

SYNT, a Synthetic Polymer Lining, to Unlock the Full Therapeutic Potential of the Small Intestine

Vasu Sethuraman, Ph.D.



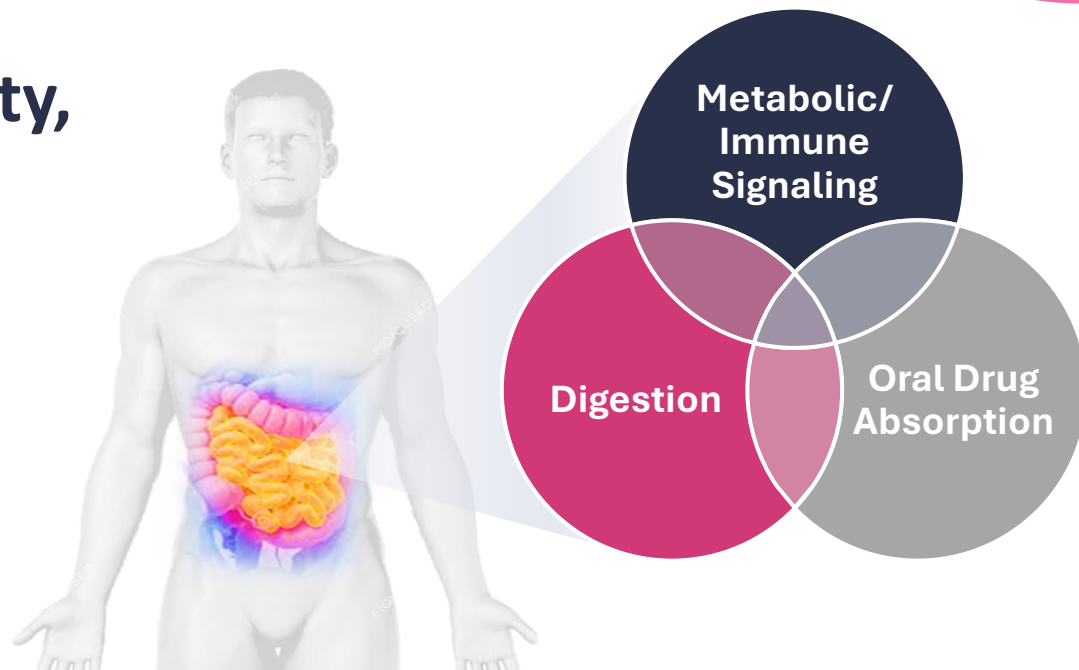
Syntis Bio

Syntis is unlocking the therapeutic potential of the small intestine with SYNT™

The nexus for metabolism, immunity, and therapeutic response

Therapeutic impact starts in the small intestine

- Metabolic Diseases
- Inborn Errors of Metabolism
- Digestive & Intestinal Disorders
- Autoimmune Conditions



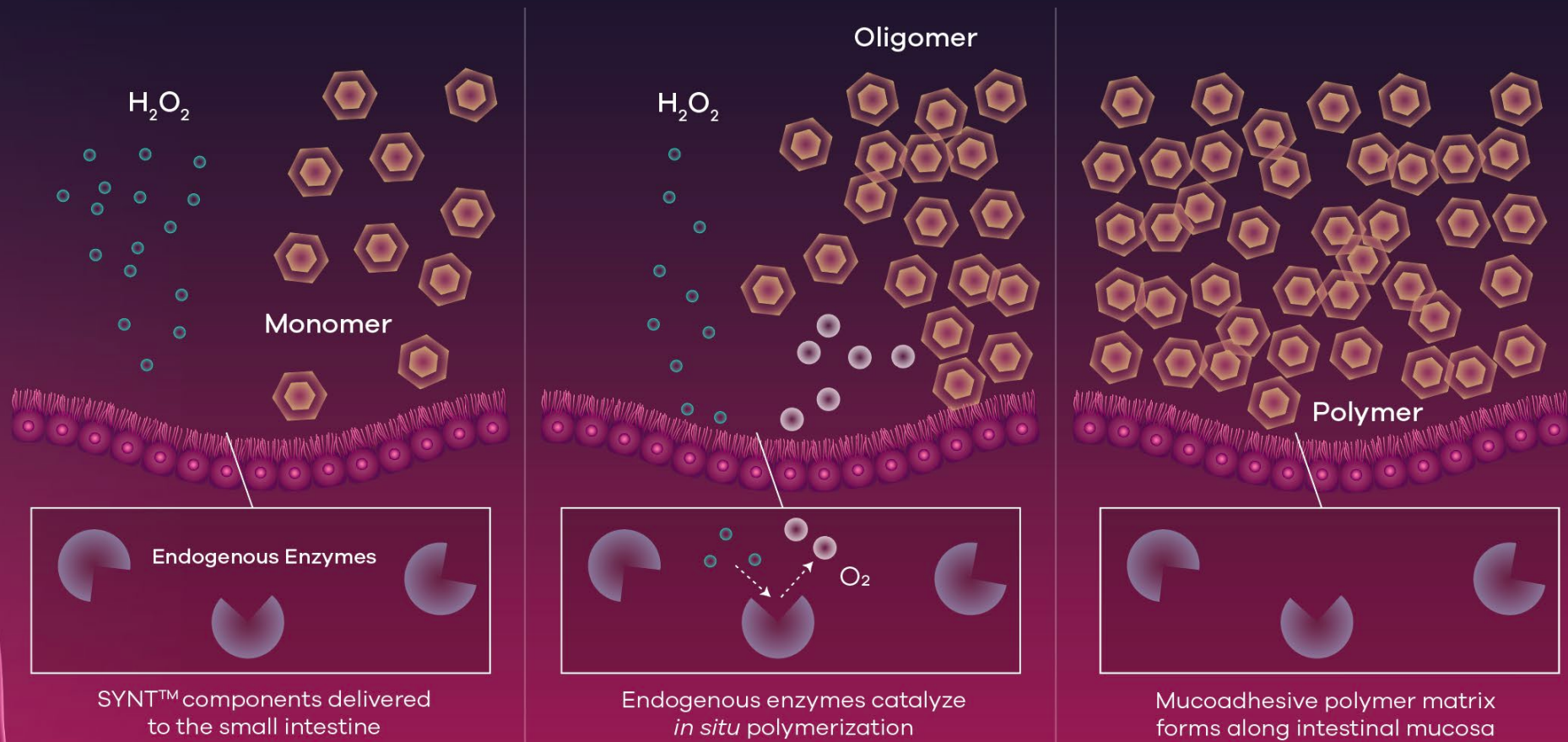
Intestinal drug targeting has been challenging due to:

- Rapid GI transit times
- Harsh proteolytic conditions
- Low absorption of biologic drugs

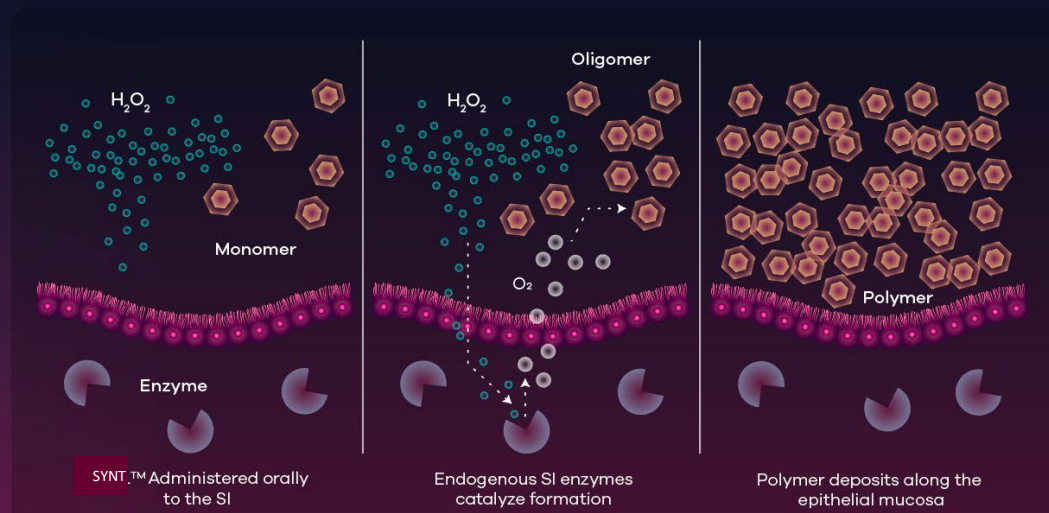


Syntis Bio

SYNT™ Targets & Sustains Therapeutic Activity in the SI

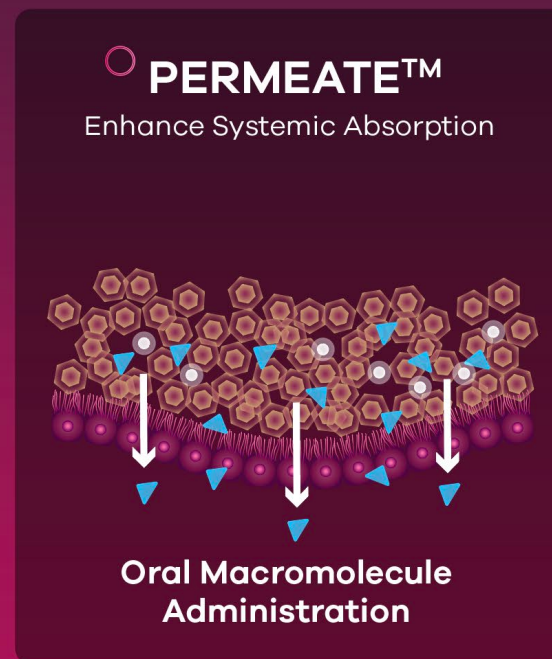
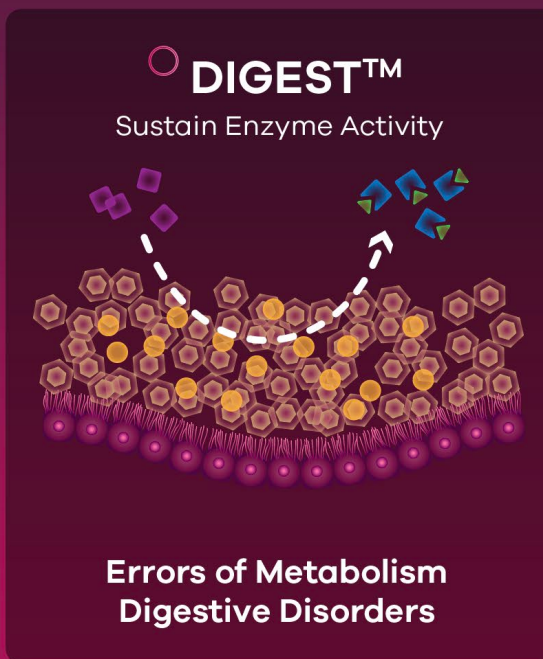
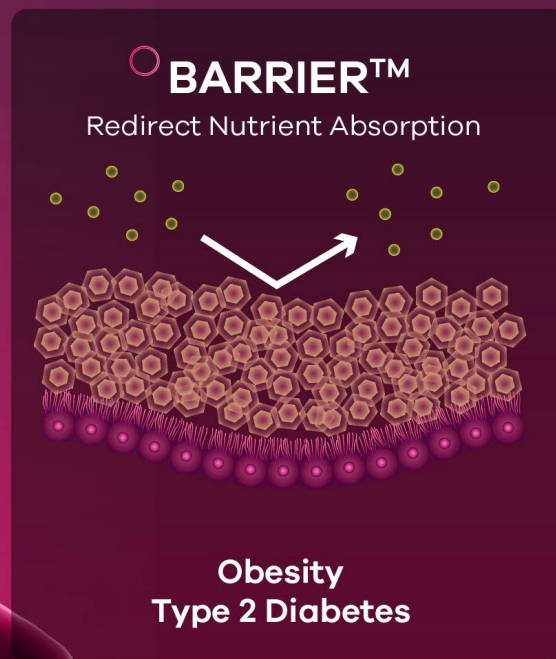


