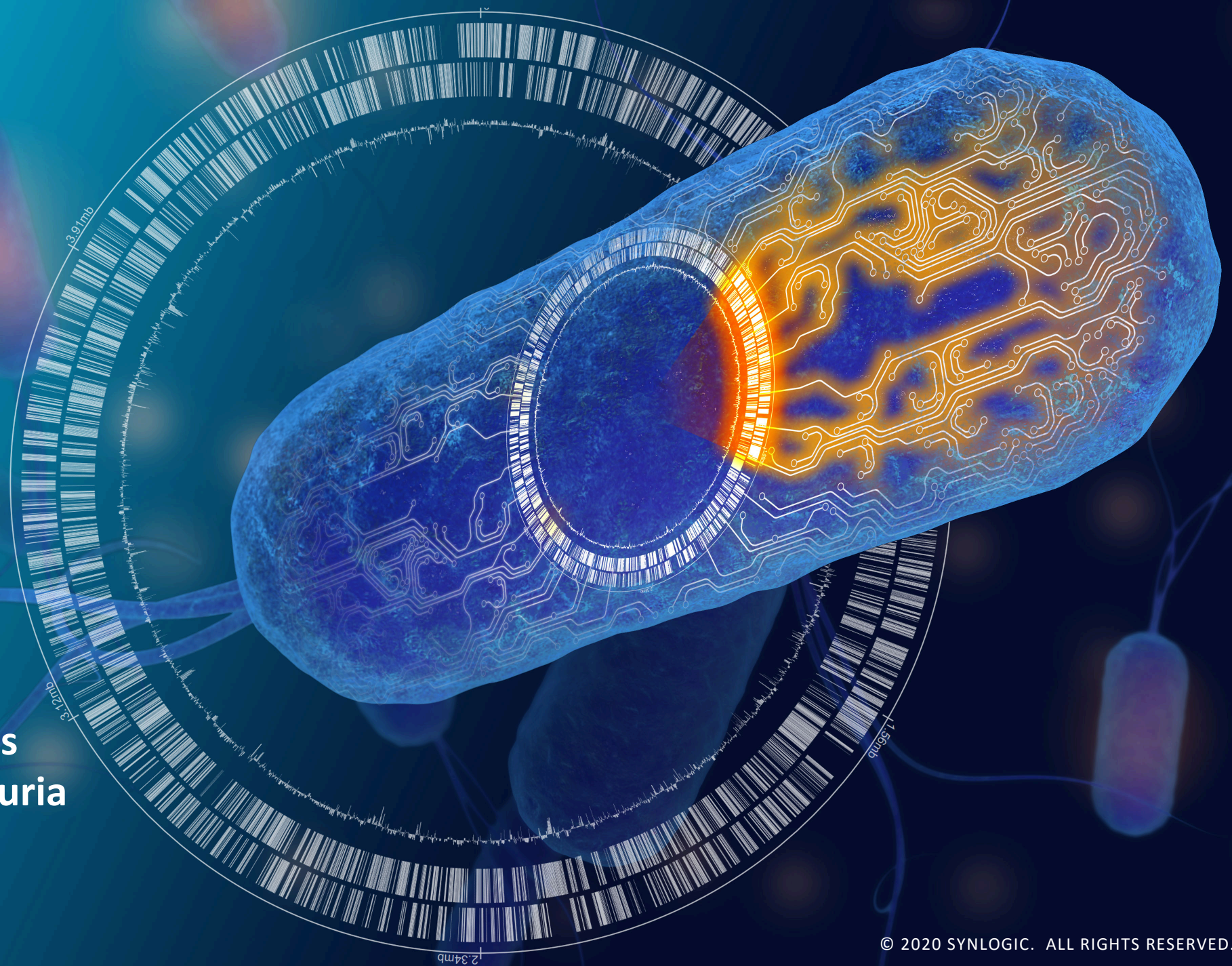


Synlogic

DESIGNED FOR LIFE

***In Silico* Simulation to
Predict Activity of a
Synthetic Biotic,
SYNB8802, in Healthy
Volunteers and Patients
with Enteric Hyperoxaluria**

