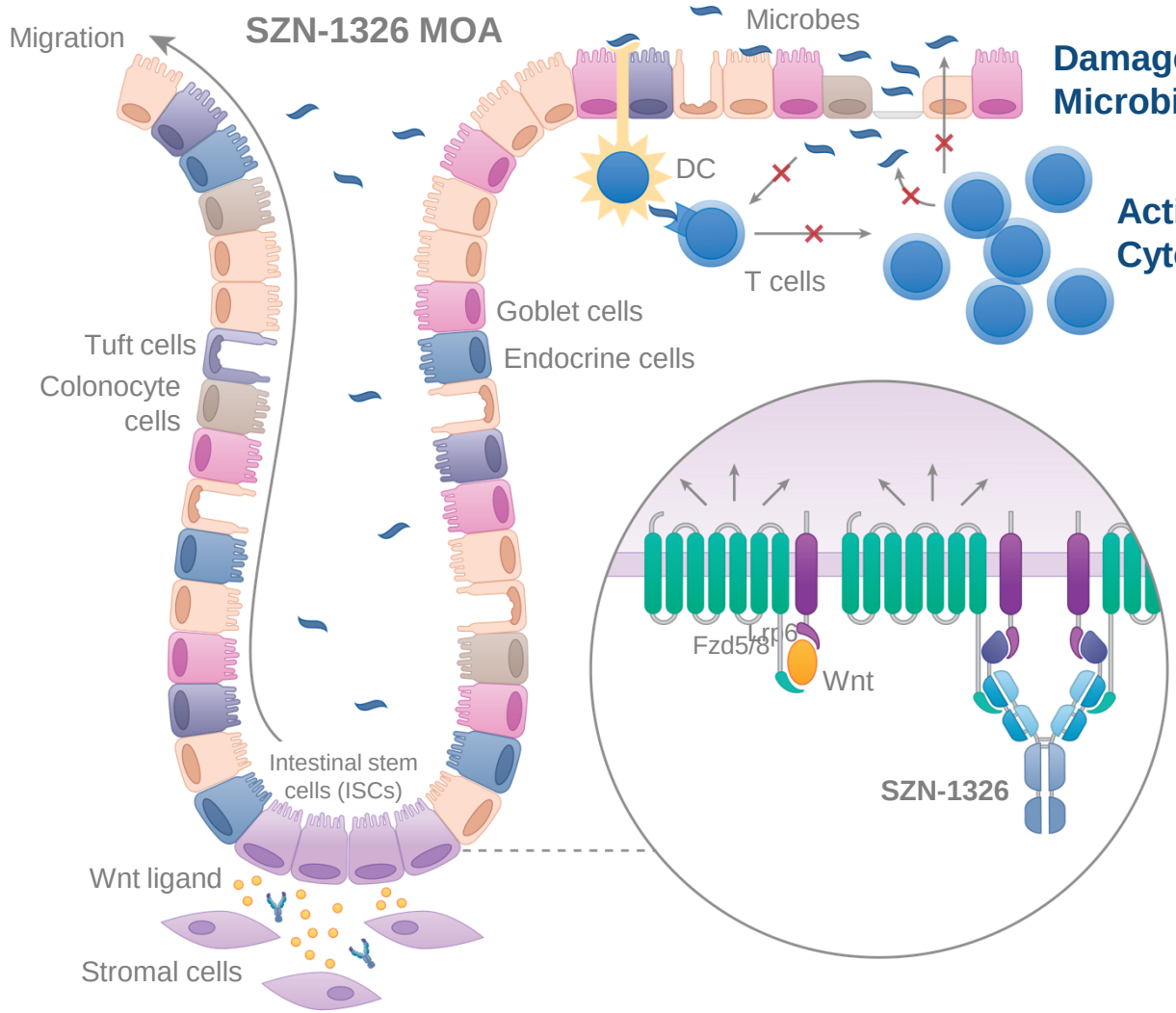
# SZN-1326 – Intestine Targeted Epithelial Restoration

## 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

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# 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 2nd and 3rd line therapies

## Differentiated Preclinical Data

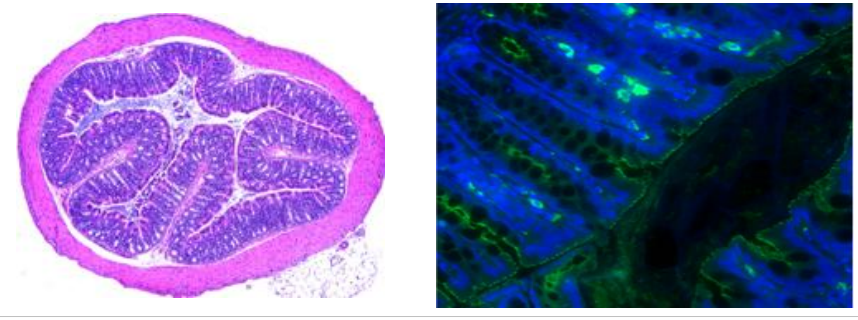
Repairs damaged colon epithelium

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

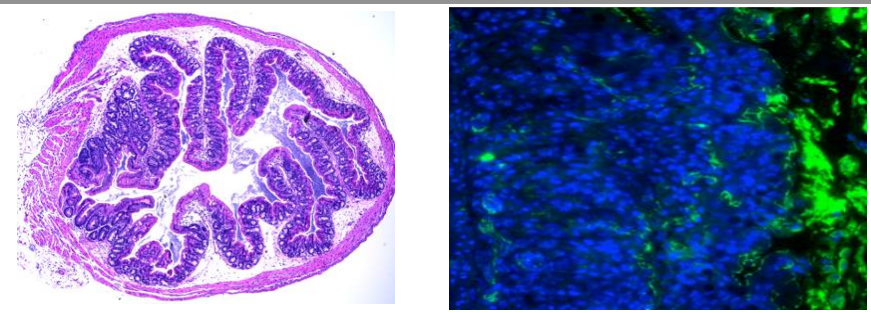
Reduces inflammation and improves disease activity index

Superior to cyclosporin and anti-TNF's

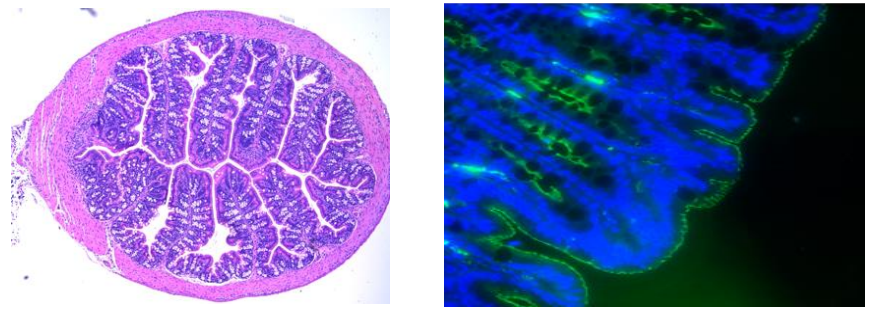
**Normal (No DSS Damage)**



**Damaged (DSS Damage)**



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



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# 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 |
|---|---|---|---|
| **Population** | Healthy | UC Patients | UC Patients |
| **N** | Up to 60 | Dose Escalation: Up to 24<br>Expansion (Mono and Combo): Up to 24 | 120-150 |
| **Key Objectives** | | | |
| **Early Efficacy** | | ○ | ○ |
| **Inform Dose** | ○ | ○ | ○ |
| **Proof of Mechanism** | | ○ | ○ |
| **Safety / PK/ ADA** | ○ | ○ | ○ |
| **Additional End-Points** | 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 |

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# SZN-043

## Severe Liver Disease


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# Potential for First Approved Treatment for Severe Alcoholic Hepatitis