Syntis Bio



- ✓ Lasts up to 24 hours
- ✓ Specific to the SI
- ✓ Orally administered
- ✓ Protects APIs from degradation
- ✓ Safe, natural excretion

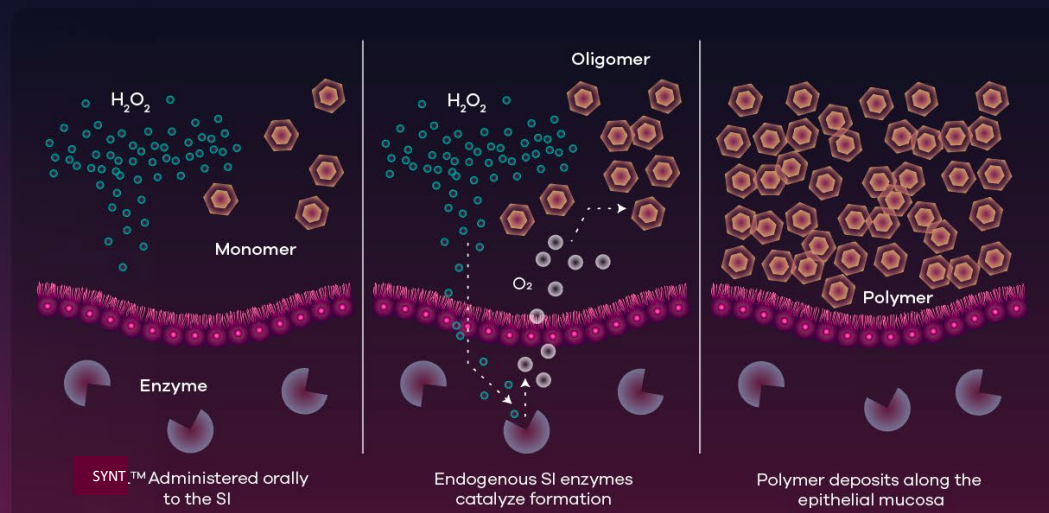
Multiple Therapeutic Platforms



Syntis is advancing a proprietary pipeline

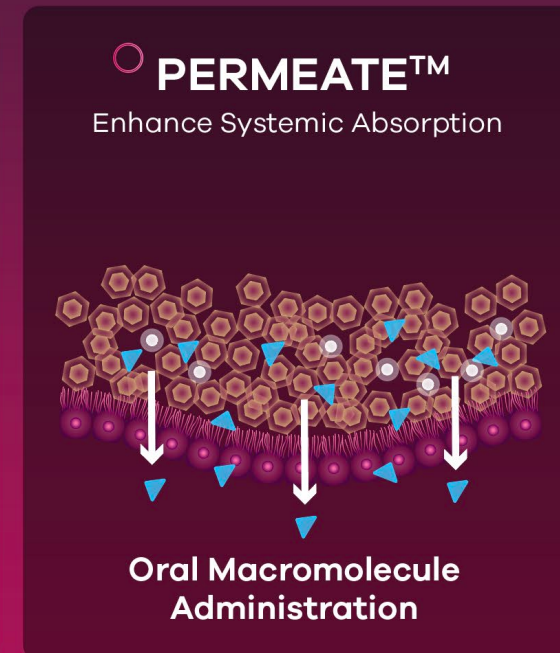
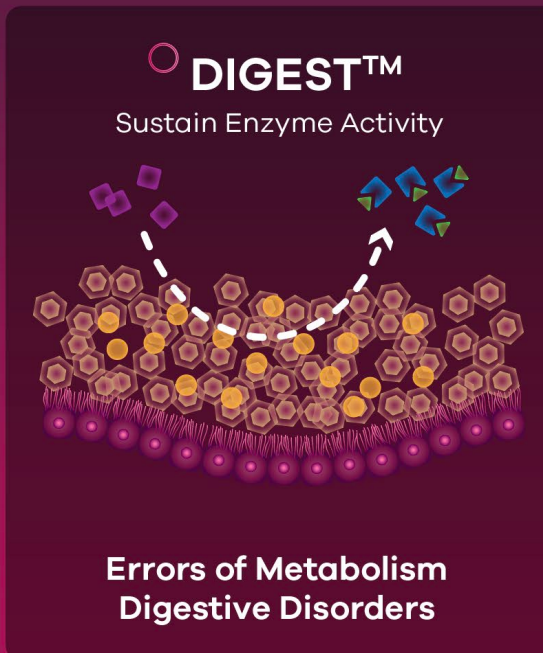
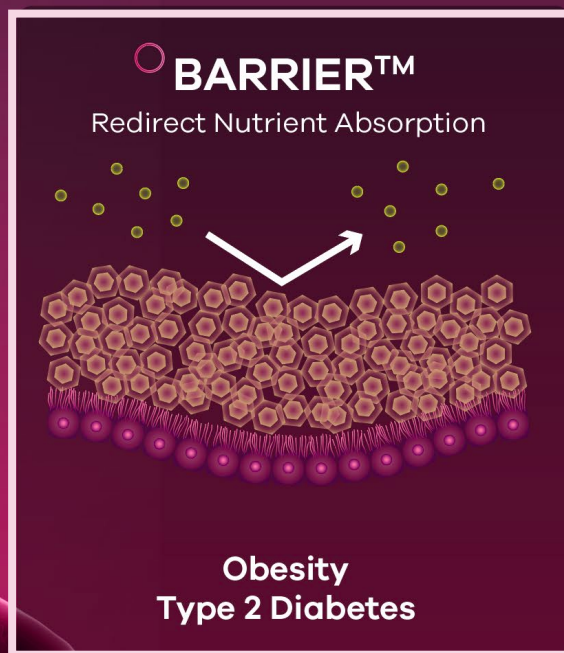
	PROGRAM	TECHNOLOGY	DESCRIPTION	STATUS
Obesity	SYNT-101	BARRIER™	✓ Daily oral pill redirects nutrient absorption to distal bowel ✓ Enhances natural satiety hormone signaling (GLP-1, etc.) ✓ Preliminary safety, tolerability, mechanism shown in humans	FIH ●●●●●
Homocystinuria	SYNT-202	GI-Stable Enzyme	✓ Proprietary enzyme engineered for GI stability ✓ Eliminates methionine (Met) accumulation in the GI tract ✓ Normalizes systemic homocysteine (Hcy) levels	INDE ●●●●●
	SYNT-212	SYNT-202 + DIGEST™	✓ Extended SYNT-202 activity w/ DIGEST™ delivery ✓ Offers continuous Met & Hcy management ✓ Designed for maximum disease control & dietary freedom	Discovery ●●●●●
Maple Syrup Urine Disease	SYNT-203	GI-Stable Enzyme	✓ Proprietary enzyme engineered for GI stability ✓ Eliminates BCAA accumulation in the GI tract ✓ Normalizes systemic BCAA levels	INDE ●●●●●
	SYNT-213	SYNT-203 + DIGEST™	✓ Extended SYNT-203 activity w/ DIGEST™ delivery ✓ Offers continuous BCAA management ✓ Designed for maximum disease control & dietary freedom	Discovery ●●●●●





