



Targeted Regeneration

January 12, 2023

JP Morgan Healthcare Conference

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Selectively Activating the Body's Natural Repair Mechanisms

*Major Diseases
with underlying tissue damage*

*Ulcerative Colitis
Crohn's Disease
Liver Failure
Retinopathies
COPD
IPF
Fuch's
Type 1 Diabetes
Wound Healing*

*Current Treatment Options –
limited opportunity for
repair/regeneration*

*Primarily limit additional
tissue damage or address
some symptoms*

*Other than organ or cell
transplant, no treatment
options that can regenerate
or reverse disease*

*Surrozen Approach:
Selectively activate natural
regeneration pathways with
antibodies*

SWAP Technology



Mimics of Wnt
pathway
associated
proteins

SWEETS Technology



Targeted to
tissue and/or
specific cells
types



Surrozen: Leaders in Wnt Biology and Targeted Regeneration

Vision

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

Focus

Severe or acute diseases with strong evidence of Wnt mediated regenerative potential : GI, Liver, Ophthalmology

Novelty and Breadth

Invented targeted, antibody-based Wnt modulating platforms with first-in-class POC in several tissue/disease areas

Clinical Stage Pipeline

Initiation of FIH clinical trials in 2Q'22

- ✓ SZN-043: Severe Liver Disease (ongoing)
 - ✓ SZN-1326: Inflammatory Bowel Disease (paused enrollment 4Q'22)
-

Corporate Partner

SZN-413: Fzd-4 targeted bi-specific initially for ophthalmology
Partnered with Boehringer Ingelheim

Balance Sheet

~\$90M cash balance*



Surrozen Science Addresses Multiple Barriers

Paving the Way to Targeted Antibody Regeneration

Characteristics of Surrozen Platform

Selectivity: Target specific Fzd or cell surface receptors

Potency: Confer potency through multivalent binding

Biology: Mimic normal physiologic responses

Manufacturing: Easily manufacturable leveraging typical antibody methods with high yields

Prominent Role in Wnt Biology Breakthroughs

nature

Surrogate Wnt agonists that phenocopy canonical Wnt and β -catenin signaling

CellPress

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

SCIENTIFIC REPORTS

natureresearch

Tissue-targeted R-spondin mimetics for liver regeneration

cmgh

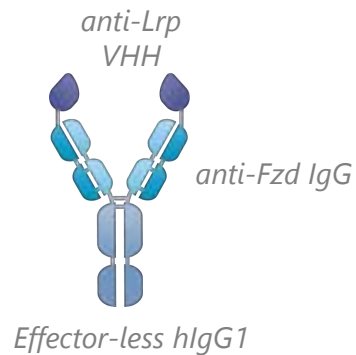
Robust Colonic Epithelial Regeneration and Amelioration of Colitis Via FZD-Specific Activation of Wnt Signaling

tvst an ARVO Journal

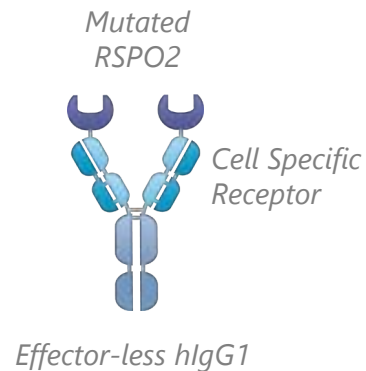
SZN-413, a FZD4 Agonist, as a Potential Novel Therapeutic for the Treatment of Diabetic Retinopathy