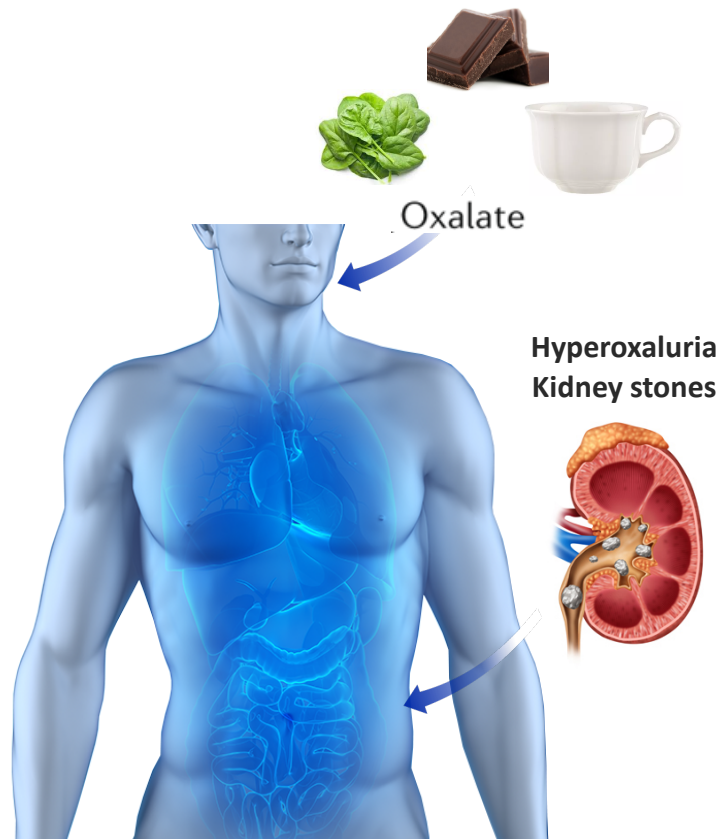
Nick Horvath
Synlogic, Inc.



Enteric Hyperoxaluria Disease Pathogenesis

Dietary Oxalate Distributes Throughout the Body Leading to Renal Complications

Dietary Sources of Oxalate



Enteric Hyperoxaluria

Pathology

Pathogenic hyperabsorption of dietary oxalate, often accompanies bowel disease or bariatric surgery

Urinary Oxalate Levels

45 – 130 mg / 24 hrs (up to 3x normal)

Onset

Adult

Clinical Mgmt

Limited nutrition options; treatment of kidney stones as they occur; nephrocalcinosis; dialysis