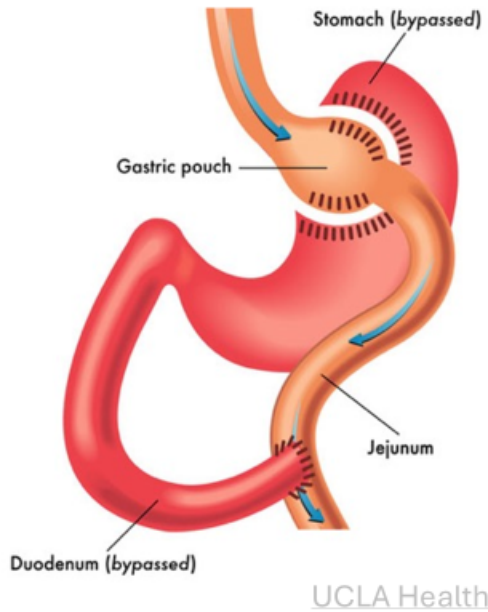
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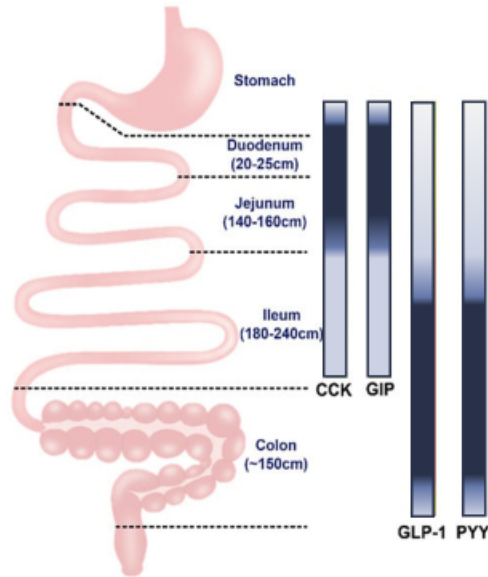


Duodenal exclusion is a proven mechanism for metabolic management

Roux-en-Y Gastric Bypass



Density of enteroendocrine cells (EECs) along GI

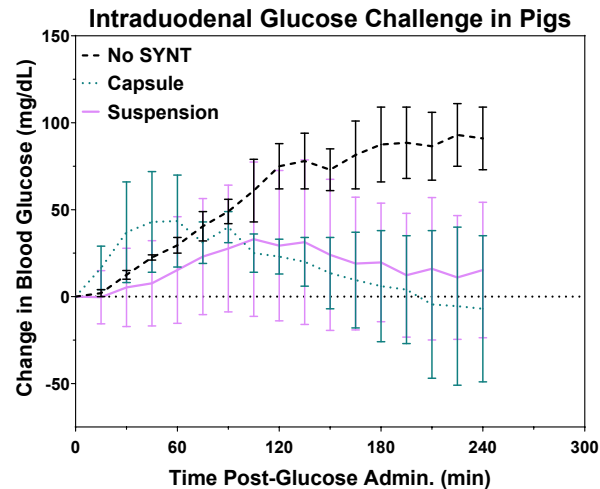


		RYGB	DJBL
% GI Intact	Stomach	10%	100%
	Duodenum	0%	0%
	Jejunum	10%	90%
	Ileum	100%	100%
Results	% TBWL	25-35%	15-25%
	% LML	20-25%	10-15%
	HbA1c Reduction	1.6% ¹	1.5% ¹
	Incretin Response	Yes	Yes

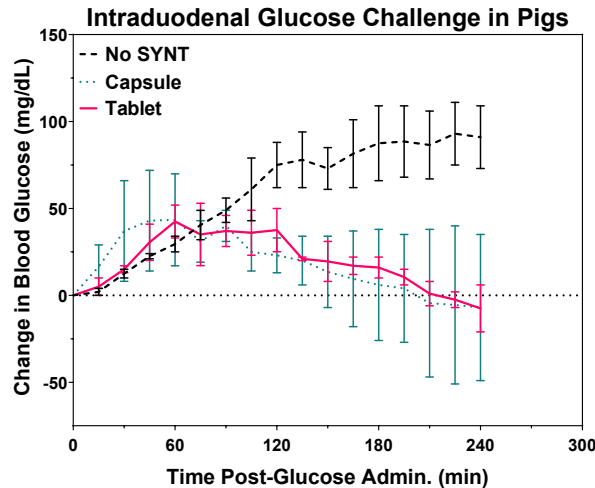
***Blocking duodenal absorption directs nutrients to the ileum,
improving postprandial neuroendocrine response and
restoring native duodenal sensitivity¹***

