



INVESTOR PRESENTATION

November 2024

NASDAQ: ONVO

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- **Attractive IBD Asset with Strong Probability Of Success in Phase 2a in Ulcerative Colitis**
- **IBD M&A Heating Up – Lilly Acquired Morphic (MORF) after Phase 2a for \$3.2B in August**
- **Lead asset with strong support for target**
 - Direct evidence in humans in IBD (variant form of gene -> greater disease); Literature support for mechanism in IBD in preclinical models (PNAS 2022)
- **Drug preclinical support – FXR314 efficacy similar to approved IBD drugs in adoptive T-cell transfer model**
- **Recent strong Ph2 data MASH, high liver fat reduction & low pruritis among FXR agonists**
 - Lawitz, “Pharmacokinetics, Safety and Efficacy of the Novel Non-bile Acid FXR Agonist FXR314 in Patients with Metabolic Dysfunction-Associated Steatohepatitis: Results from a Phase 2 Study”, American Association for the Study of Liver Diseases (AASLD), Nov. 17, 2024.
- **Strong differentiation within IBD, where substantial unmet need persists**
 - New mechanism is complementary to approved therapies; Oral once daily with high potency

Pipeline Summary

Program	Indication	Discovery	Phase 1	Phase 2	Areas of Clinical Focus
FXR314	Inflammatory Bowel Disease				Ulcerative Colitis
FXR314	Liver Fibrosis				MASH
Novel Drug to Undisclosed Target	Inflammatory Bowel Disease				Inflammatory Bowel Disease

Value Catalyst Opportunities

Program	Indication	2024	2025	Areas of Clinical Focus
FXR314	Inflammatory Bowel Disease	Combination Therapy Data Clinical Study Start Pharma M&A/Licensing	Clinical Ph.2a Readout Pharma M&A/Licensing	Ulcerative Colitis
FXR314	Liver Fibrosis	Pharma Partnerships	Combination Therapy Data Pharma Partnerships	MASH
Novel Drug to Undisclosed Target	Inflammatory Bowel Disease	IND Filing	Ph1 Start	Inflammatory Bowel Disease

M&A Opportunities For FXR314

- Ulcerative Colitis global market size of \$6.6 billion² in 2021; Total IBD market with Crohn's Disease will reach \$100B by 2032
- Many large, deep-pocketed pharmas have strong Immunology focus, interest, and aging pipelines
- Lilly buying Morphic (MORF) for \$3.2B
- Morphic has completed successful Phase 2a in Sept. 2023 for Ulcerative Colitis, entering Ph2B
- FXR314 entering Phase 2a as next step

NOTES:

1. iHealthcareAnalyst, Inc., "Global Inflammatory Bowel Disease Market Landscape and Future Outlook"
2. Future Market Insights, "Ulcerative Colitis Treatment Market Overview (2022 to 2032)"

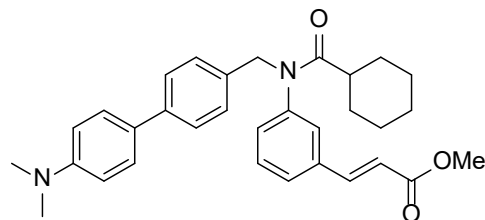


FXR314 in Liver Disease
April 2024 MASH Results

Organovo FXRs Have Distinct Structure and Profile That Can Provide Superior Therapeutic Benefit



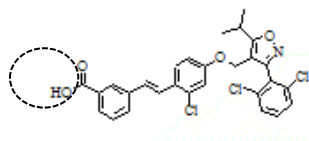
Unique Chemical Scaffold



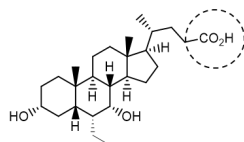
Fexaramine Scaffold

- Proprietary, non-steroidal, non-bile acid scaffold
- In contrast to other chemotypes, activates FXR without carboxylic group (dotted circle)
- >2,500 compounds generated through rational SAR design

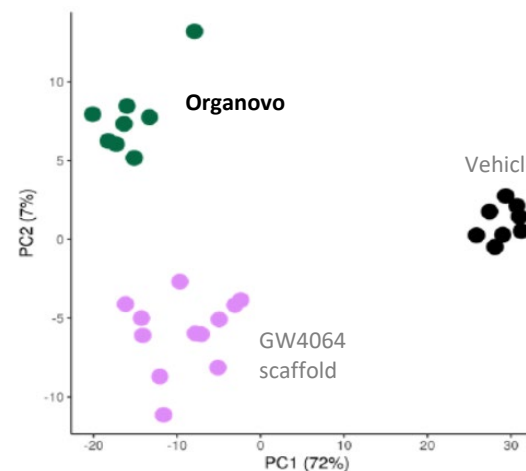
GW4064 scaffold



Bile acid scaffold



Differentiated Gene Regulation



- Distinct signature relative to other agonists as shown in Principal Component Analysis plot
- Potential for translating into a differentiated clinical profile