Proprietary Technologies Enable Selective Wnt Signaling

SWAP Technology



SWEETS Technology



Mimic normal physiologic response

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

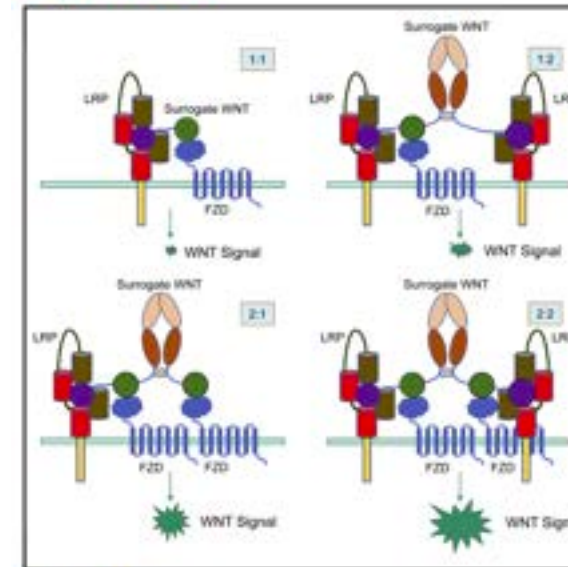
Customized for each disease state

Targeted with Fzd receptor selectivity or cell specific receptors

Cell Chemical Biology

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

Graphical Abstract



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In Brief

WNT molecules have the potential to induce tissue regeneration and repair. However, their biophysical characteristics and lack of selectivity have hindered their application as therapeutics. Chen et al. have developed a platform for potent, selective WNT surrogate generation, and identified key requirements for maximal signaling.

Highlights

- Developed a flexible system to generate potent and selective surrogate WNTs
- Multivalent binding to FZD and LRP is a requirement for maximal activation
- Active receptor complexes can contain different ratios of receptors
- Recruitment of two different FZDs together with LRP induces efficient signaling

Wnt Biology and Regeneration Underpins a Compelling R&D Pipeline

Lead Programs	Indication(s)	Research	Preclinical	Phase 1	Phase 2	Phase 3	Partnerships	Status
SZN-043	Severe Alcoholic Hepatitis							Ph 1 Ongoing
SZN-1326	Moderate to Severe IBD							Enrollment paused; Next steps TBD
SZN-413	Retinopathies						Boehringer Ingelheim	

Research Programs

Tissue	Indications	Discovery	Proof of Concept	Lead Candidate/s
Lacrimal Gland	Severe Dry Eye (Sjögren's)			
Cornea	Fuchs' Dystrophy			
Skin	Wound Healing			

SZN-043 Potential to Transform Patient Outcomes in Severe AH

Targeted antibody designed to induce hepatocyte proliferation and improve liver function

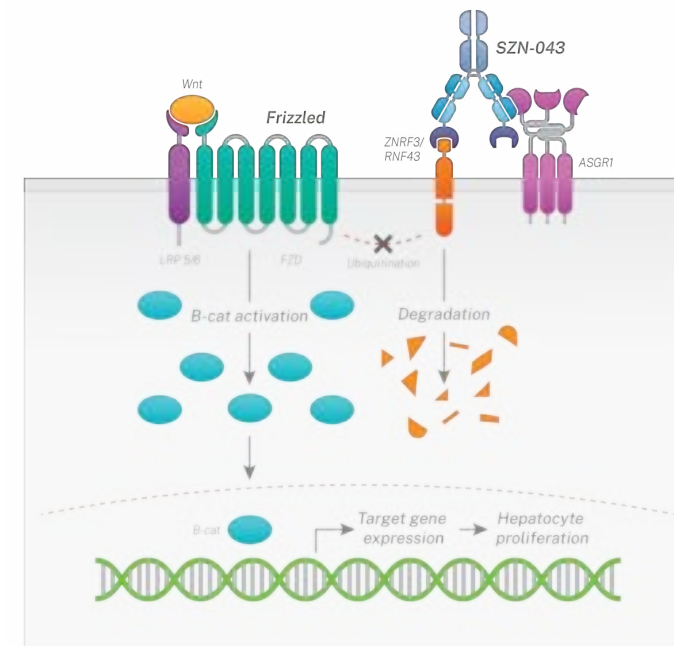
Unmet Need in SAH

- 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 survival benefit at 3 months
 - Liver transplants: limited supply, costly and often denied

SWEETS Technology – A Targeted Solution

MOA: SZN-043 designed to address underlying pathophysiology

- Hepatocyte proliferation correlated with increased survival
- Upregulation of Wnt signaling implicated in improved liver function
- Hepatocyte targeted effect achieved through ASGR1 binding