SYNT-101 is Effective as a Suspension, Capsule or Tablet

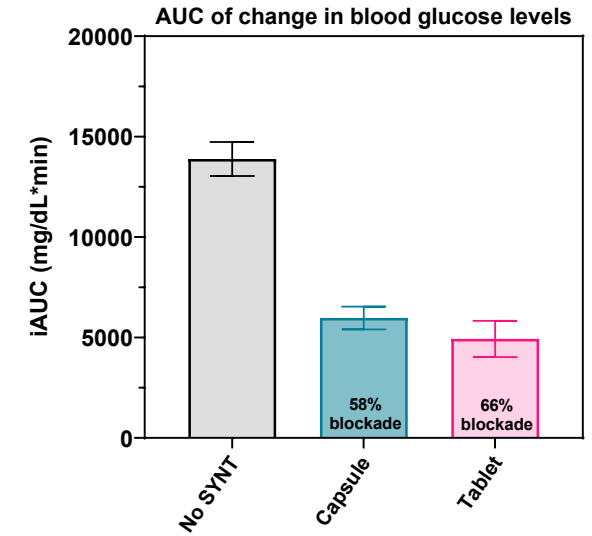
SYNT formulations maintain performance in vivo in suspension and solid dosage forms in a pig model



Suspension translates to capsule

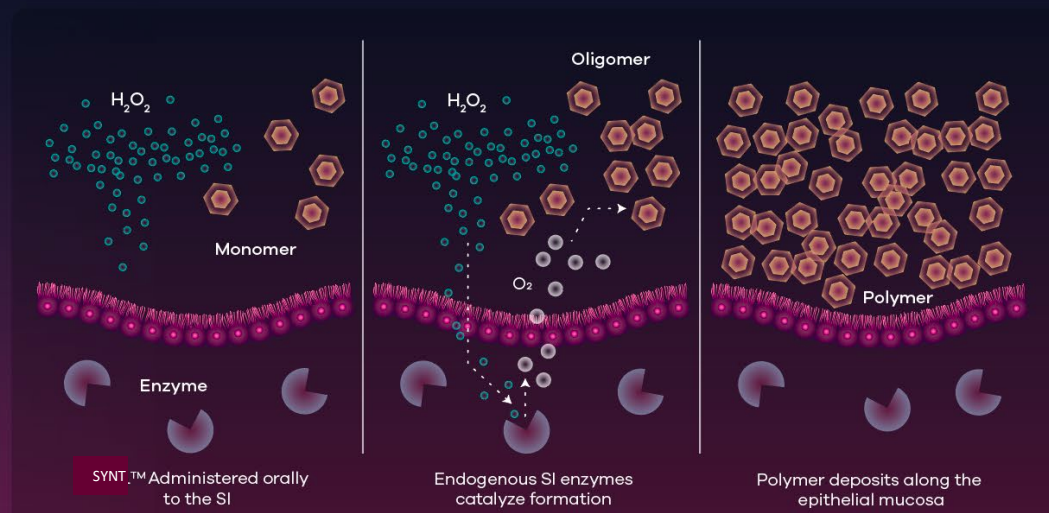


Tablets reproduce performance with higher consistency



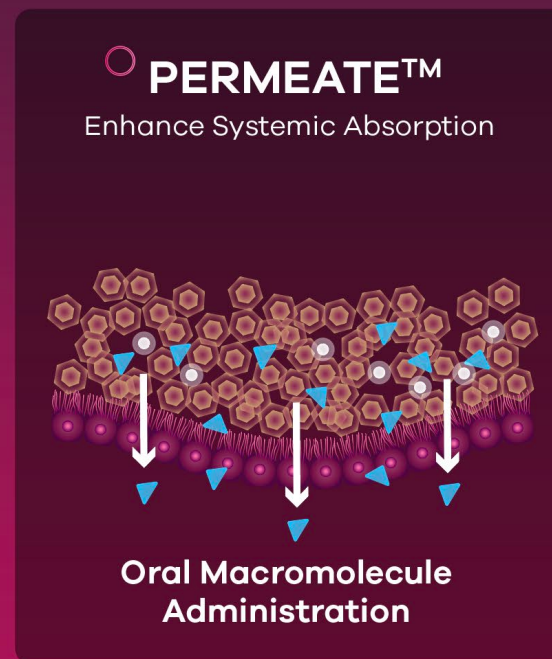
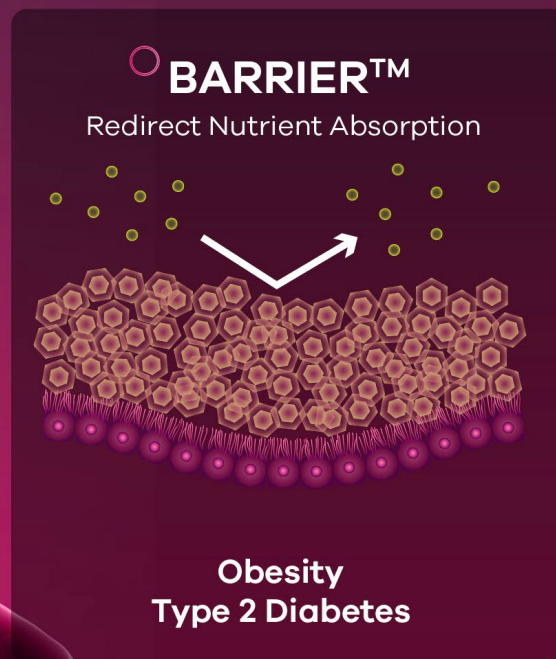
Mechanism of action is slightly more effective in tablets

The dissolution of the SYNT-101 tablets can be optimized by modification of the controlled release polymers for optimal site-specific formation of the synthetic epithelial lining in the small intestine.