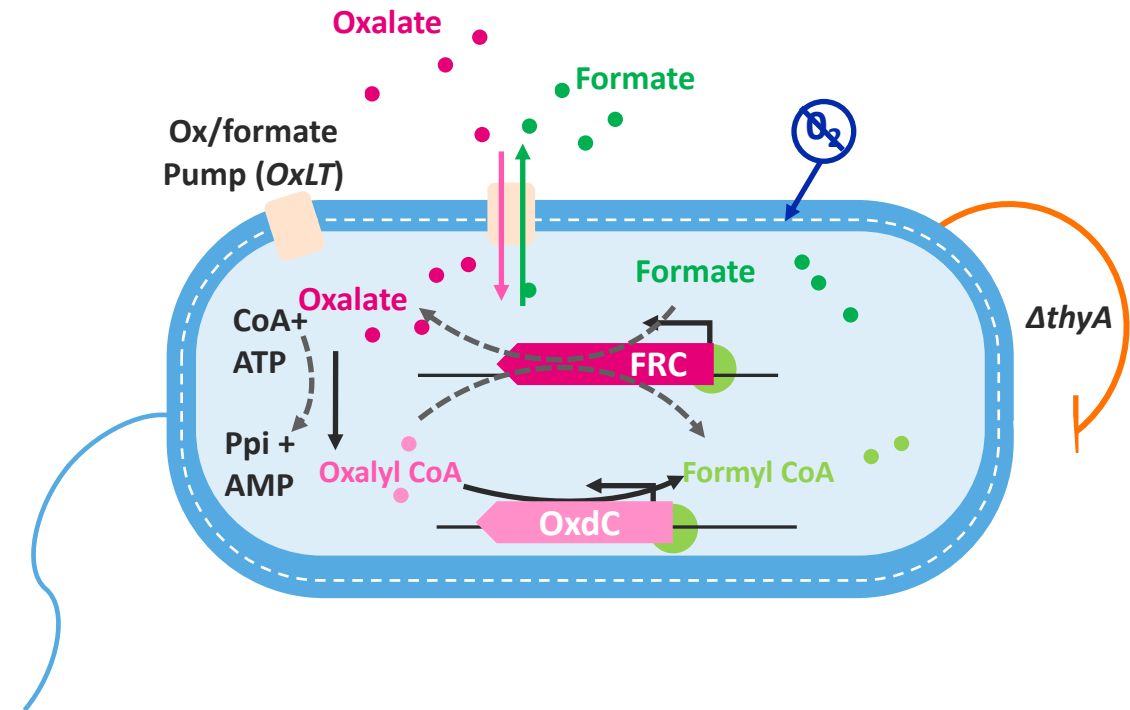
U.S. Epidemiology

200,000 – 250,000

SYNB8802 Design

Engineered to Convert Oxalate to Formate for the Treatment of Enteric Hyperoxaluria

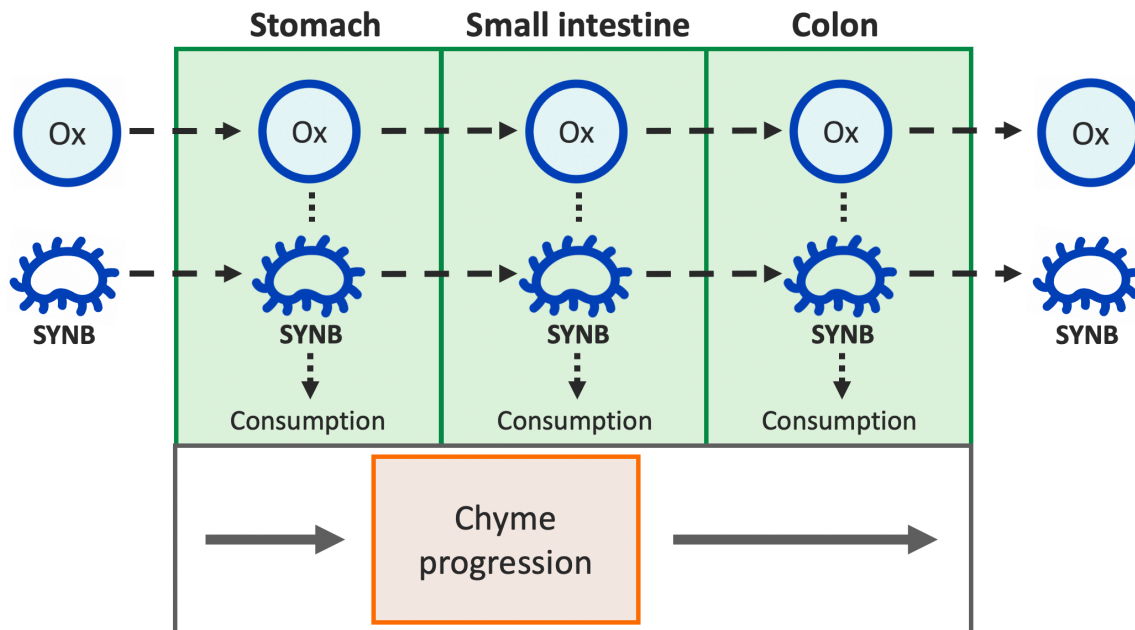
Component	Approach	Benefit
Bacterial Chassis	<i>E. coli</i> Nissle	Decades of human use
Switch	FNR promoter	Inducer-promoter pair
Pump	<i>OxLT</i>	Pumps oxalate in & formate out
Effector 1	<i>OxdC</i> and associated components	Catalyzes conversion of oxalate to formate
Safety Features	$\Delta thyA$	Controls growth