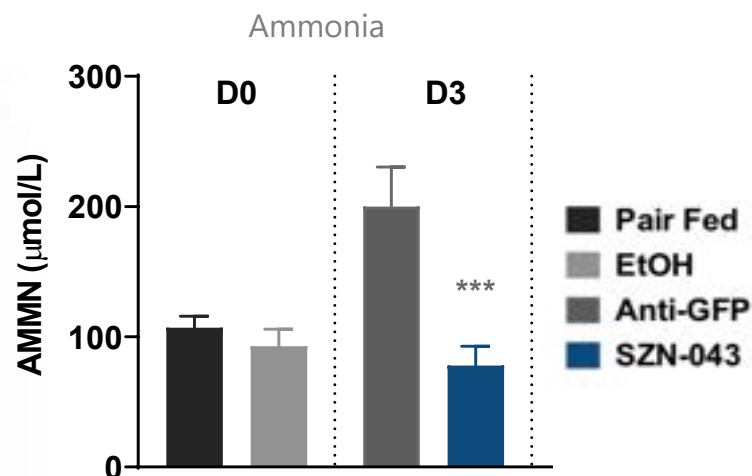
SZN-043 In Vivo Effects

Liver Specific Proliferation, Functional Improvement, Fibrosis Regression

Improvement in Liver Function in Multiple Liver Injury Models

Compelling Preclinical Data

- >25 preclinical studies conducted
- Selectively activates Wnt Signaling
- Induces hepatocyte proliferation
- Rapidly improves liver function
- Reduces markers of liver injury & inflammation

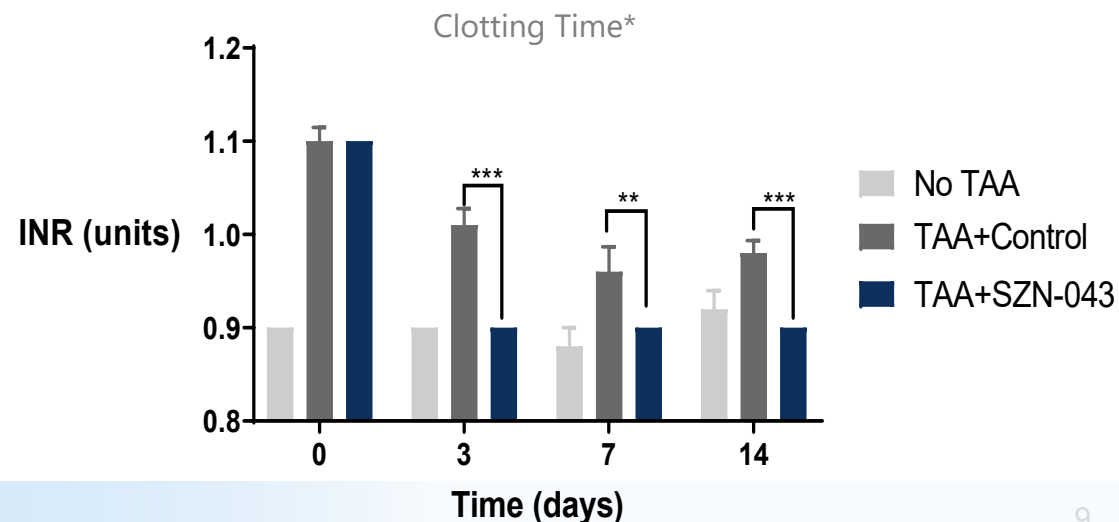


Rodent alcohol liver injury model

- Alcohol injury model phenocopies alcoholic hepatitis
- Similar hepatocyte loss and functional impact
- Increased ammonia as seen in AH
- SZN-043 treatment induces hepatocyte proliferation
- SZN-043 treatment rapidly lowers ammonia

Rodent thioacetamide liver injury model

- TAA liver injury model induces functional loss
- Increased clotting time (synthetic function)
- SZN-043 treatment induces hepatocyte proliferation
- SZN-043 treatment rapidly normalizes clotting time (INR)