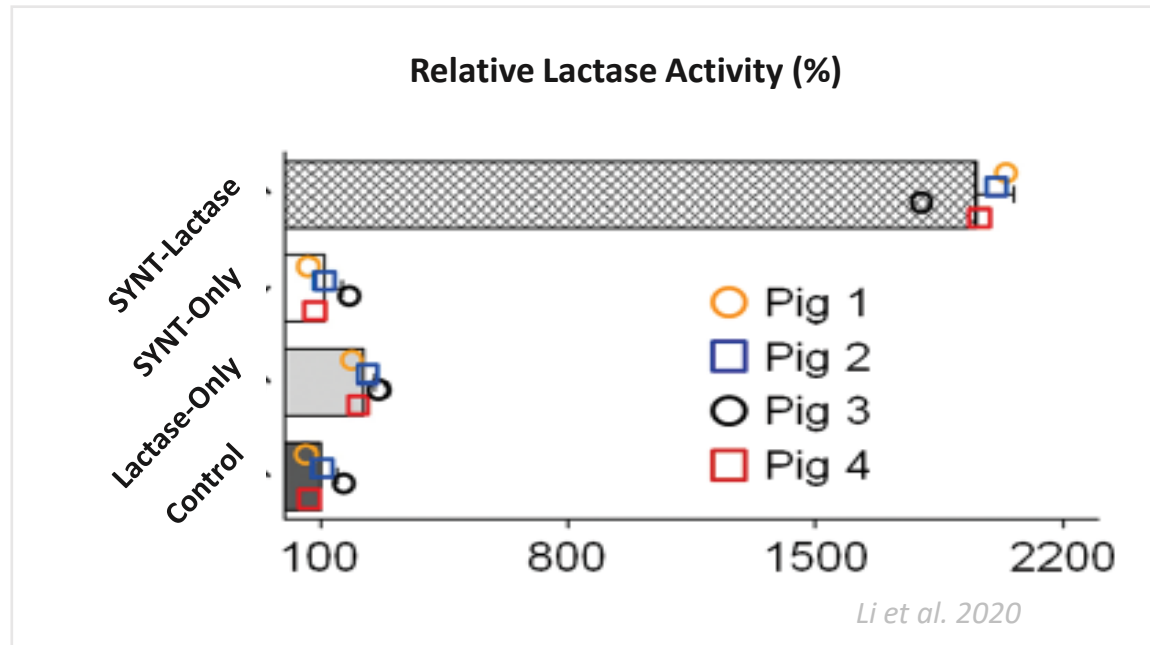


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Multiple Therapeutic Platforms

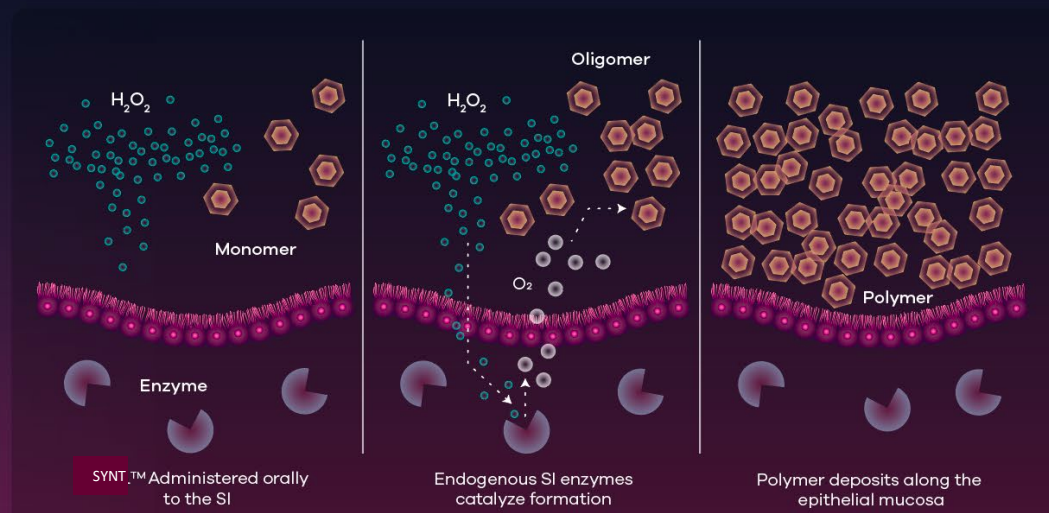


DIGEST™ enables durable intestinal enzyme therapy



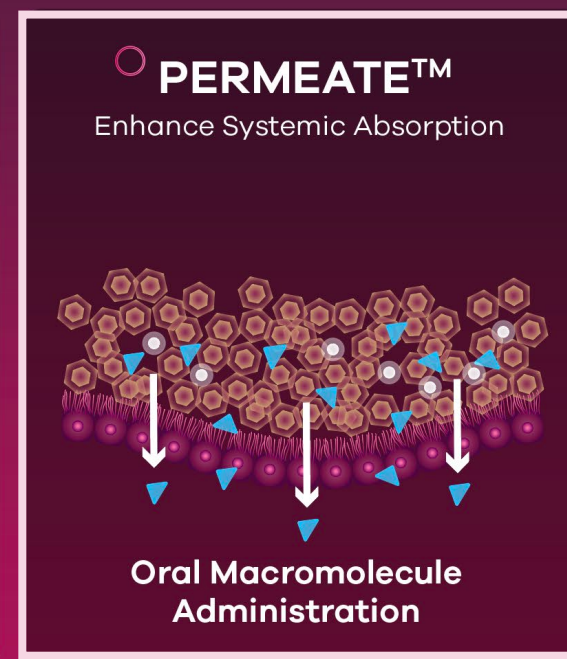
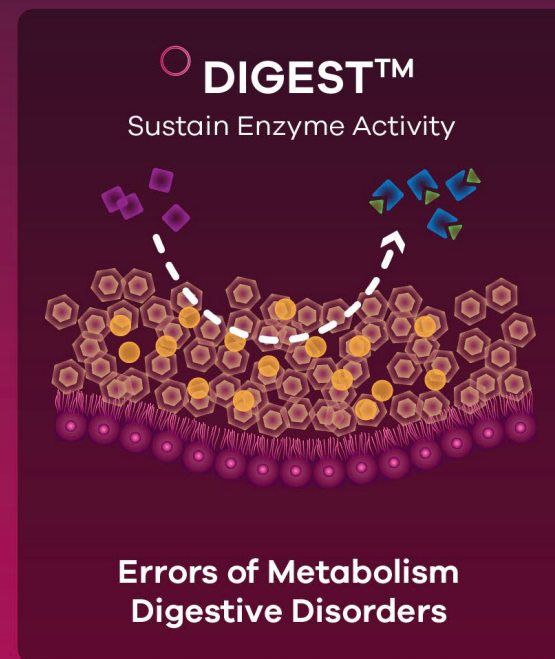
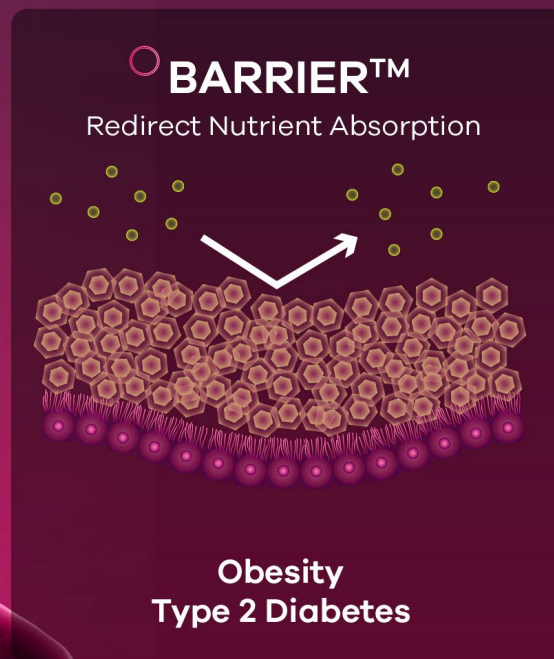
- » Sustained lactase residence via mucoadhesive polymer coating
- » ~20-fold *in vivo* activity vs. enzyme alone after simulated gastric emptying
- » Non-disruptive to nutrient absorption or brush border activity