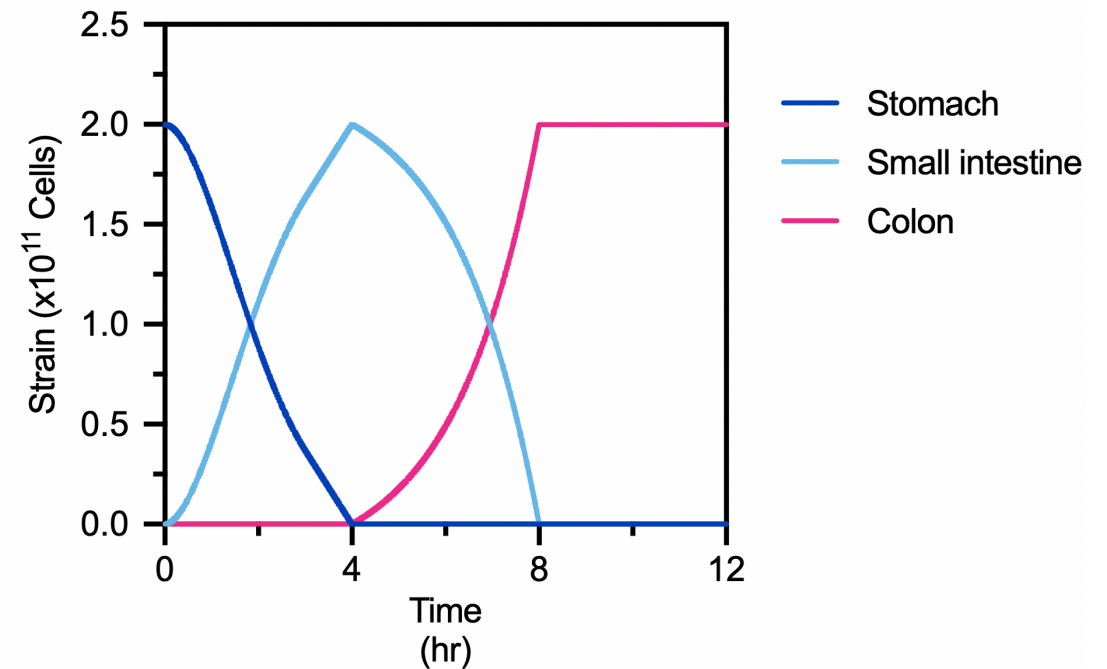
In Silico Simulation (ISS): a Mechanistic Modeling Approach