Source: Smith et al, AASLD Emerging Trends in NAFLD Conference, 2017

FXR314 Has Excellent Efficacy and Tolerability Profile Within FXR Agonists – Phase 2 Results



	FXR314 3 mg	Ocaliva 25 mg	EDP-305 2.5 mg	Cilofexor 100 mg	Tropifexor 0.2 mg
Liver Fat Reduction (using Std DEV)	22.8 ± 3.6% p=0.0010 v. placebo	17%	16%	15%	21%
Subjects with ≥30% Liver Fat Reduction	29% p=0.0023 v. placebo	NR	45%	39%	64%
Overall pruritus rate	5%	51% (72 wk)	47%	>14% (24 wk)	53%
Pruritus-related treatment discontinuation	0%	9% (72 wk)	21%	2% (24 wk)	6%
Potency EC50 (nM)	2-5	99	8	43	0.2

Sources:

FXR314: Organovo press release 15Apr2024;
Lawitz, “Pharmacokinetics, Safety and Efficacy
of the Novel Non-bile Acid FXR Agonist
FXR314”, AASLD, Nov. 17, 2024.
Ocaliva: Sanyal, J Hep, 2023
EDP-305: Ratziu, J Hep, 2023
Cilofexor: Patel, Hep, 2020
Tropifexor: NCT02855164, EASL 2019

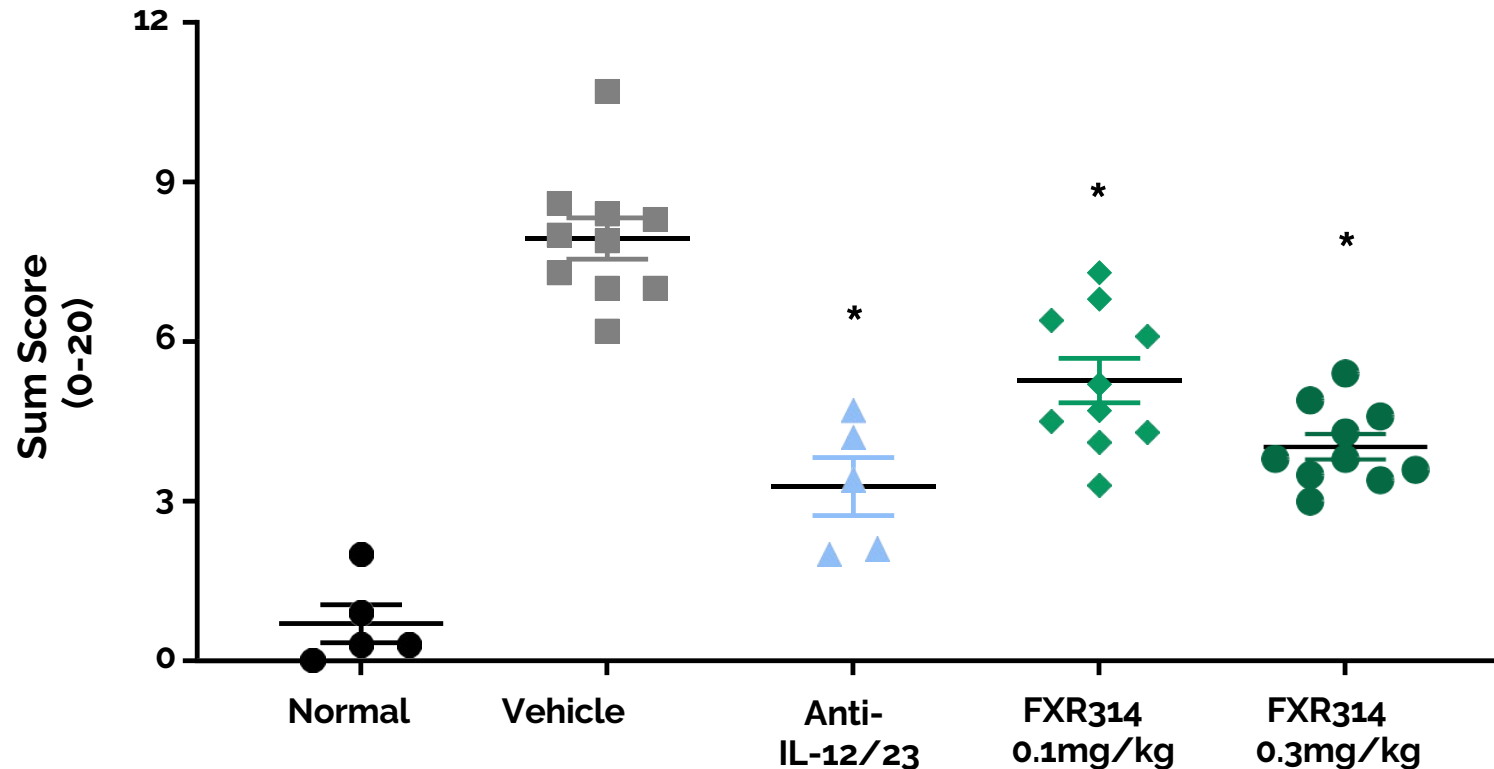
- FXR314 has demonstrated excellent potency and specificity, limiting safety and liver tox concerns
- Unlike Ocaliva (OCA) and some others, FXR314 is a non-steroidal non-bile-acid FXR agonist, has demonstrated top tier fat reduction with encouraging safety profile – very low pruritis and no liver tox signals