## Liver Specific Wnt Activation and Regeneration


**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

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

## High Unmet Need

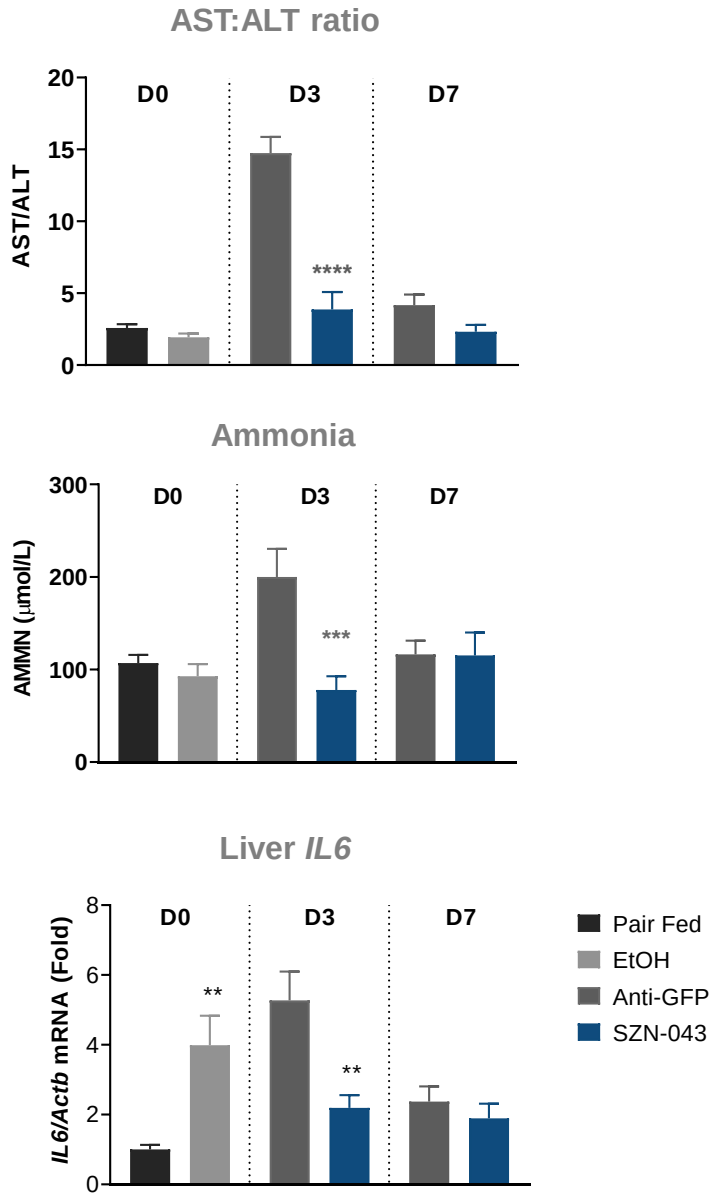
No approved drugs: SOC: steroids

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

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# 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 |
|---|---|---|---|
| **Pop** | HV/Early cirrhosis | Severe Alcoholic Hepatitis | Severe Alcoholic Hepatitis |
| **N** | 30-45 | Up to 30 | 300 (placebo controlled) |
| **Key Objectives** | | | |
| **Early Activity/Clinical Efficacy** | ○ | ○ | ○ |
| **Inform Dose** | ○ | ○ | ○ |
| **Proof of Mechanism** | ○ | ○ | ○ |
| **Safety / PK** | ○ | ○ | ○ |
| **Additional End-Points** | PD markers (angiogenin, Lect2, Methacetin) | 7day Lille score, MELD score PD markers | 90-day mortality |

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# Beyond Intestine and Liver…

## Broad Opportunities in Ocular Disease

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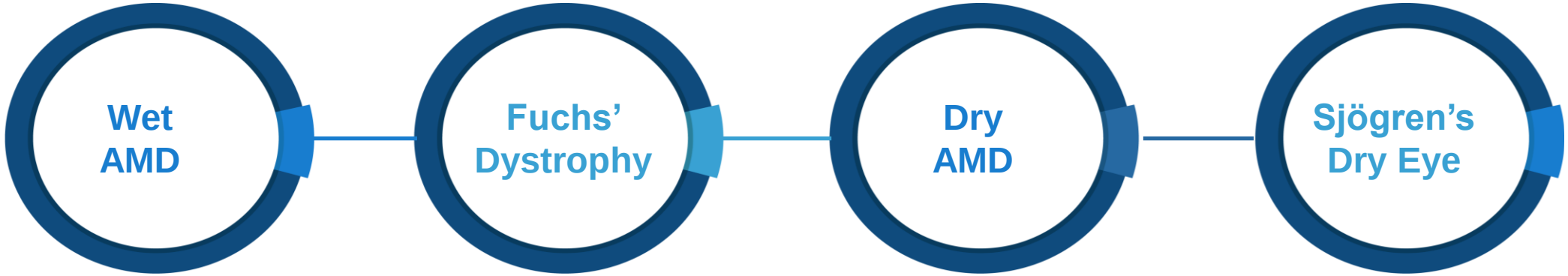
# Preclinical Data Supports Advancement of Ocular Programs

## Broad Set of Opportunities in Ocular Diseases




- Fzd4 maintains & restores the blood-retina barrier
- SWAP antibodies activating Fzd4 inhibited vascular leakage
- 1.5M US patients

- Wnt involved in corneal endothelial cell proliferation
- In-vitro, SWAP antibodies stimulated proliferation of primary human endothelial cells
- 4% US patients over 40

- Wnt involved in retinal pigment epithelial (RPE) cells and photoreceptor regeneration
- In-vitro, SWAP antibodies stimulated RPE proliferation & differentiation
- 1M US patients with dry AMD

- Wnt involved in acinar cell proliferation
- Human lacrimal gland explant cultures respond to SWAP antibodies
- 70,000 US patients with Sjogren's

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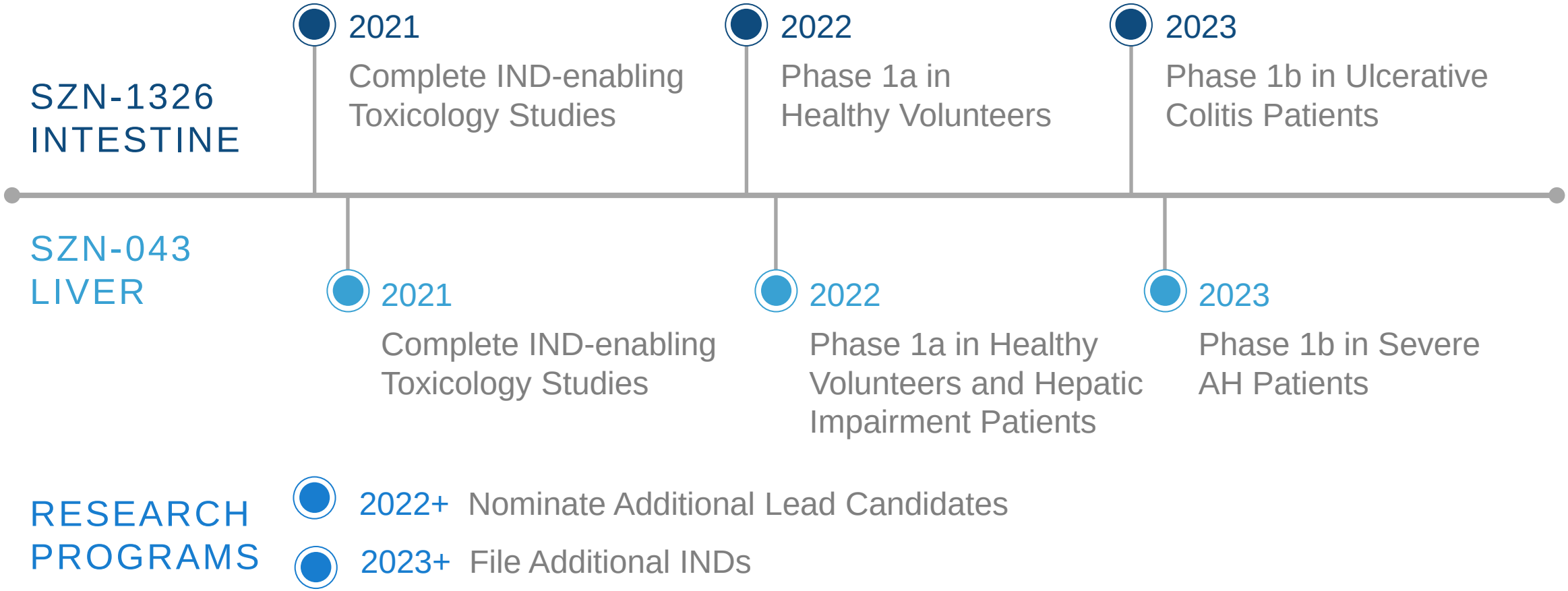
# Near Term Outlook and Potential Milestones

## Multiple Clinical Milestones with Potential for Early Proof of Concept

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# The Wnt Company - Targeted Regeneration