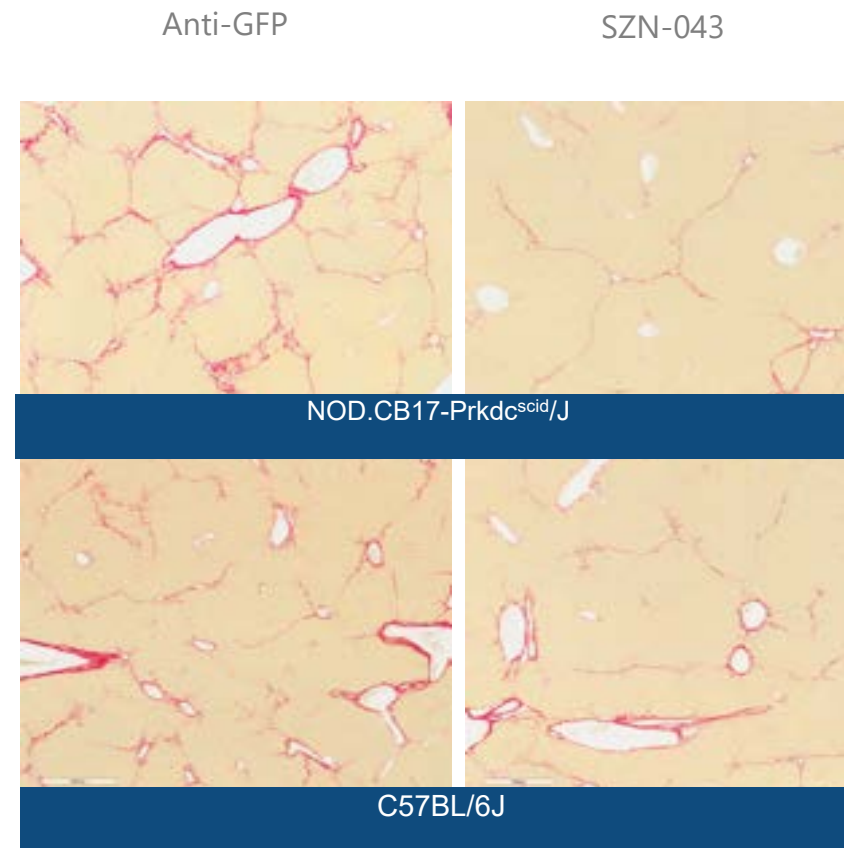
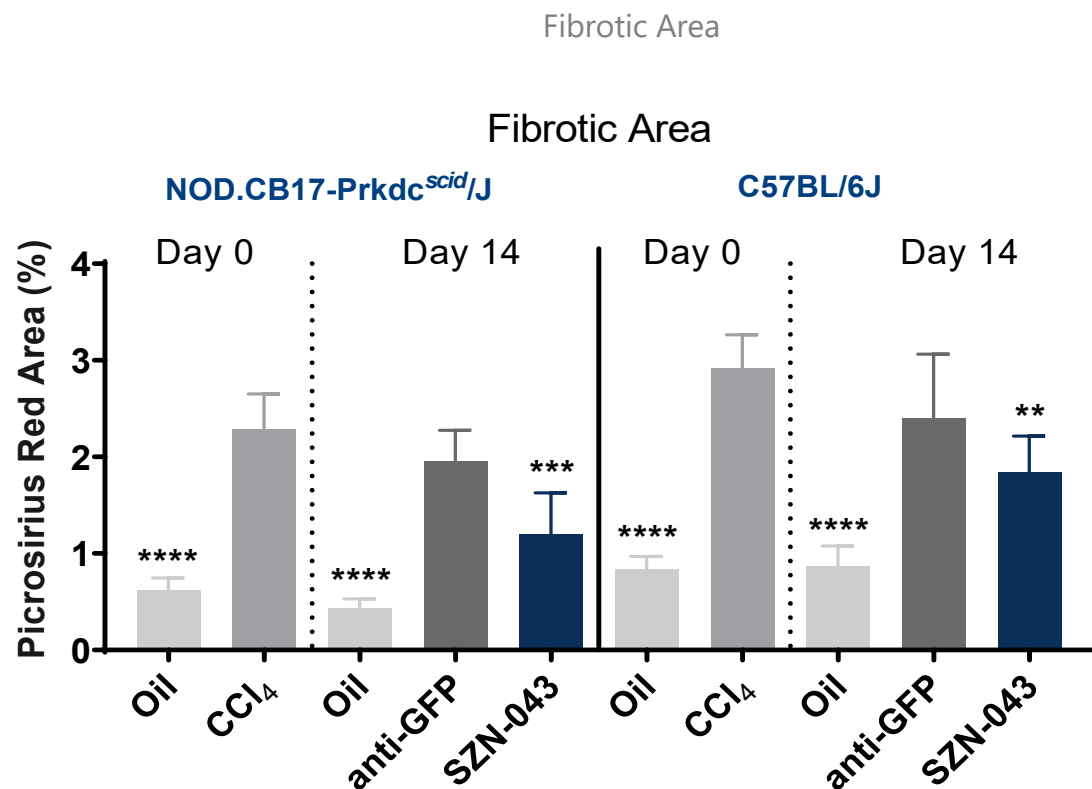