FXR314 in Inflammatory Bowel Disease

FXR314 Improves Colitis Similarly to Approved IBD Therapies

Colon Histopathology Sum Score



* $p < 0.0001$, vs Vehicle,
One-Way ANOVA with Dunnett's post test
Source: Internal data

- FXR314 dose-dependently improves measures of ulcerative colitis in an adoptive T- Cell transfer preclinical model
- Effects are similar to approved drug treatments that are current market leaders

FXR314 Phase 2a Trial in Ulcerative Colitis

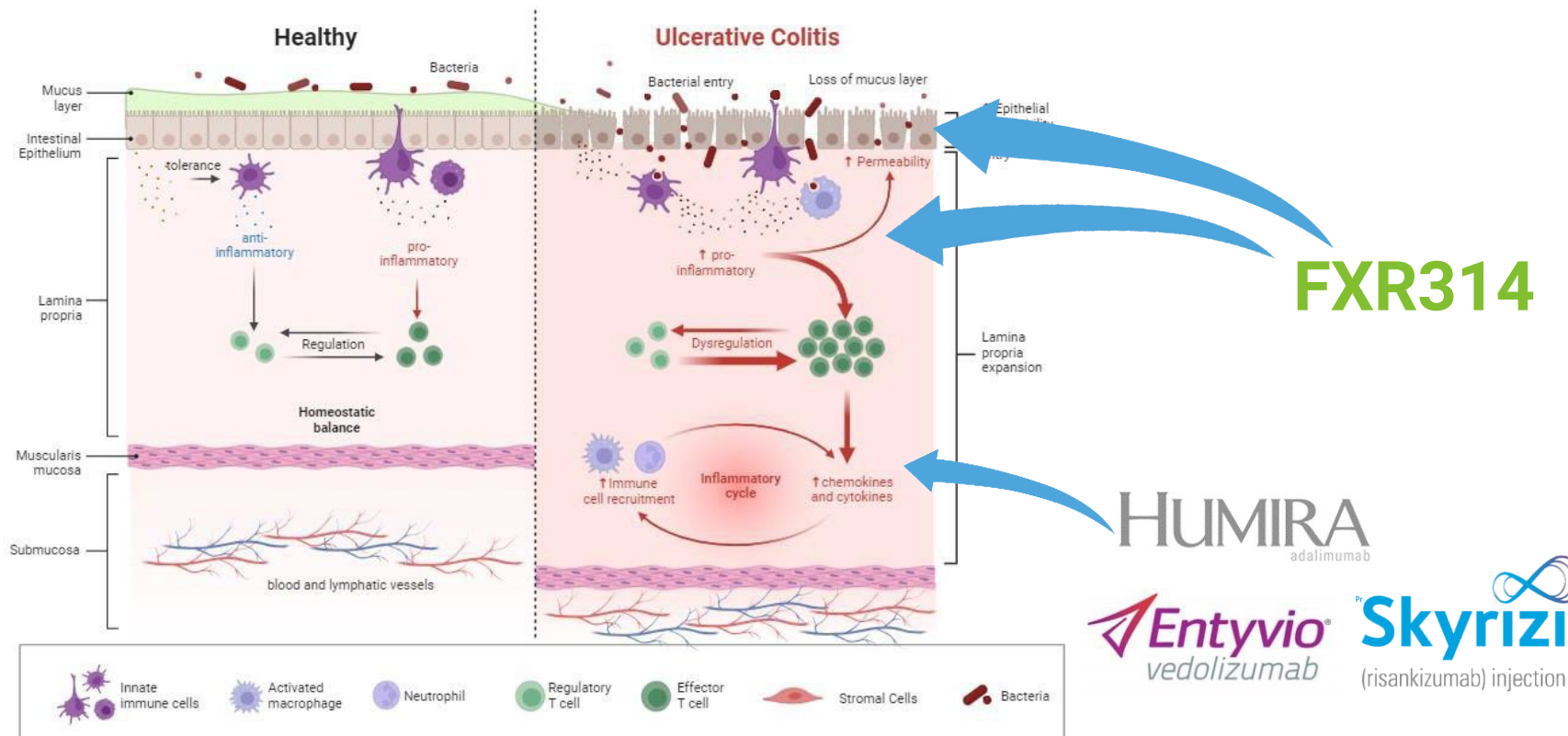
Phase 2a RCT Study to Demonstrate POC

- Target enrollment of 75 patients, 2:1 drug:placebo
- FXR314 6mg vs. placebo
- 12 weeks of treatment, oral once daily
- Diagnosis of moderate to severe UC > 3 months prior to screening defined by clinical and endoscopic evidence, supported by histopathology report
- Primary objective: improvement in UC severity and symptoms via the modified Mayo score (mMS). Secondary objectives include: to evaluate the safety and tolerability of FXR314 in subjects with moderate to severe UC
- Enrollment expected to begin Q1 2025
- Study readout expected 1H 2026