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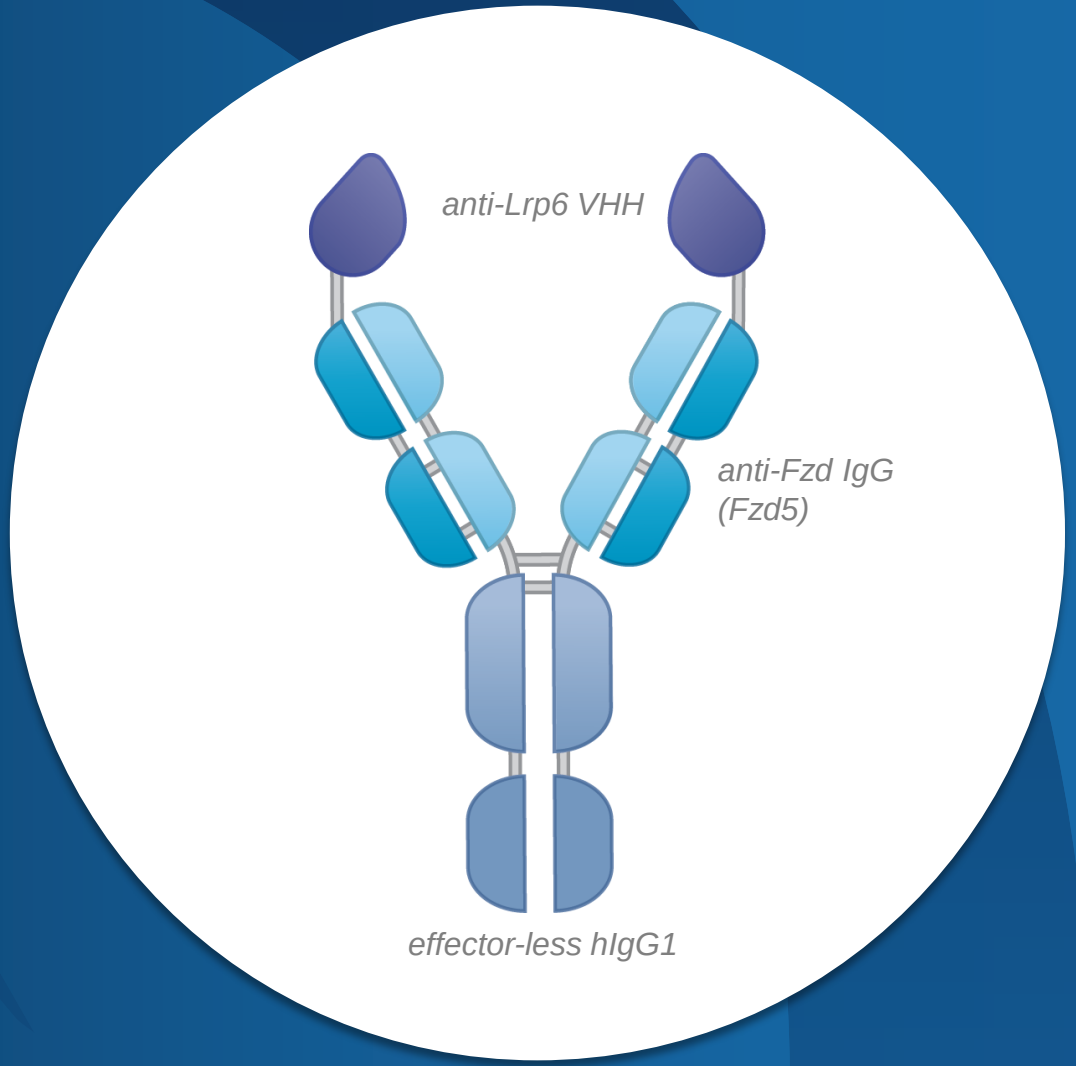
# Appendix

2021

# SZN-1326

## Preclinical Data

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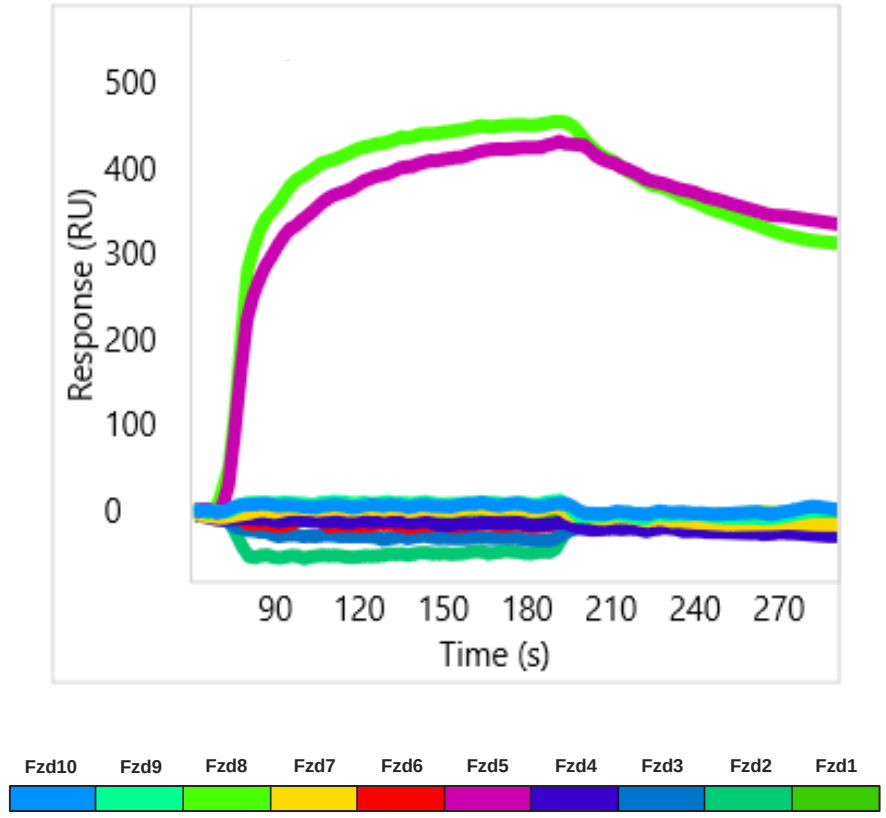
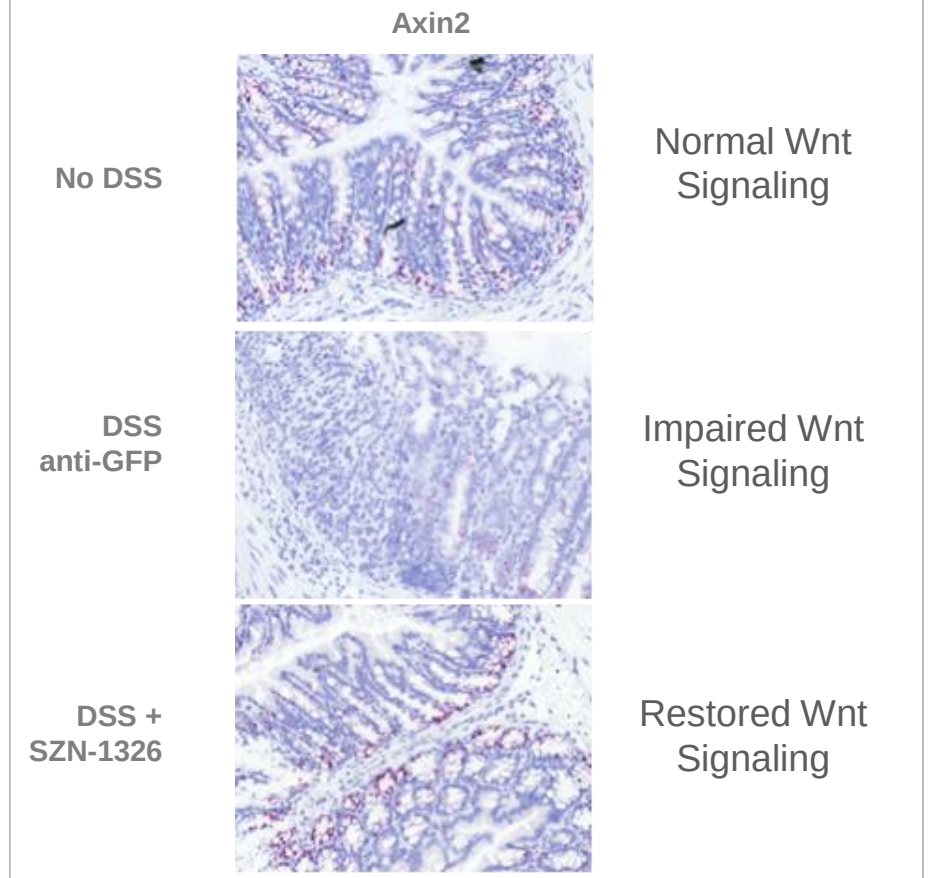
# SZN-1326 – Restores Wnt Signaling in Damaged Intestine