SZN-043 In Vivo Effects

Liver Specific Proliferation, Functional Improvement, Fibrosis Regression

Regression of Fibrosis

Rodent CCL₄ liver injury 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

2 randomized cohorts
(IV)

Safety

PK

Ph 1b – SAD

Early cirrhosis

PK

PD marker indicative
of liver disease
severity

Ph 1b

Severe Alcoholic
Hepatitis (AH)

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

Potential for Fast
Track
and Breakthrough
Designation

Key Endpoints

Ph 1a SAD:

- Safety, ADA
- PK/PD

Ph 1b SAD - (early cirrhosis)

- Safety
- PK/PD (Hepquant)
- ADA

Ph 1b Severe AH

- Lille and MELD scores
- Mortality

SZN-043 Phase 1 Clinical Trial Ongoing

Initial Clinical and Laboratory Observations in Healthy Volunteers

Objectives

To characterise the safety and tolerability of single ascending doses of SZN-043 in healthy volunteers (HVs)

To characterise the pharmacokinetics (PK) of single IV doses of SZN-043 in HVs

To evaluate the immunogenicity (measured as antidrug antibodies [ADA]) to SZN-043 in HVs

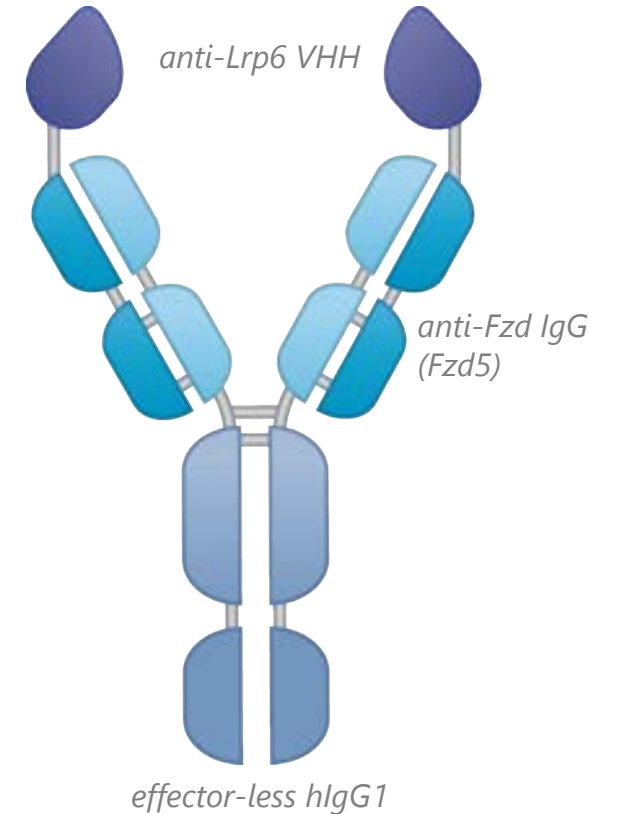
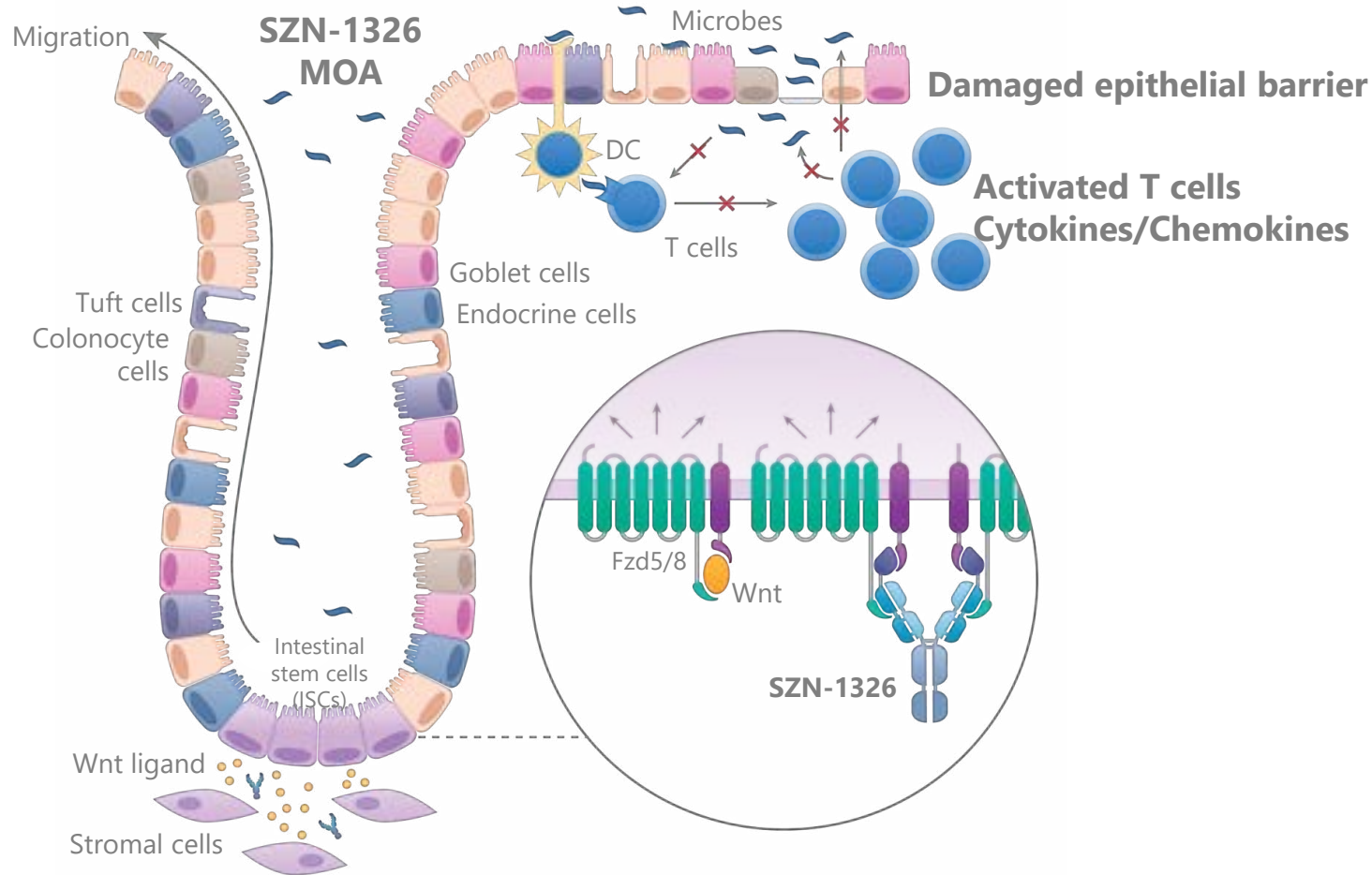
Observations