FXR314 MoA Linked to Epithelial Repair, Upstream of Anti-inflammatory Treatments

- Potential to achieve priority utilization over anti-inflammatory therapies
- Epithelial repair would negate cytokine release
- Preference for safety (no immunosuppression) & convenience (oral once daily)



FXR314 Next Steps In Liver Fibrosis / MASH

Drug Successful in Phase 2 Studies; Opportunity for Development

- Next Step: Preclinical evaluation of combination opportunities to complete in 2024
- Likely combination therapy with GLP-1, especially oral
- Combination study with GLP-1 in preclinical setting will be run, with results expected by end of calendar 2024
- Results will indicate potential dose and clinical phase 3 opportunity for MASH development
- Will engage in partnering discussions; regarding development of FXR314 in MASH as well

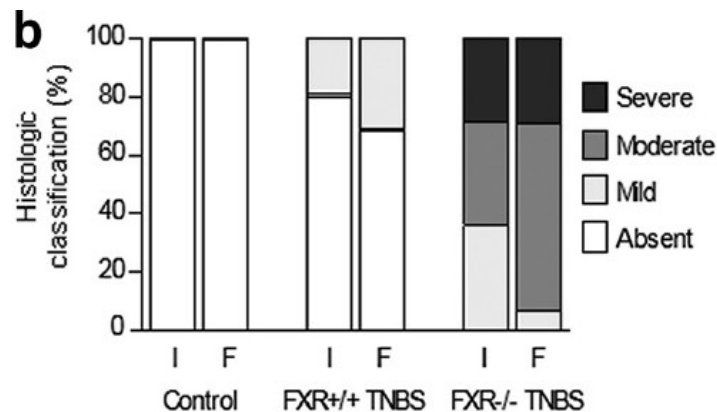


FXR314 Preclinical Support

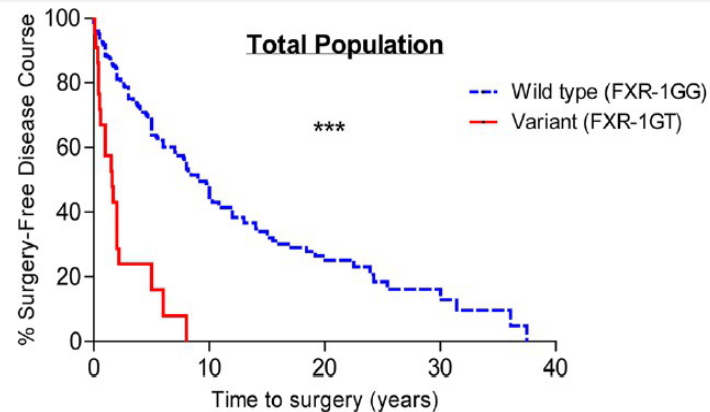
Evidence For A Role Of FXR Agonism In Inflammatory Bowel Disease (IBD)

- FXR is a nuclear hormone receptor critical for maintaining bile acid, lipid and intestinal homeostasis
- Studies in null mice demonstrate a protective role of FXR in IBD
- FXR SNP associated with IBD
 - FXR SNP rs56163822 (FXR-1G->T) leads to reduced protein expression
 - Patients with Crohn's disease (CD) carrying the FXR-1G->T variant exhibit greater disease severity and earlier progression to surgery
- The biomarker of intestinal FXR activity, FGF-19, is reduced in CD patients

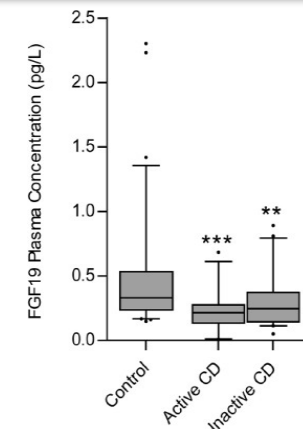
FXR Protects Mice From TNBS-induced Colonic Inflammation