- ☑ **Selective Wnt activation**
- ☐ Epithelial repair
- ☐ Inflammation reduction
- ☐ Functional improvement

## Selective Binding Profile




## Restores Wnt Signaling in Damaged Intestinal Epithelium




**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

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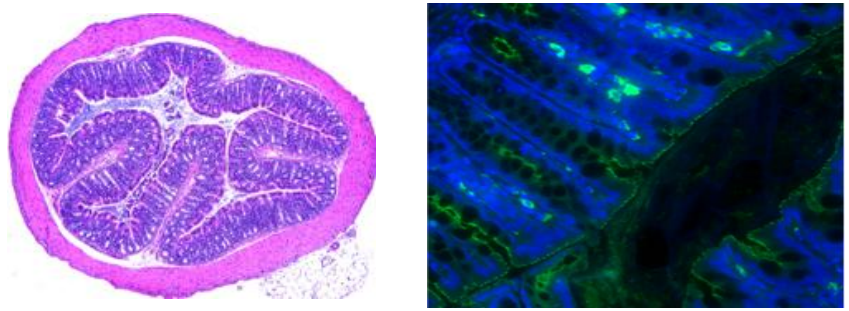
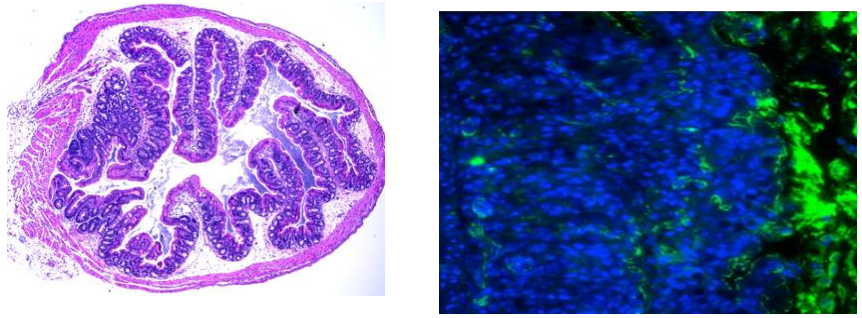
# SZN-1326 – Repairs Damaged Colon Epithelium

- ☑ Selective Wnt activation
- ☑ **Epithelial repair**
- ☐ Inflammation reduction
- ☐ Functional improvement

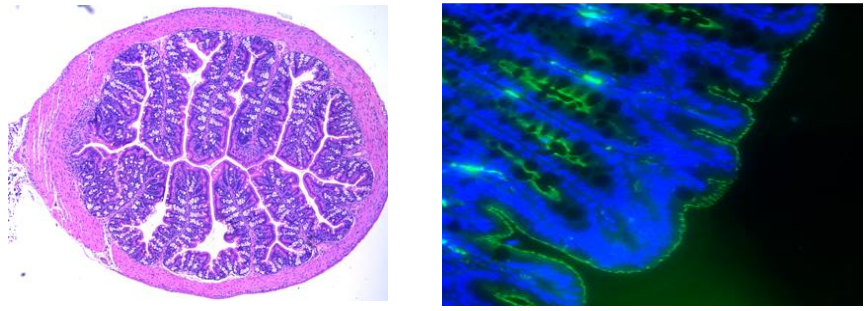
**Normal (No DSS Damage)**



**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

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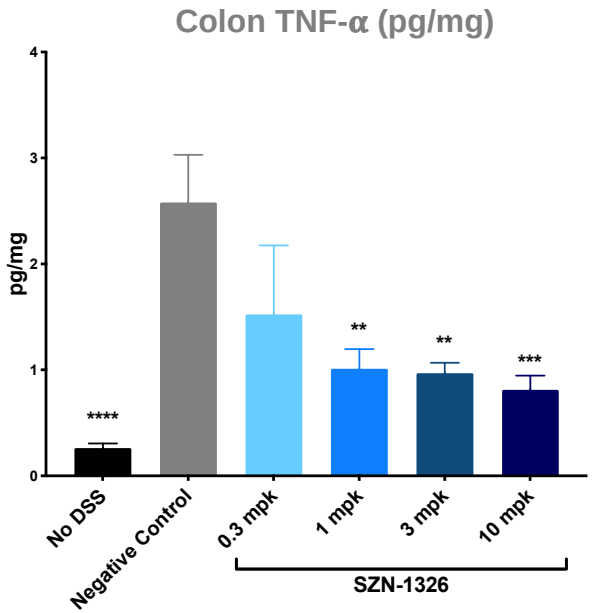
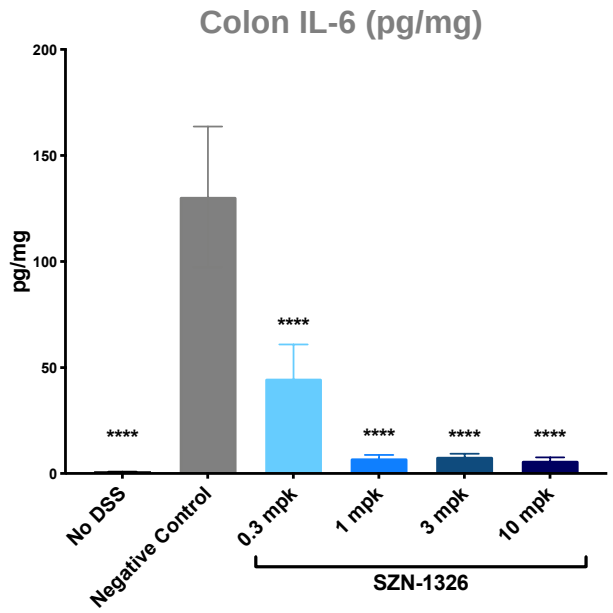
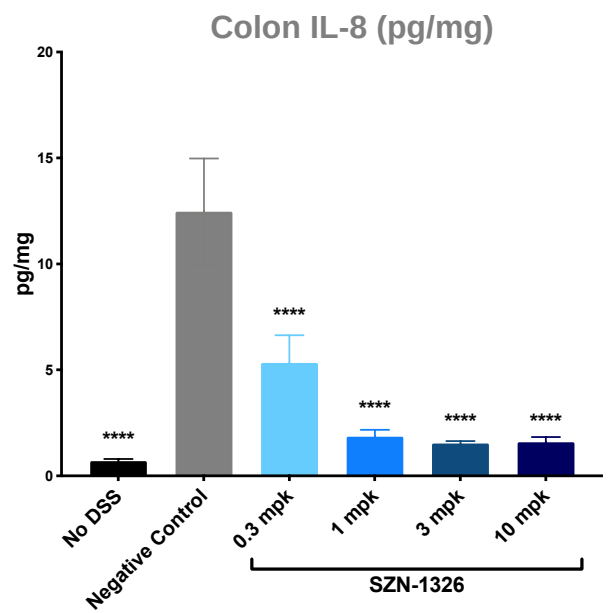
# SZN-1326 – Reduces Inflammatory Cytokines

- ☑ 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.