Well tolerated
No serious Adverse Events
Grade 1 and 2 treatment-related asymptomatic transaminase elevations (ALT, AST)
No corresponding increase in total bilirubin or GGT
No changes in liver function markers (coagulation or albumin)
No other clinically significant laboratory abnormalities
Transaminase increases resolved spontaneously

Consistent with predictions from other species
Dose dependent exposure

SZN-1326 – Intestine Targeted Epithelial Restoration

Potential New Treatment Paradigm in Inflammatory Bowel Disease

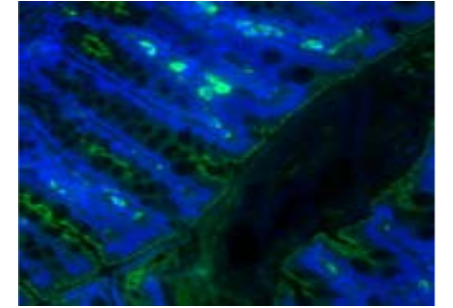


Intestine-Targeted Regeneration and Functional Improvement

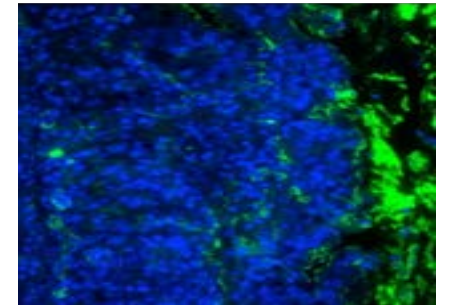
Initial Preclinical Data

- 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

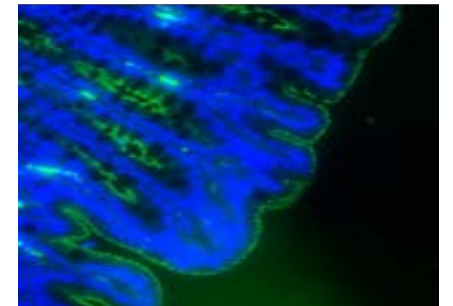
Normal
(No DSS Damage)