FXR Variant Causes Increased Disease Severity



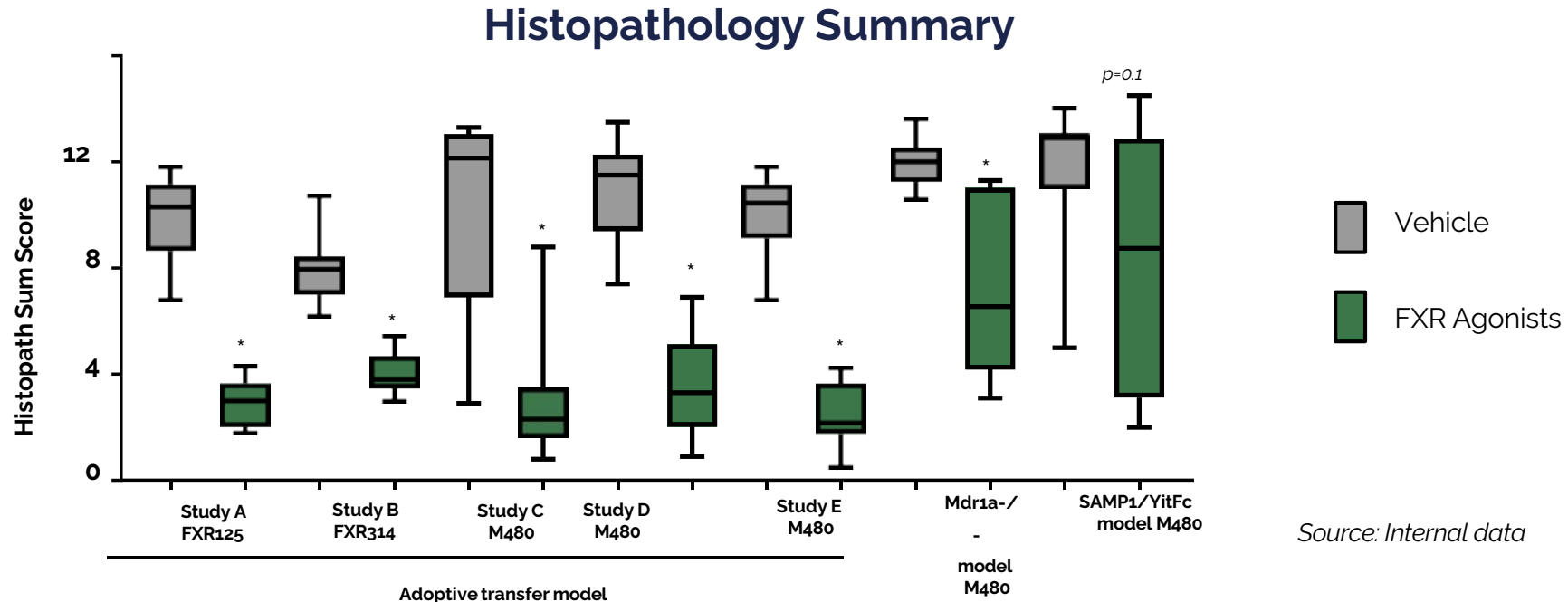
Biomarker Of FXR Activity Reduced In CD Patients



Source: Internal data

FXR314 And Analogs Improve Colitis In Multiple Chronic IBD Models

- Efficacy demonstrated in various chronic IBD models of different modalities
- All studies conducted in treatment mode
- Adoptive transfer model: colitis triggered by abnormal T-cell activation
- Mdr1a null model: colitis triggered by disrupted gut barrier function
- SAMP1/YitFc model: spontaneous Crohn's disease-like ileitis