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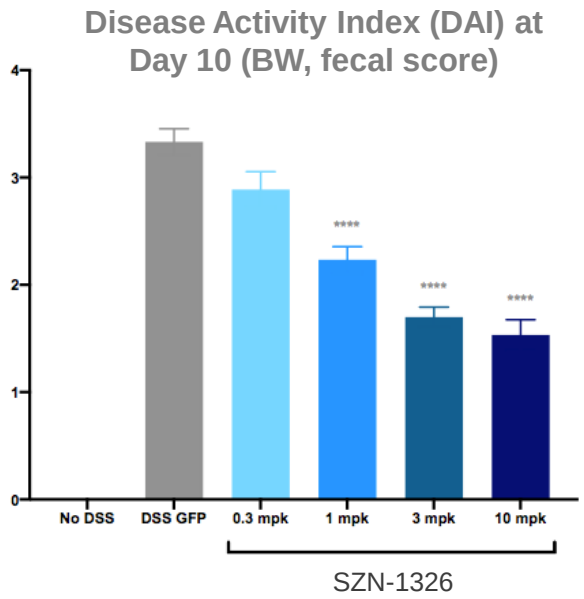
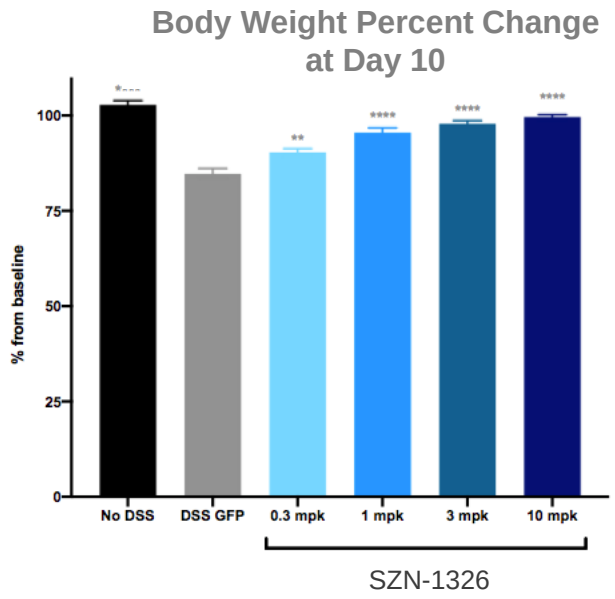
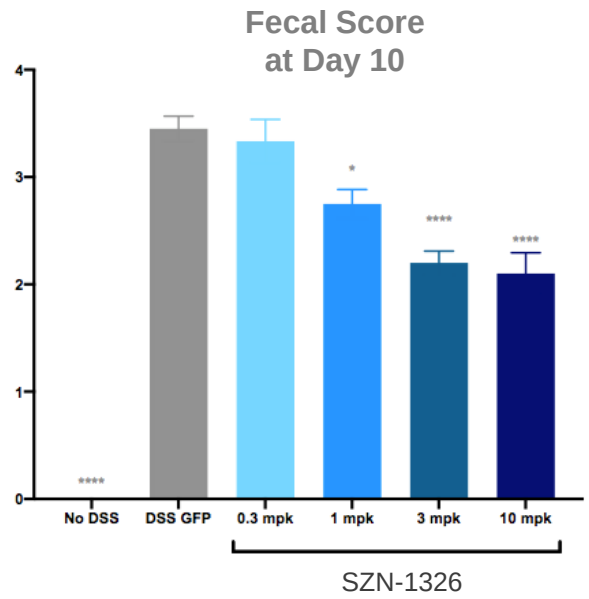
# SZN-1326 – Reduces Disease Activity

- ☑ 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.

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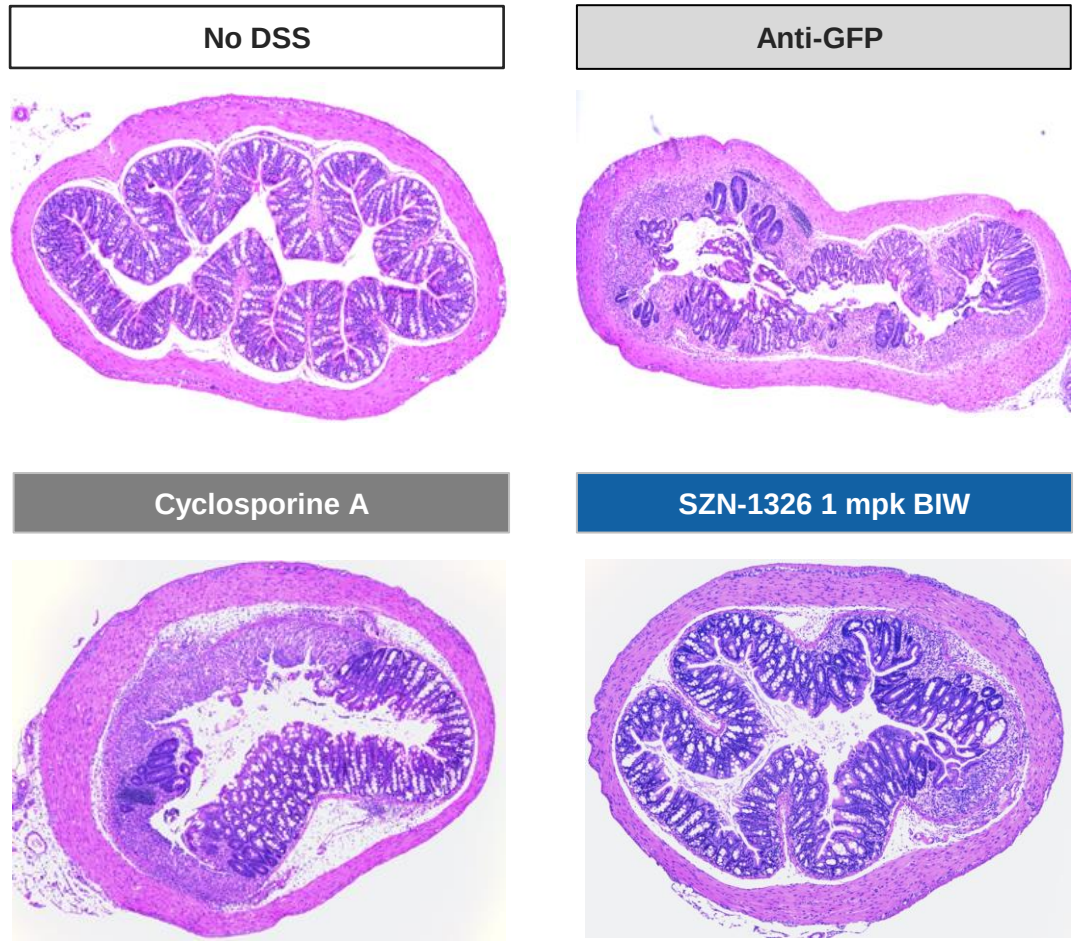
# SZN-1326 – Repairs Colon Epithelium *In Vivo* More Than Cyclosporine

- ☑ Selective Wnt activation
- ☑ **Epithelial repair**
- ☐ Inflammation reduction
- ☐ Functional improvement

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




**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.

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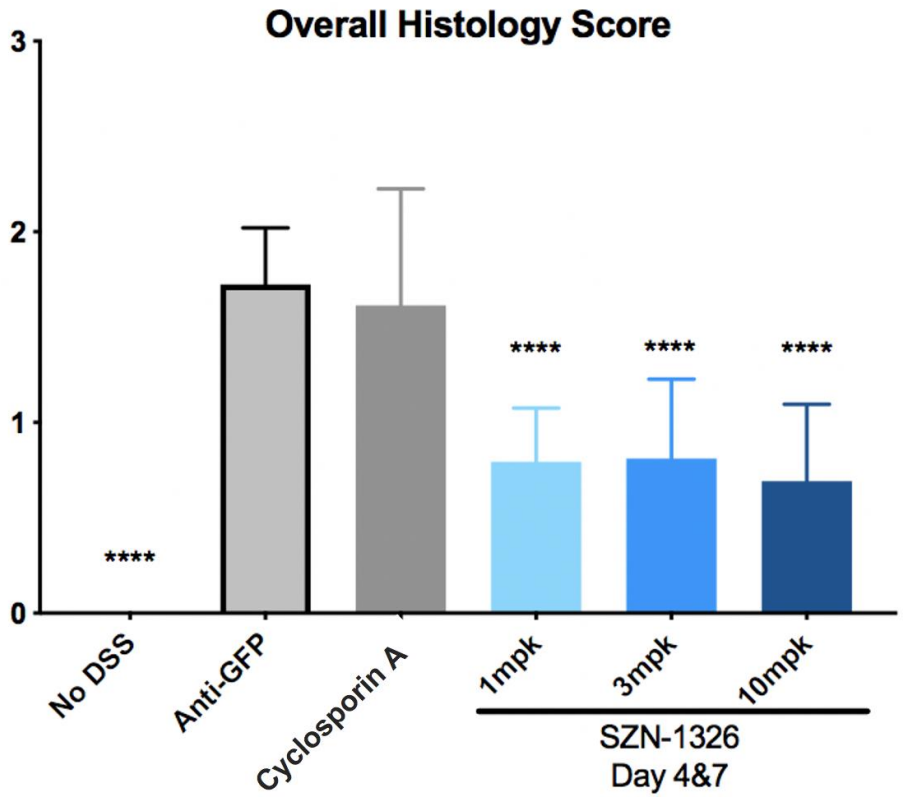
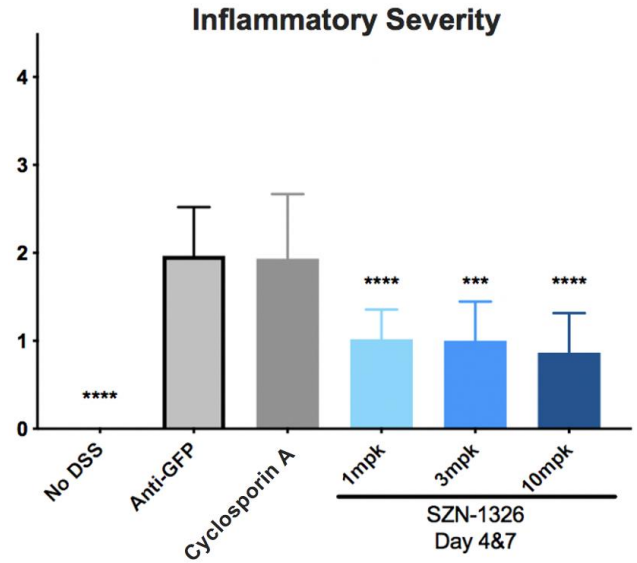
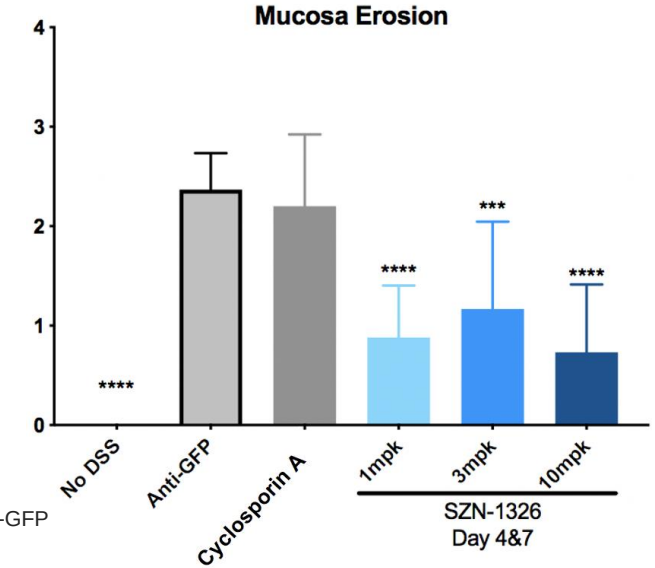
# SZN-1326 – Improves Colon Histology Score *In Vivo* More Than Cyclosporine