Damaged
(DSS Damage)



Restored
(DSS Damage + SZN-1326)



SZN-1326 Phase 1 Clinical Trial Paused

Initial Clinical and Laboratory Observations in Healthy Volunteers

Objectives	Observations
To characterise the safety and tolerability of single ascending doses of SZN-1326 in healthy volunteers (HVs)	Well tolerated Grade 1 and 3 treatment-related asymptomatic transaminase elevations (ALT, AST) No corresponding increase in total bilirubin or GGT No changes in liver function markers (coagulation or albumin) No other clinically significant laboratory abnormalities Transaminase increases resolved spontaneously
To characterise the pharmacokinetics (PK) of single IV doses of SZN-1326 in HVs	Higher exposure than predicted from other species Dose dependent exposure
To evaluate the immunogenicity (measured as antidrug antibodies [ADA]) to SZN-1326 in HVs	No Anti-Drug Antibodies (ADA) detected

Robust Activity in Multiple Preclinical Ophthalmology Models

Retinal Vascular Program

SZN-413 addresses retinal non-perfusion and vascular leakage simultaneously

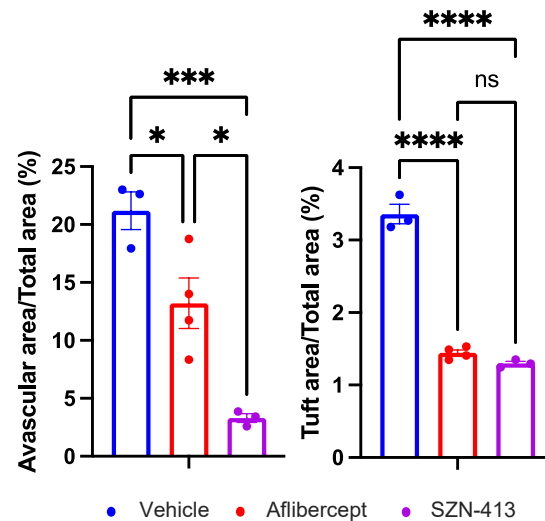
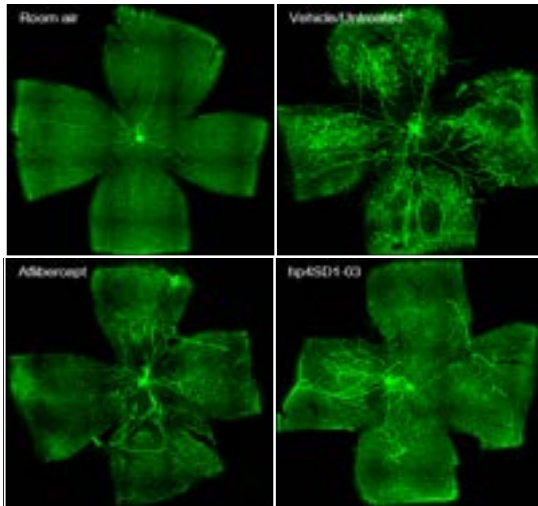
Fzd4 signaling plays critical role in retinal vasculature integrity