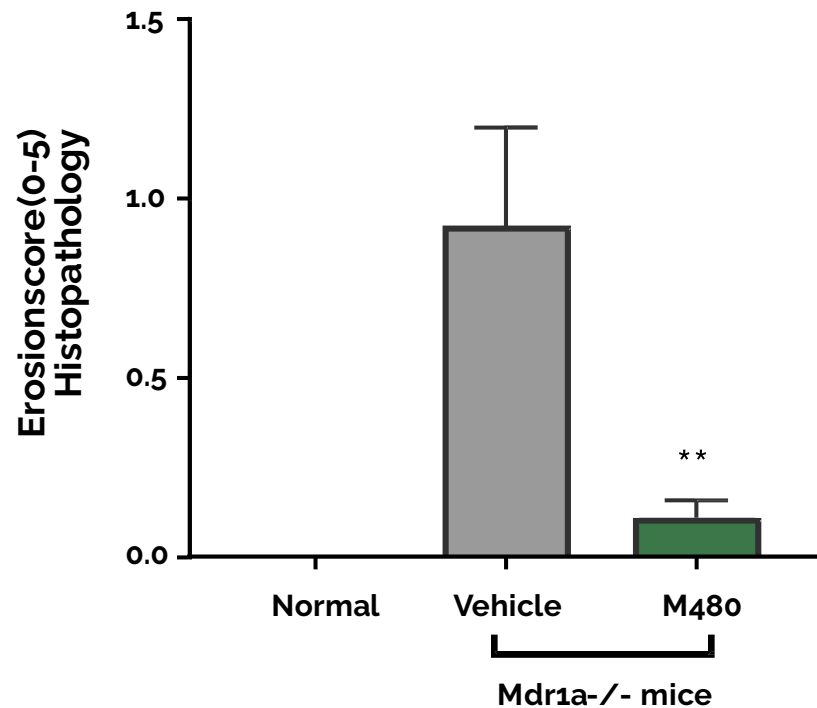


Source: Internal data

FXR Agonists Improve Intestinal Lining

Protection of Intestinal Barrier

Colon Epithelium Erosion

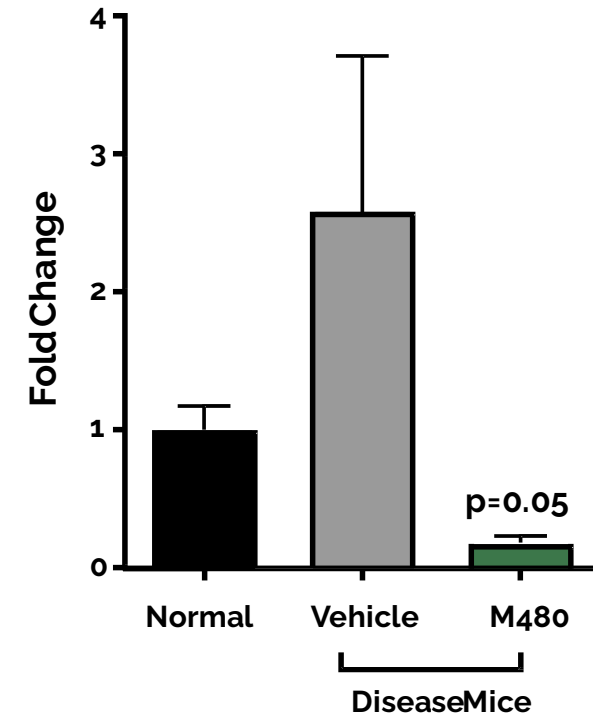


* p<0.01 vs Vehicle, ANOVA

Mdr1 Null Colitis Model

Direct Anti-bacteria Effects

Reduced Bacterial Load in Intestine (16s rRNA)



Adoptive T-Cell Transfer model

Source: Internal data

Market Opportunities For FXR314

- 13mm prevalent cases of ulcerative colitis globally in 2022
- 2.1mm in North America¹
- Global market size of \$6.6 billion² in 2021
- Anticipated to reach \$122 billion by 2032
- Growing steadily at a CAGR of 6.0%²
- Driven by the increasing prevalence of ulcerative colitis, and introduction of several new therapies



NOTES:

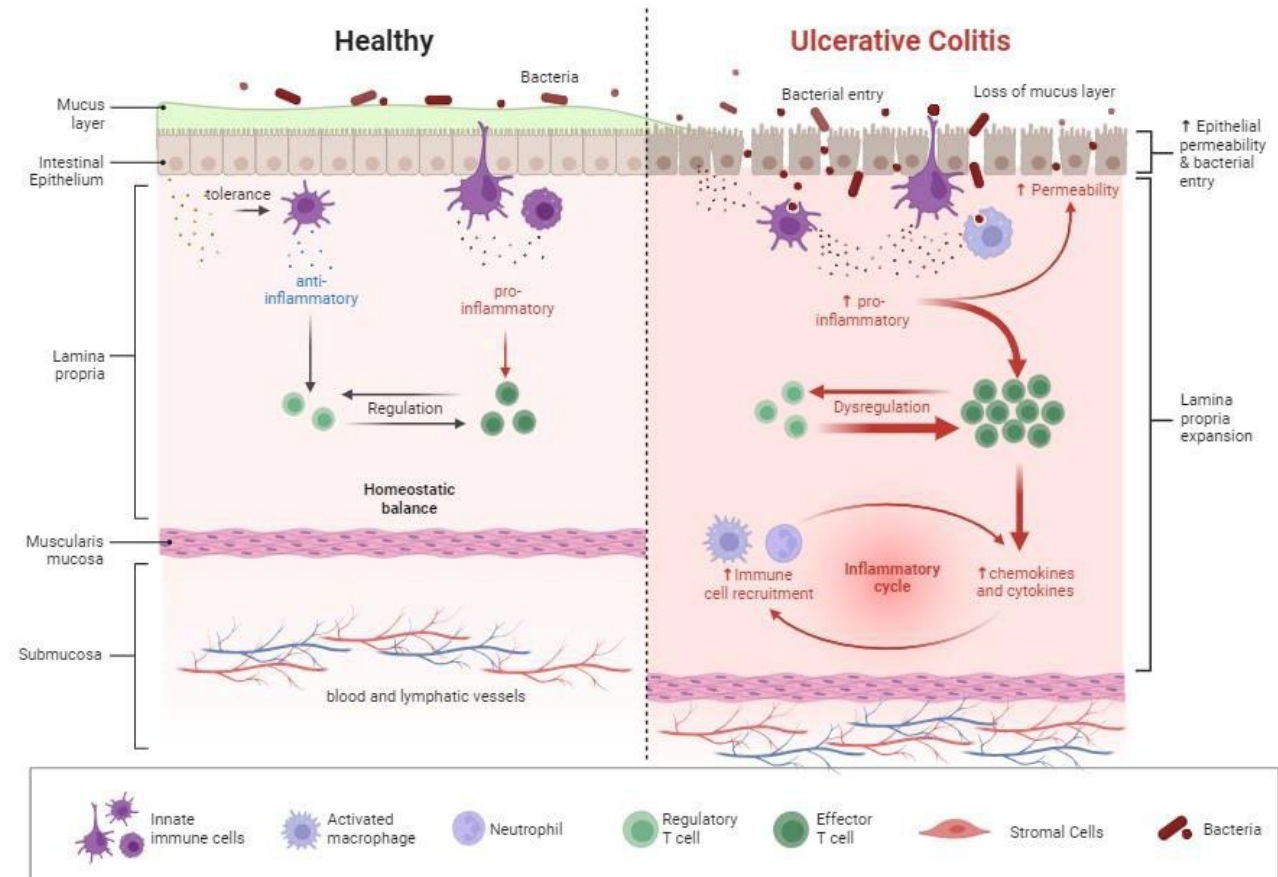
1. iHealthcareAnalyst, Inc., "Global Inflammatory Bowel Disease Market Landscape and Future Outlook"
2. Future Market Insights, "Ulcerative Colitis Treatment Market Overview (2022 to 2032)"