Physiological Basis for Gastrointestinal Transit and Strain Activity

Strain Activity in GI



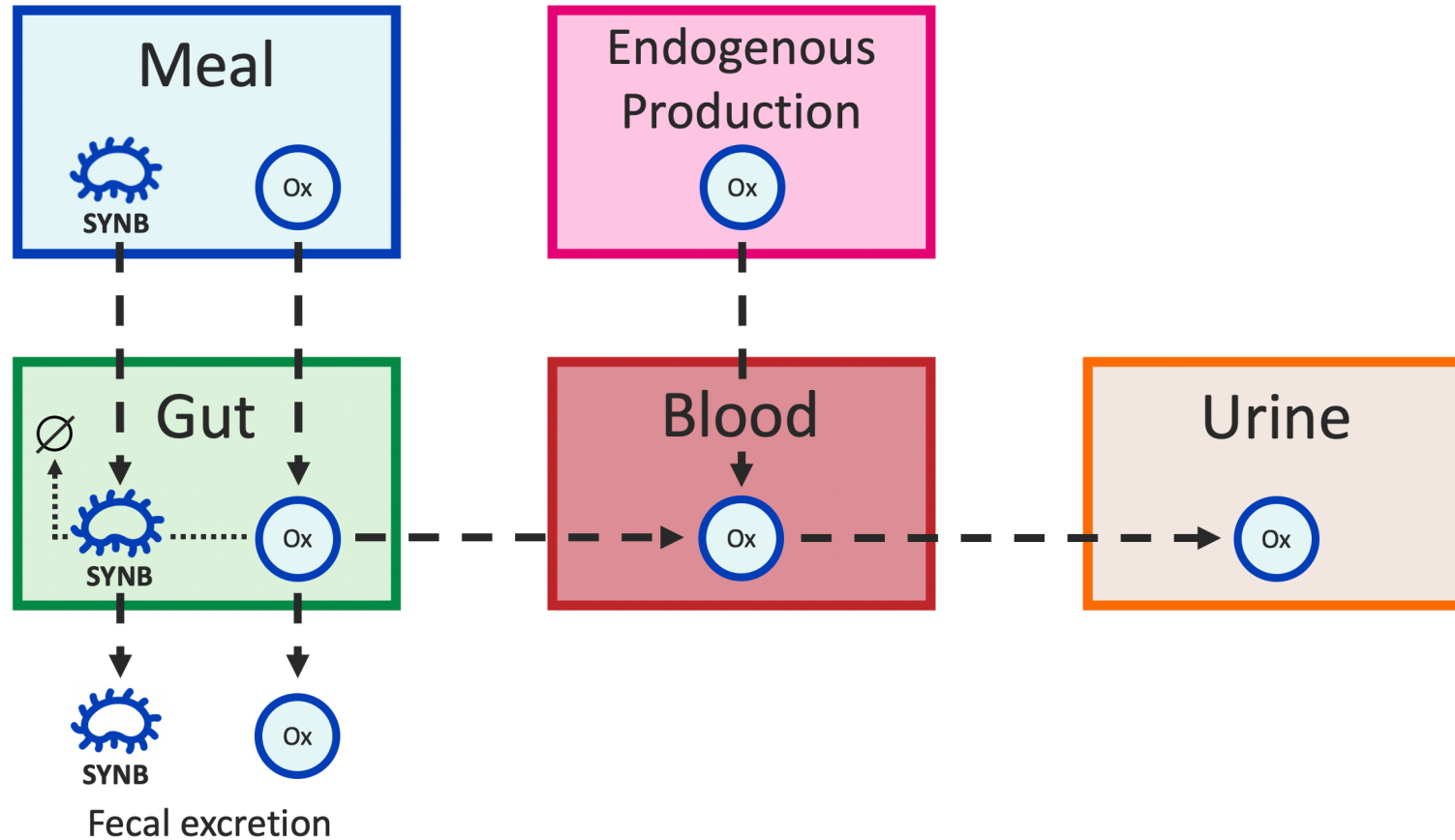
Strain Transit



In Silico Simulation (ISS): a Mechanistic Modeling Approach

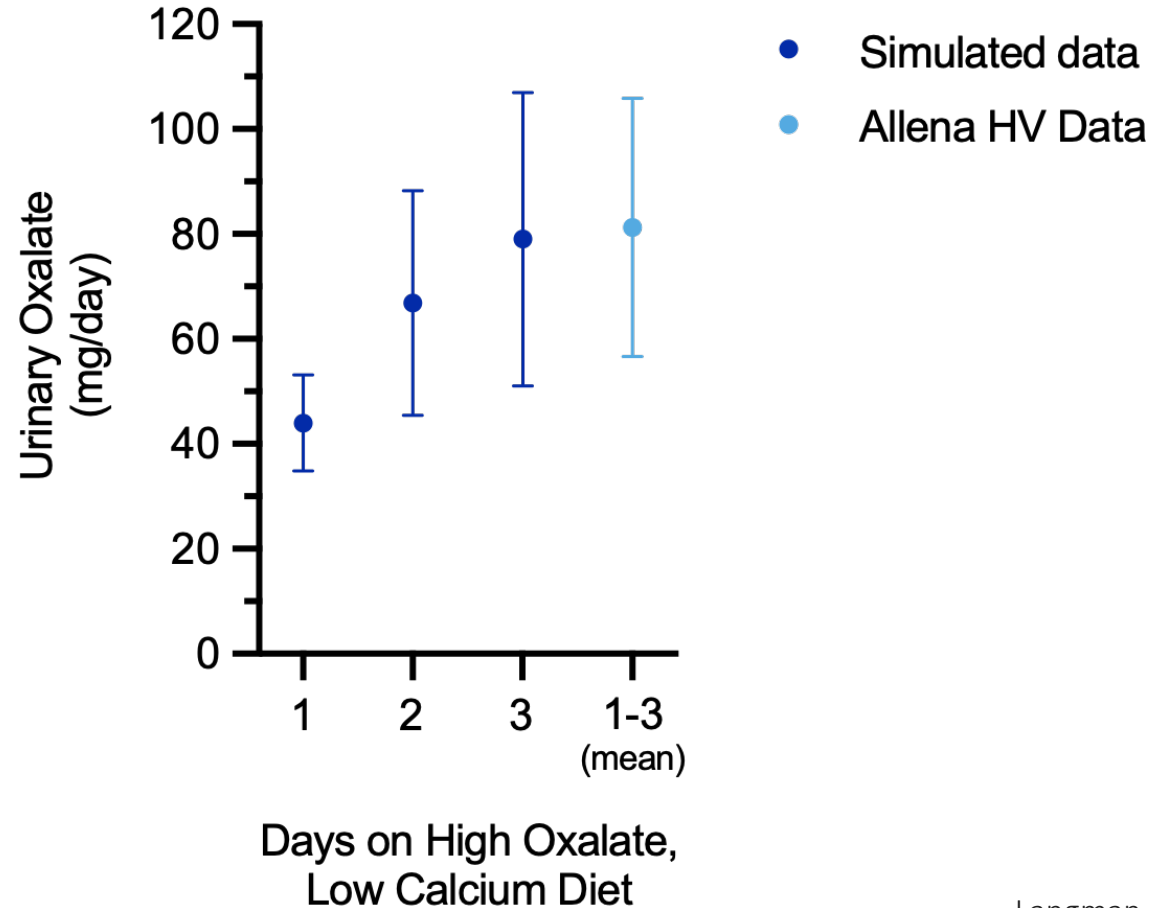
Two Components: Gastrointestinal Strain Activity and Human Disease Biology

SYNB8802 ISS Model



Establishing Confidence in the *In Silico* Simulation (ISS) Approach

Validation Using Clinical Data from Allena Oral Enzyme Study



Phase 1 study by Allena of their oral enzyme for oxalate degradation (ALLN-177)