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



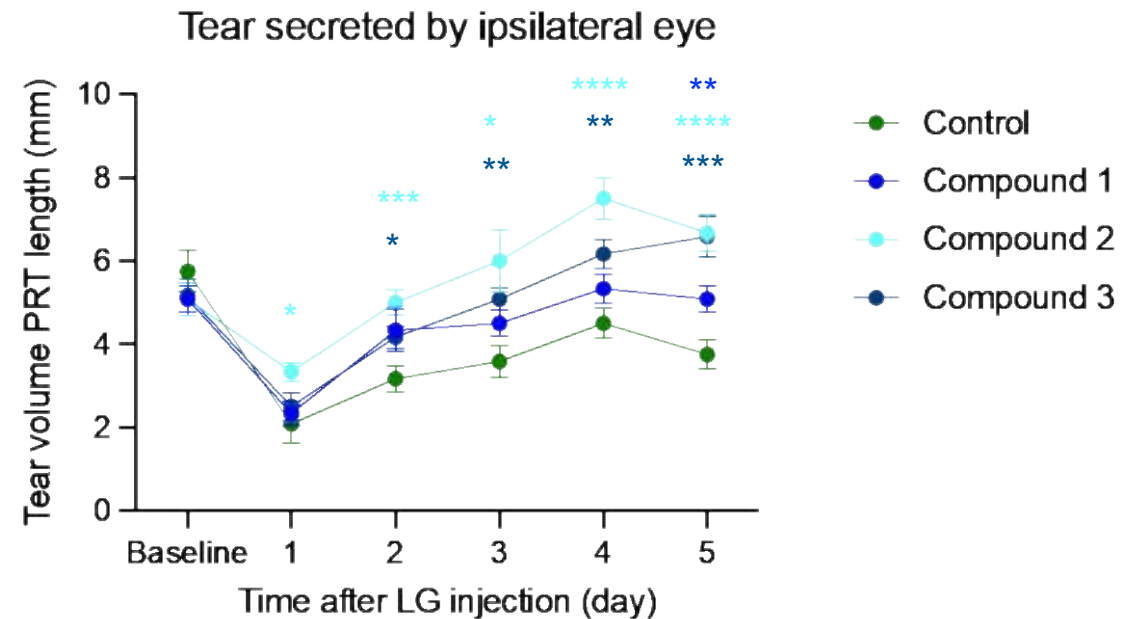
Lacrimal Gland (LG) Program

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



Strategic Partnership with Boehringer Ingelheim



SZN-413 treatment potential –

Regeneration of healthy eye tissue, not only halting retinal disease, but potential for full reversal of patient's disease

Optimizing SZN-413 through worldwide (WW) partnership

- Provides external validation of Wnt pathway activation and SWAP technology
- Leverages Boehringer Ingelheim's commitment to retinal health, R&D expertise and first-in-class treatments
- Provides up-front and milestone payments; obviates future capital commitment by Surrozen for development of SZN-413

Exclusive WW partnership to research and develop SZN-413 for retinal diseases

- Following joint research period, BI assumes WW development and commercial responsibilities for Fzd4-targeted Wnt agonist program in eye diseases

Financials:

- \$12.5M upfront (4Q'22)
- Clinical, regulatory and commercial milestones of up to \$586.5M
- Mid-single digit to low-double digit royalties on commercial sales



Targeted Regeneration

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Glossary

ACLF – Acute-on-chronic liver failure–
ACTA2 – actin protein
ADA – Anti-drug antibodies
AE – Adverse events
AH – Alcoholic hepatitis
ALT – Alanine Aminotransferase
AMD – Age-related macular degeneration
ASGR1 – Asialoglycoprotein receptor 1
AST – Aspartate aminotransferase
AT1/AT2 – Alveolar type epithelial cells
BW – Body weight
CCL4 - carbon tetrachloride
COPD – Chronic Obstructive Pulmonary Disease
DC – Dendritic cell
DME – Diabetic macular edema
DSS – Dextran sodium sulfate
EtOH – Ethyl alcohol
FIH – First in humans
FSGS – Focal segmental glomerulosclerosis

Fzd – Frizzled
GFP – Green fluorescence protein
GI – Gastrointestinal
GLP – Good laboratory practice
GGT – gamma-glutamyl transpeptidase
HNF alpha - Hepatocyte nuclear factor 4 alpha
HV – Healthy volunteer
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
Lrp – Lipoprotein receptor-related protein
MELD – Model for end-stage liver disease score
MOA – Mechanism of action

Mg – Milligrams
MS – Multiple sclerosis
PD – Pharmacodynamics
Pg – Picogram
PIPE – Private investment in public equity
PK – Pharmacokinetic
SC – Subcutaneous
MAD – Multiple ascending dose
SAD – Single ascending dose
SAH – severe alcoholic hepatitis
SOC – Standard of care
SWAP – Surrozen Wnt signal activating proteins
SWEETS – Surrozen Wnt enhancer engineered for tissue specificity
TAA – Thioacetamide
TBD – To be determined
VHH – Single variable domain on a heavy chain (VHH) antibodies