- ☑ 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.

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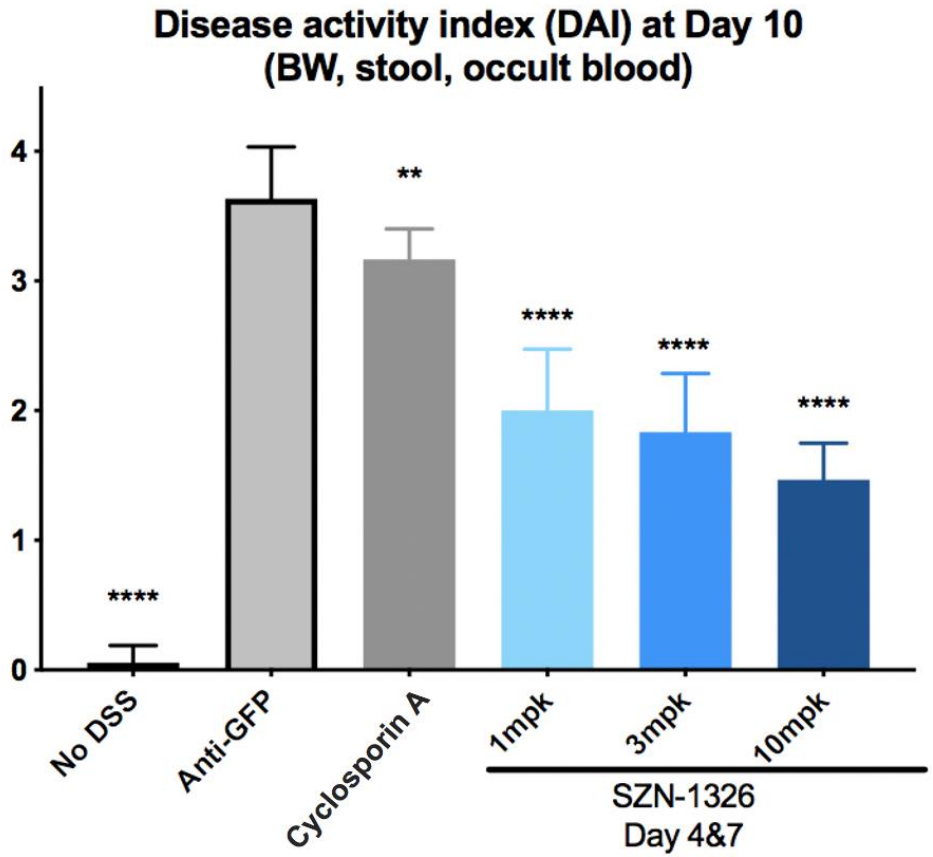
# SZN-1326 – Improves Disease Activity *In Vivo* More Than Cyclosporine

- ☑ Selective Wnt activation
- ☑ Epithelial repair
- ☑ Inflammation reduction
- ☑ **Functional improvement**

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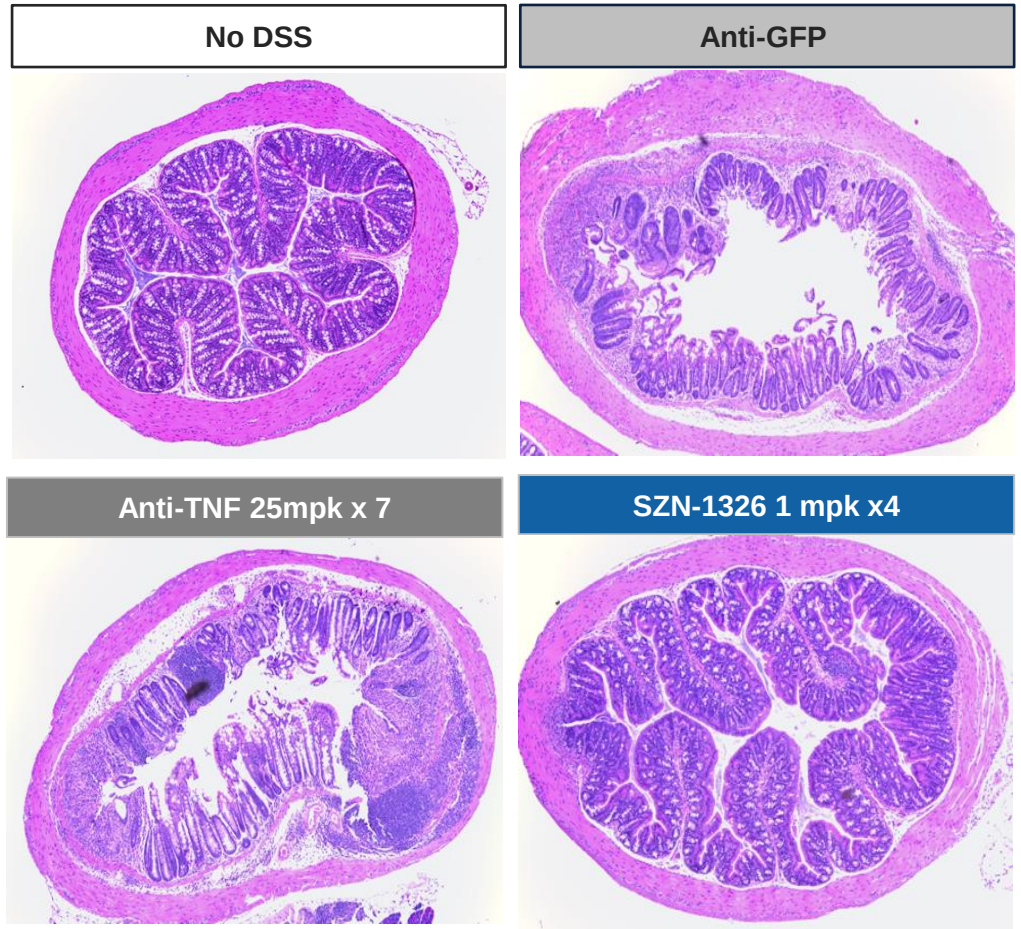
# SZN-1326 – Repairs Colon Epithelium Better Than Anti-TNF in Chronic *In Vivo* Model

- ☑ 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.