**Organovo's 3D Human Inflammatory
Bowel Disease Model And Path To **FXR314****

IBD Is Characterized By Epithelial Barrier Breakdown And Inflammatory Response

- Intestinal epithelium damage
- Disruption of epithelial layer
- Bacterial ingress into tissue
- Inflammatory response
- Cytokine release, T-cell recruitment



Source: Hoffmann et al. Pathobiology (2003) 70 (3): 121-130.
<https://doi.org/10.1159/000068143>

Approved treatments address the inflammatory response, but Organovo seeks to avoid epithelial damage, work earlier in disease

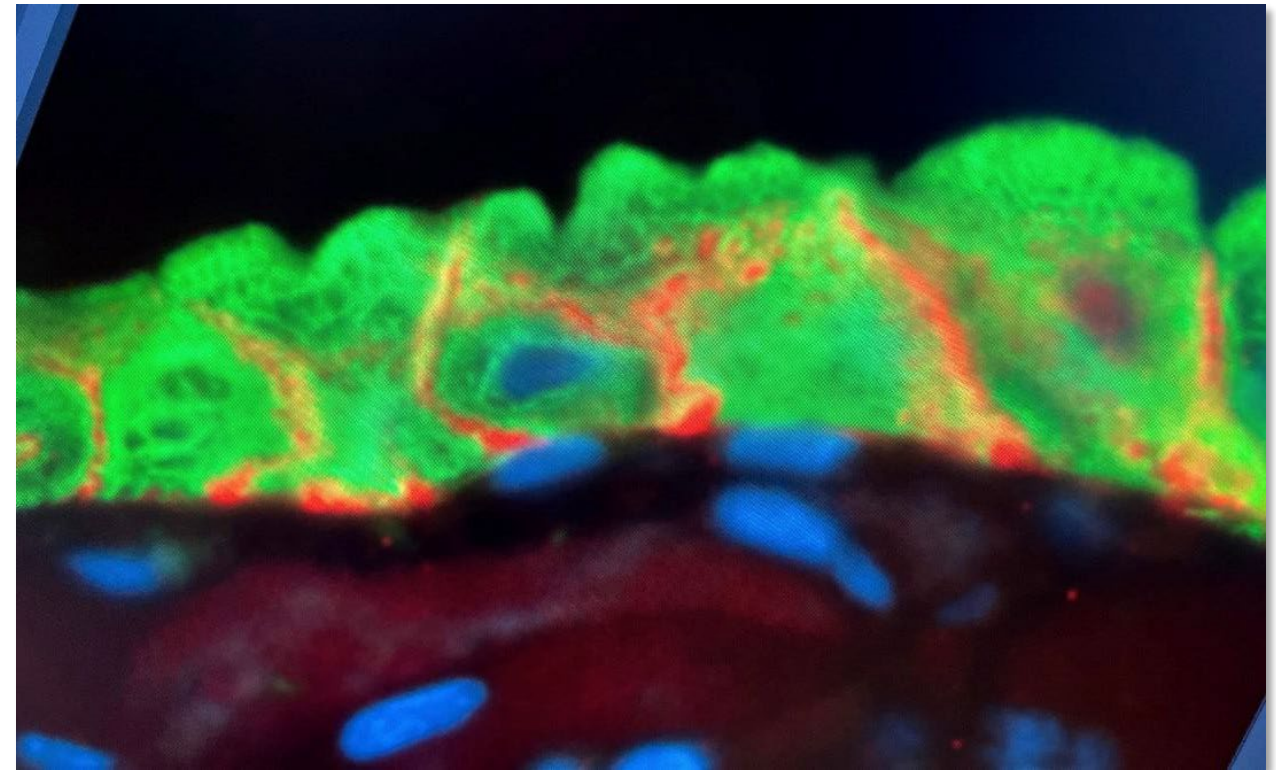
Organovo 3D Disease Models Can Enable Better Clinical Outcomes