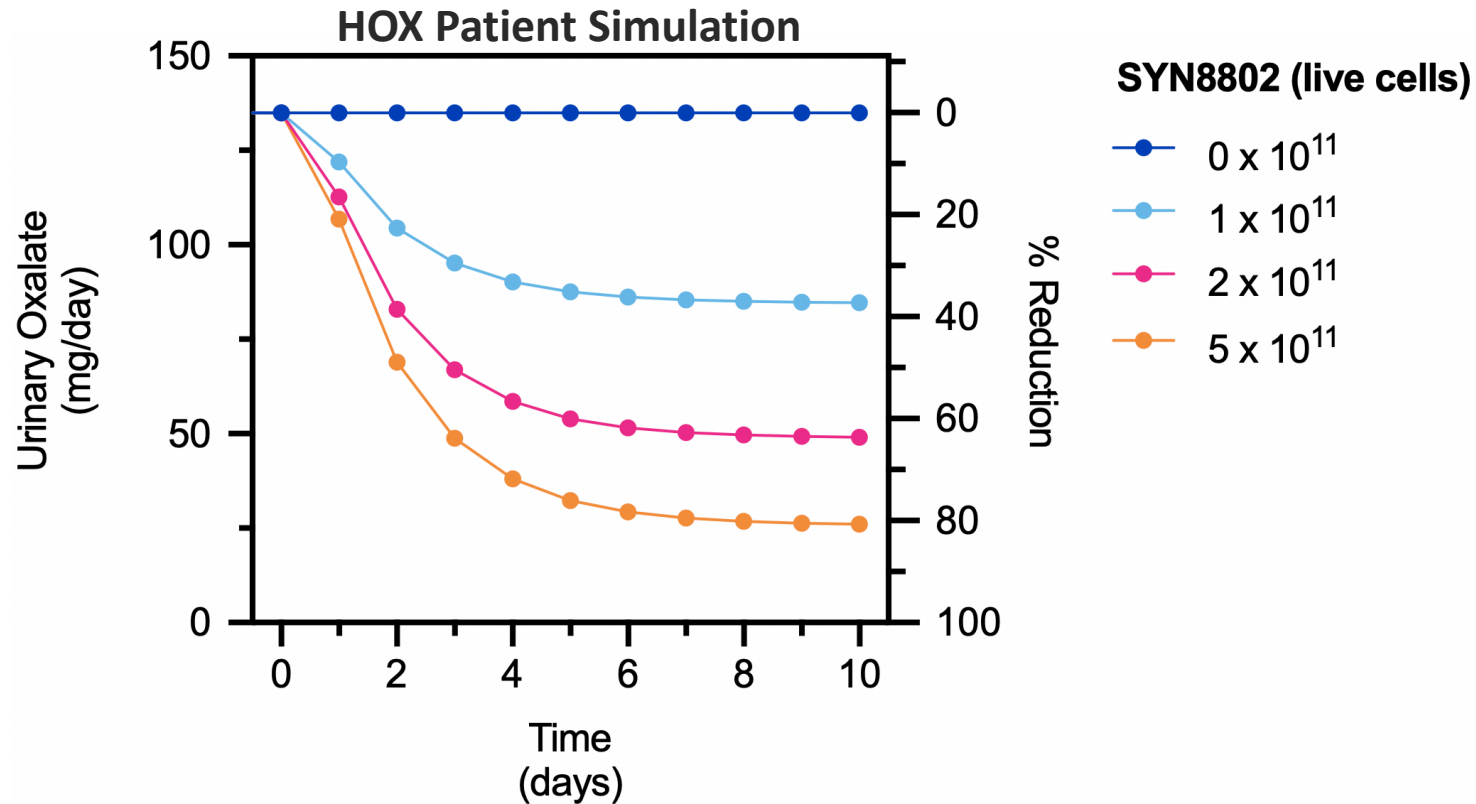
The study began with a 3-day period on a **high-oxalate** low-calcium (HOLC) diet, before the drug was administered

Simulations of the disease biology model agree with the observed impact of **high dietary oxalate**

Langman CB, Grujic D, Pease RM, Easter L, Nezzar J, Margolin A, Brettman L. A Double-Blind, Placebo Controlled, Randomized Phase 1 Cross-Over Study with ALLN-177, an Orally Administered Oxalate Degrading Enzyme. *Am J Nephrol* 44 (2016): 150-8.

Predicting Synthetic Biotic Potential

Urinary Oxalate Reduction as a Function of SYN8802 Dose



In Silico Simulations (ISS)

predict a change in baseline of the clinical endpoint (urinary oxalate)

Urinary oxalate lowering by various doses can be compared to target product profile to inform **candidate selection**



Enteric Hyperoxaluria: Hyperabsorption of Dietary Oxalate Leading to Renal Complications



SYNB8802 Predicted to Meaningfully Lower Urinary Oxalate in EH Patients



SYNB8802 Phase 1 Clinical Study Initiated Ahead of Schedule



synlogic

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Questions?

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Synlogictx.com