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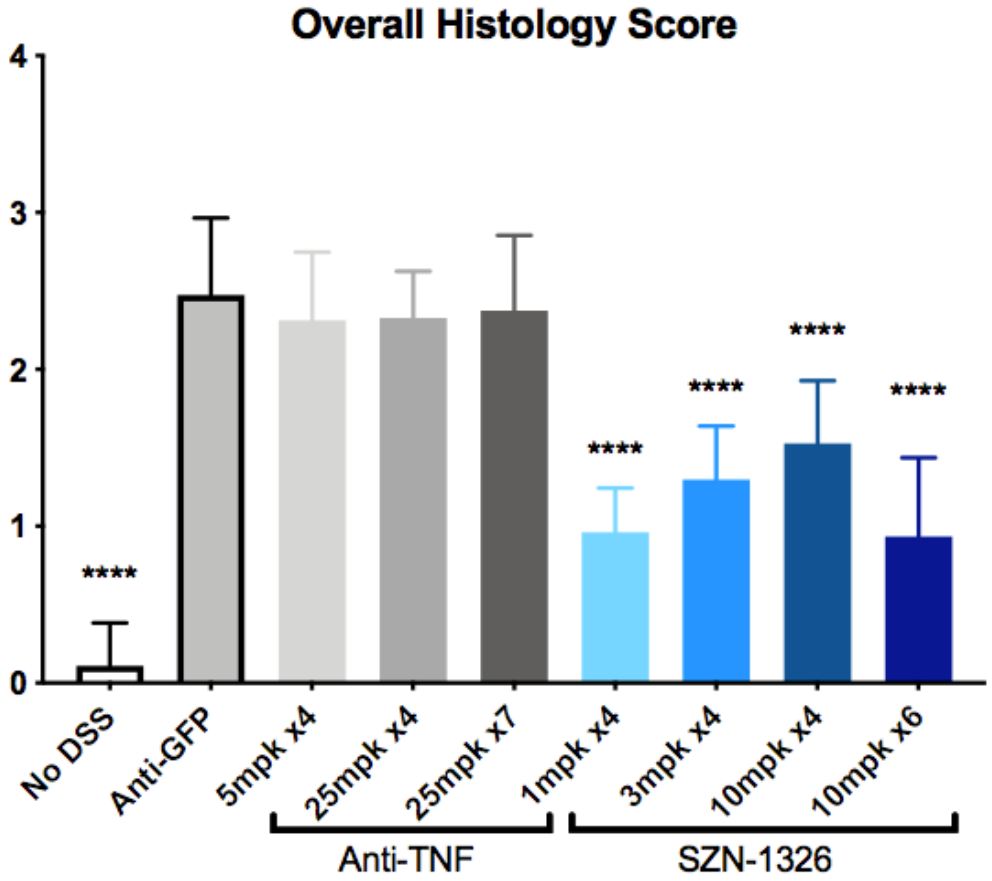
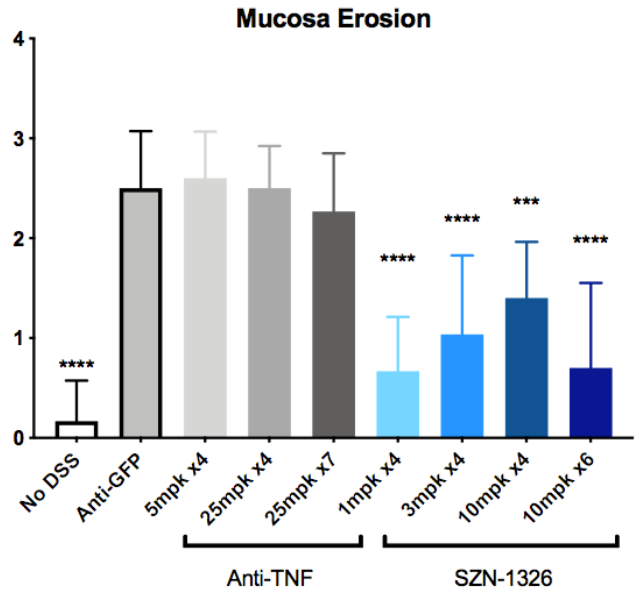
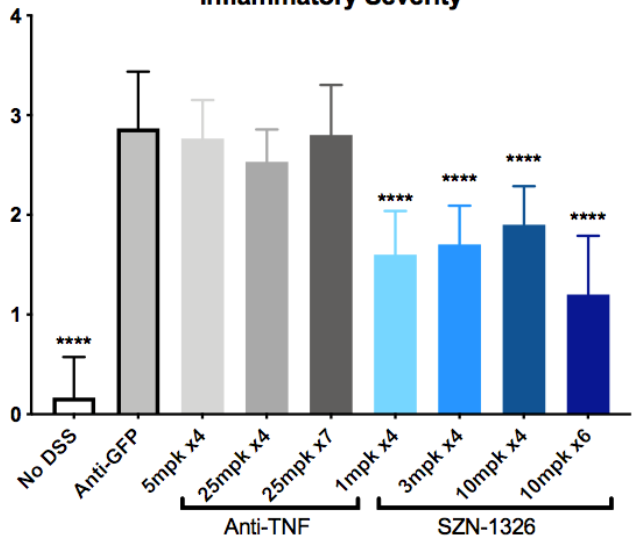
# SZN-1326 – Improves Colon Histology Score More Than Anti-TNF in Chronic *In Vivo* Model

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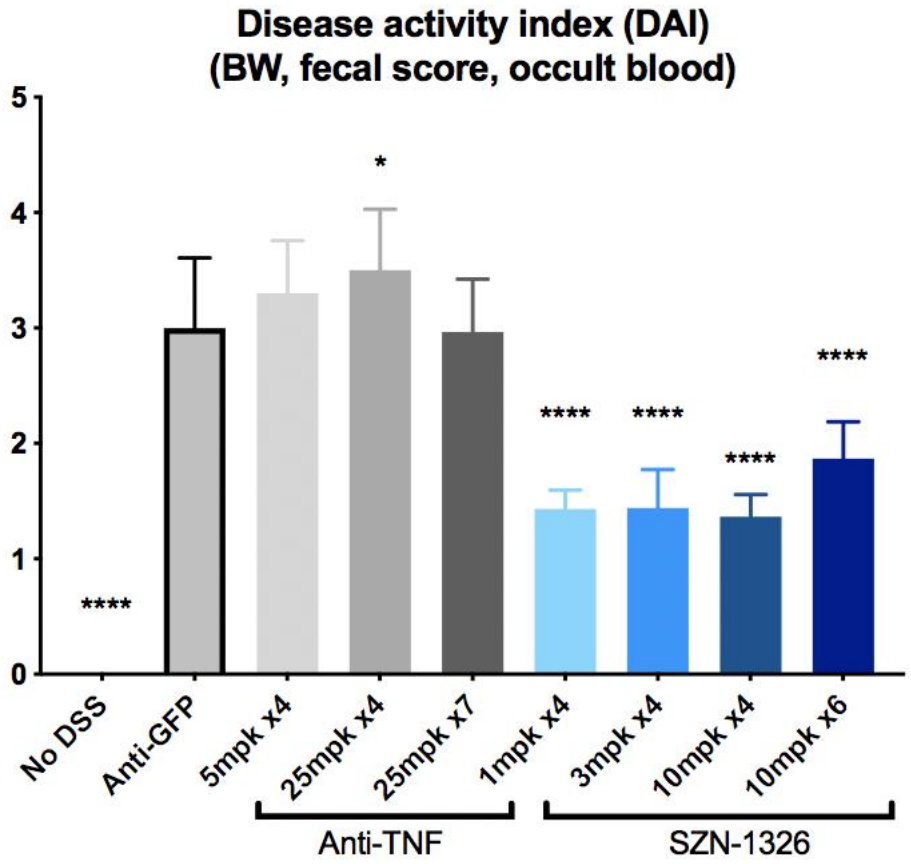
# SZN-1326 – Improves Disease Activity More Than Anti-TNF in Chronic *In Vivo* Model

- ☑ Selective Wnt activation
- ☑ Epithelial repair
- ☑ Inflammation reduction
- ☑ **Functional improvement**