organovo®

- Organovo creates exceptional 3D models using bioprinting and other 3D tissue technologies
- 3D tissue models created with cells taken directly from patients (UC or CD patients, biologic naïve or exposed, varying disease severity)
- Models can be used to test compounds, siRNA, etc. to validate targets or study drug effects
- Testing broad donor sets from a biobank allows us to understand population response to a drug or to target modulation

3D Tissue Intestinal Wall Model Has Accurate Structure With Intact Epithelium

- Polarized epithelium
- Interstitial layer with smooth muscle, fibroblast, capillaries
- Tight junctions – cadherin (orange)
- Specialized epithelial cell types
- Expresses functional, inducible CYP450 enzymes
- Physiological barrier function
- Functional P-gp and BCRP transporters

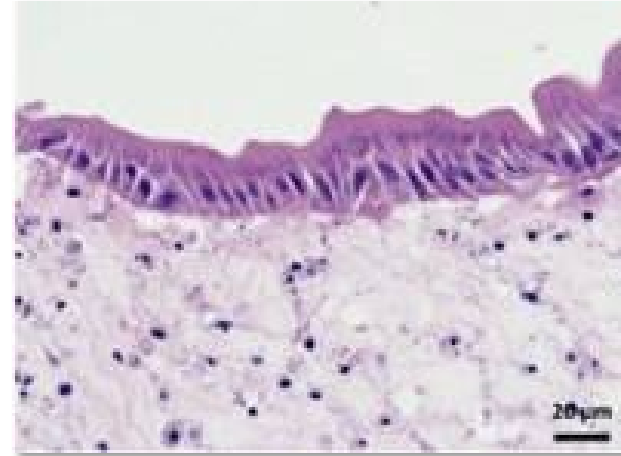


Tissue consists of human primary epithelial, sm. muscle, fibroblast, endothelial cells, either from healthy donor (shown) or diseased

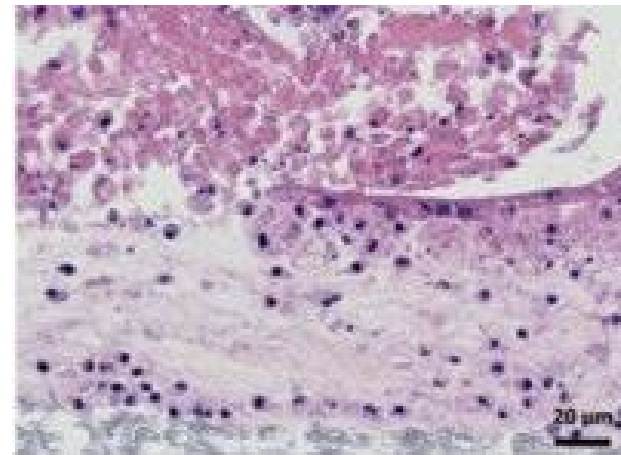
Source: Internal data

3D Tissue From Diseased Donor Cells Correctly Demonstrates Disease Phenotype

- Our ability to see the earliest changes in the intestinal epithelial lining in the model led us to see value of FXR agonism in our tests
- FXR314 significantly reduces epithelial disruption in 3D disease donor model
- FXR314 similarly reduces epithelial disruption in preclinical animal models (slide 10)
- Prevention of bacterial ingress and cytokine release, acts earlier in disease course
- May prevent need for inflammatory cytokine blockade, resulting in superior safety



Healthy donor cells



Diseased cells

Source: Internal data

Investment Summary

- Strong human genetics and preclinical support for target, FXR agonism
- Drug preclinical support – FXR314 works similarly to approved IBD drugs
- Strong differentiation within IBD, where substantial unmet need persists
 - New mechanism is complementary to approved therapies
 - High potency oral therapeutic delivery which is dosed once daily
- Ulcerative colitis Phase 2a POC result is expected in 2H 2025
- FXR314 is effective in 3D human models, showing improvement of intestinal epithelium in cells of UC for its lead therapeutic molecule FXR314
- FXR agonism: Organovo is also advancing FXR314 for the treatment of other Inflammatory Bowel Diseases including Crohn's Disease as well as diseases of the Liver including NASH and Primary Biliary Cholangitis
- 2nd target: Organovo began medicinal chemistry in 2023 to create a novel drug for another, as yet undisclosed, target. The target was validated in our 3D tissue models of Crohn's disease. IND expected by the end of 2025

Source: Internal data



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