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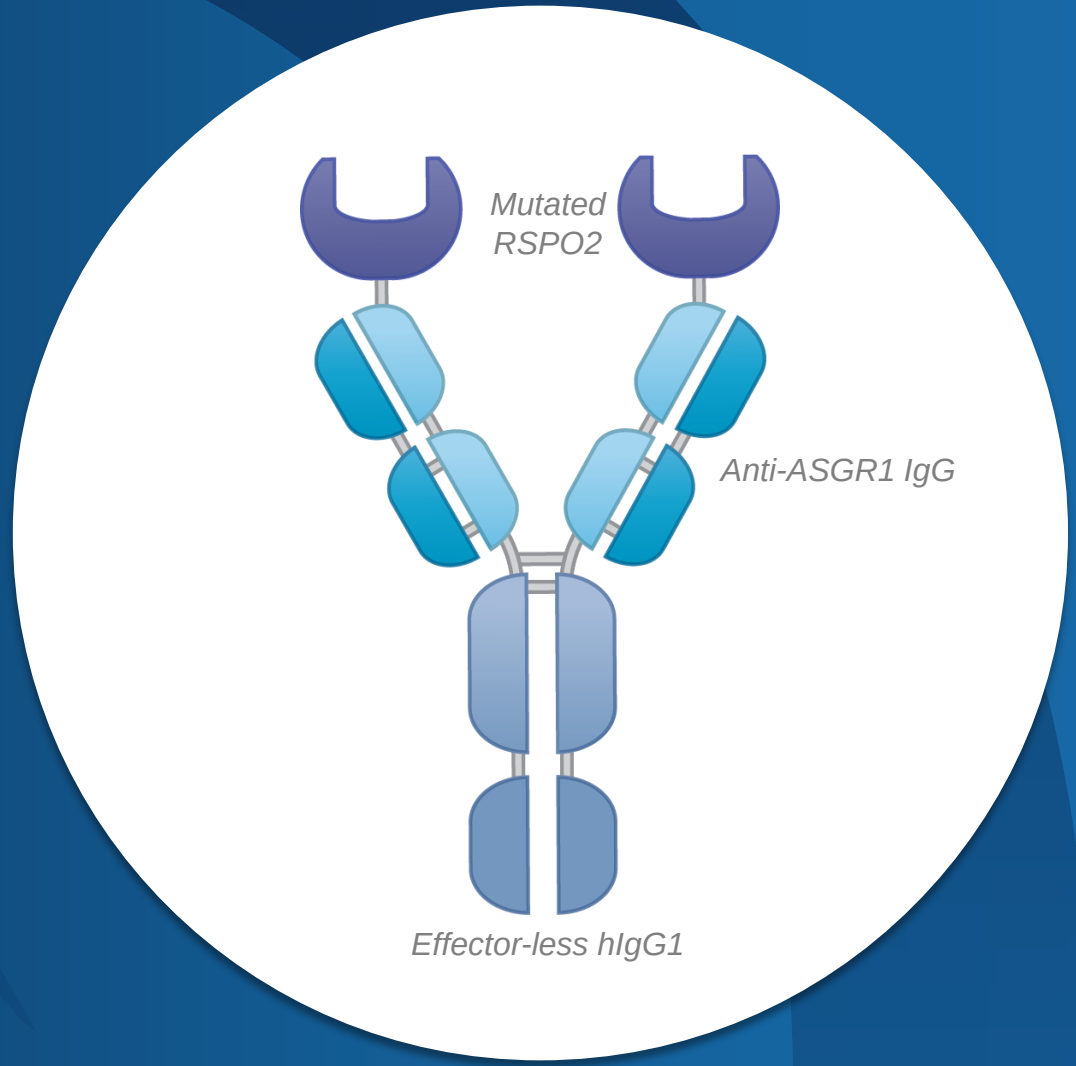
# SZN-043

## Preclinical Data

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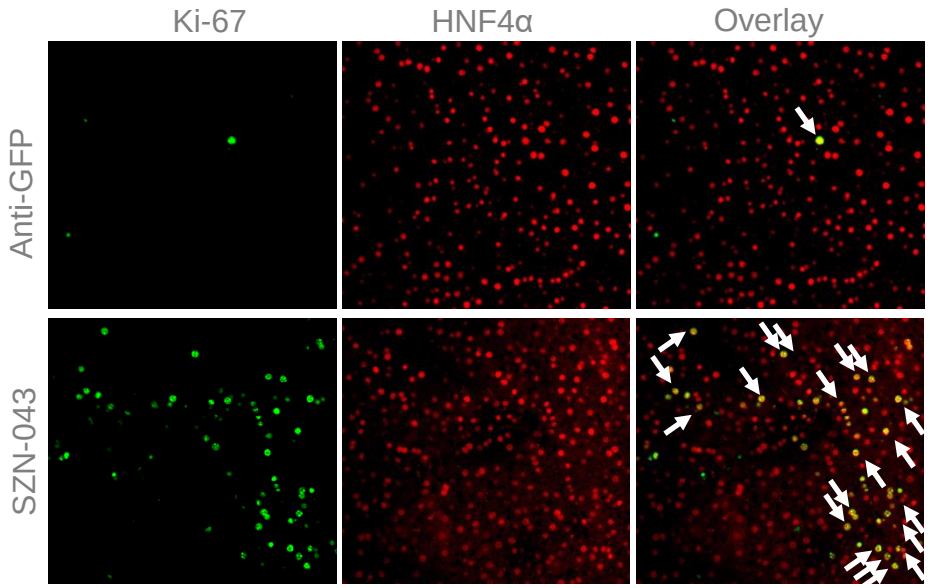
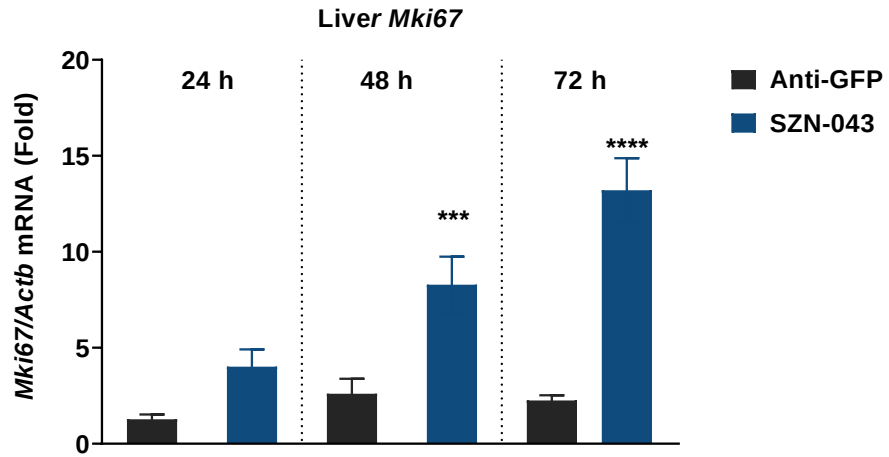
# SZN-043 Selectively Stimulates Hepatocyte Proliferation

## 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.

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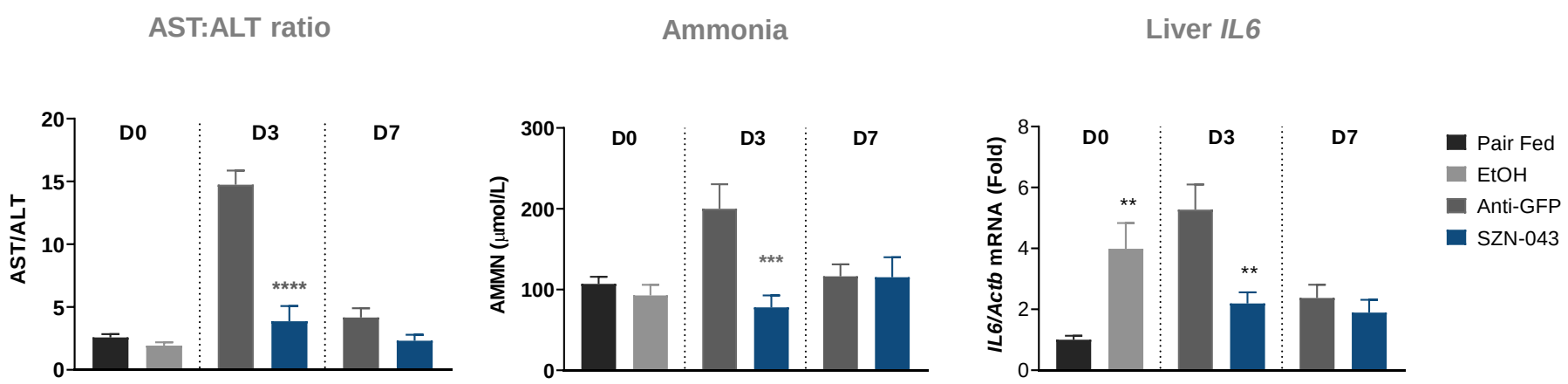
# SZN-043 Reduces Markers of Liver Injury and Inflammation

## 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, IL1β, and IL6

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# 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

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