The location of the enzyme for prolonged residence can be optimized by modification of the controlled release polymers for optimal site-specific formation of the synthetic epithelial lining in the small intestine and enzyme entrapment.



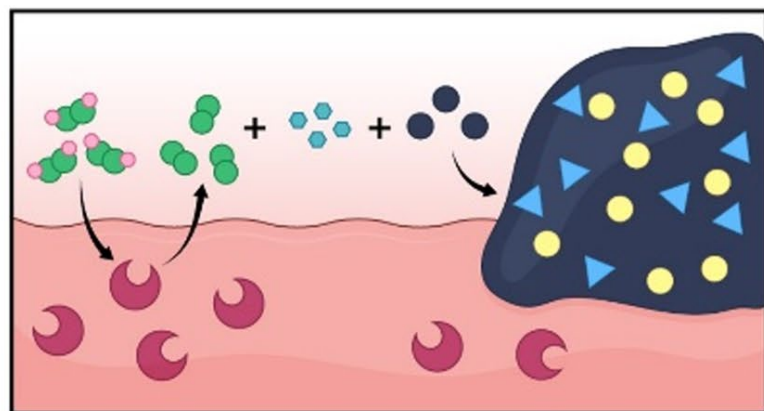
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PERMEATE™ Mechanism

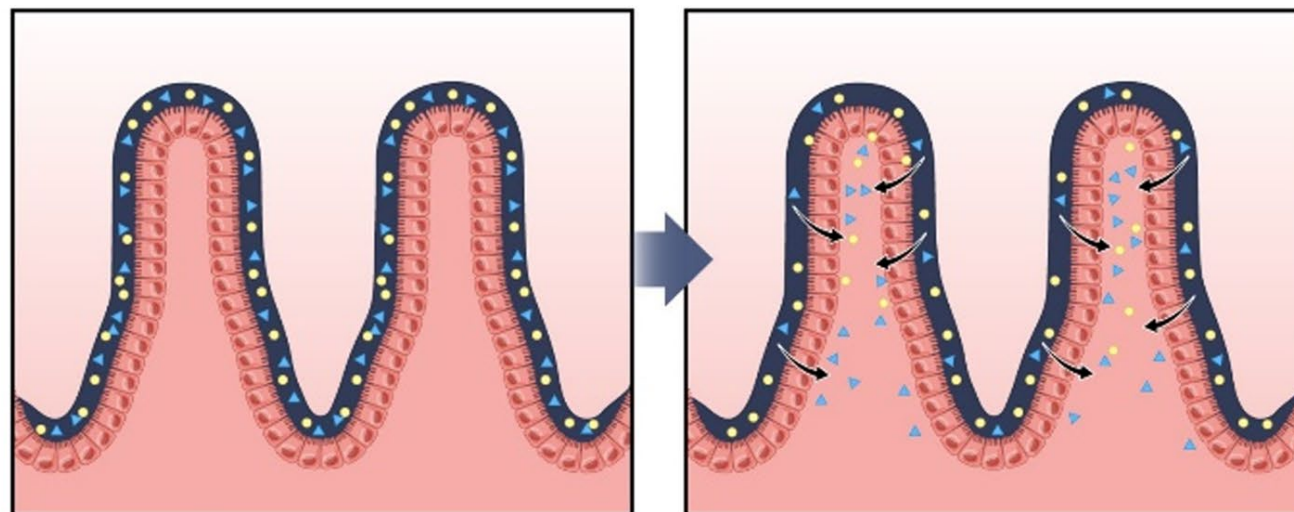
A SYNT formation mechanism



Treatment components:

 Catalase	 Dopamine	 H ₂ O ₂
 Oxygen	 API	 PDA nanoparticle
	 PE	

B PERMEATE mechanism



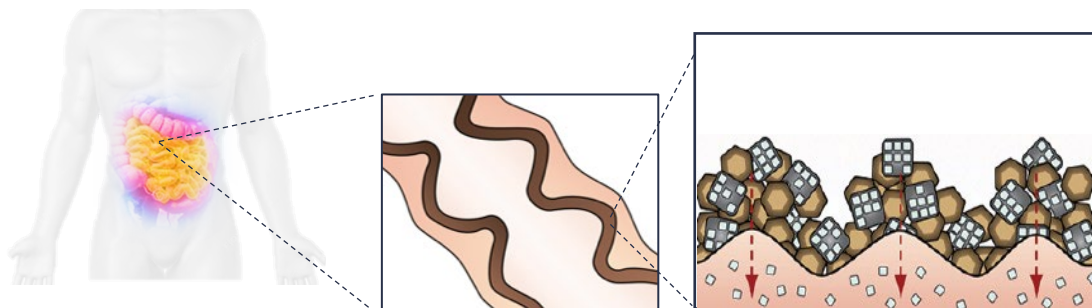
drug colocalization

Enhanced drug absorption over 24h



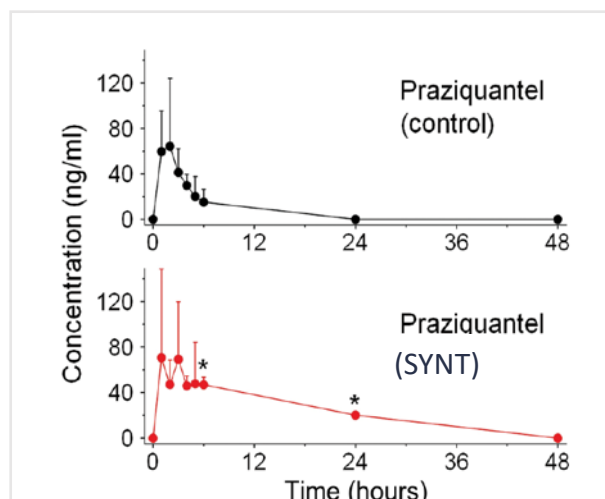
PERMEATE™ increases oral bioavailability

PERMEATE™ = SYNT™ + API + PE



POC: Small Molecules

- ✓ 10-fold increase in T1/2
- ✓ 4-fold increase in AUC
- ✓ Compatible with biologics



SYNT™ alone increases duration and oral bioavailability of small molecules.



PERMEATE™ combines SYNT™ with PEs and APIs to maximize absorption of multiple modalities.

Compatible Modalities

- Small molecules
- Peptides
- Antisense Oligos
- siRNA
- mAbs
- Nanoparticles



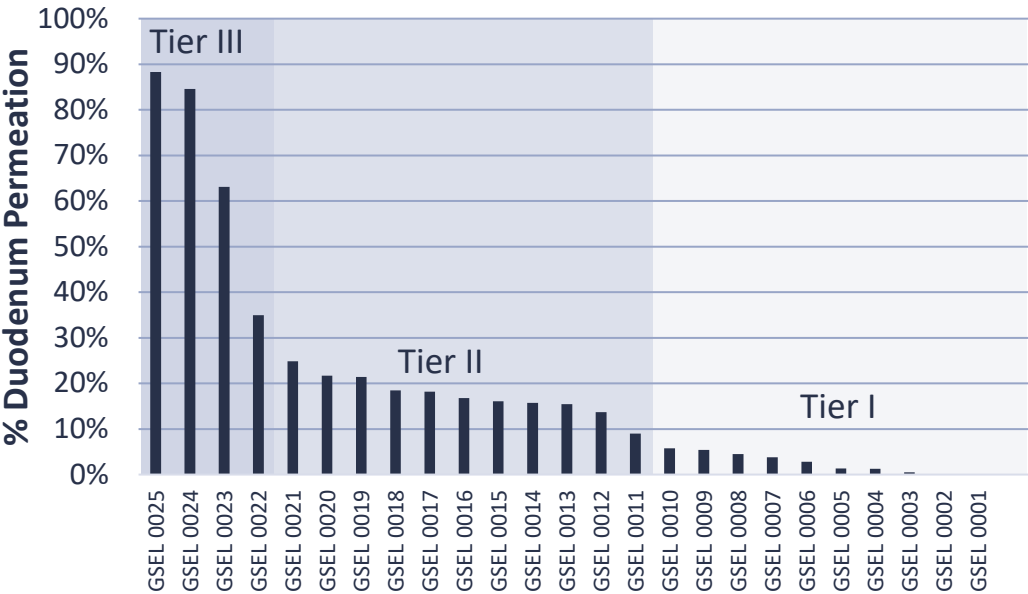
SYNT™ alone extends GI absorption of small molecules



PERMEATE™ is currently being evaluated for the oral delivery of biologics

PERMEATE™ delivers oral bioavailability of biologics

Peptide Permeation Tunable by Formulation

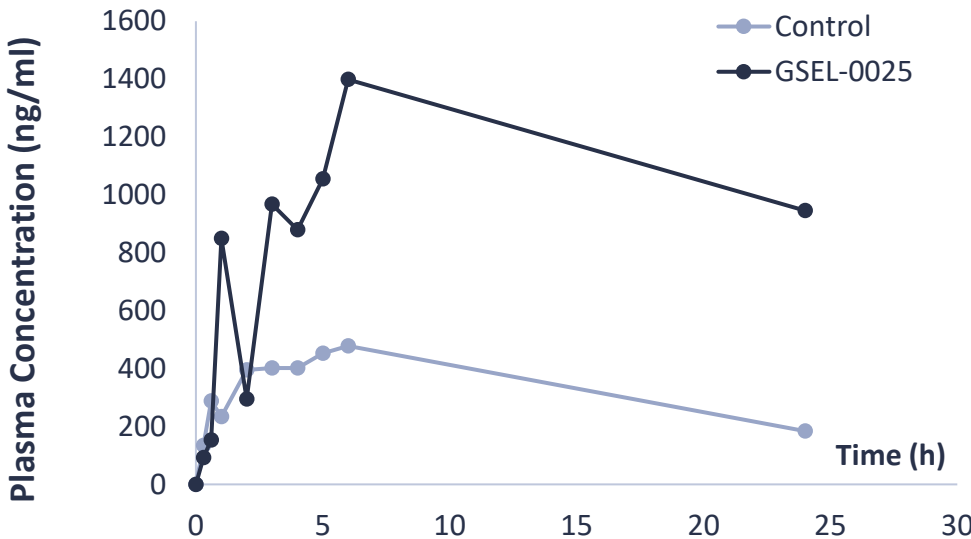


Unpublished

Formulation Applications:	
Tier I	GI-Restricted
Tier II	GI-Penetrant
Tier III	Systemic Delivery

SYNT formulations can be fine-tuned to dial up, or down, permeation levels of model peptide

Systemic Delivery of Model Peptide Demonstrated in Pigs

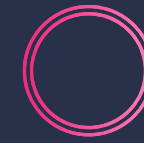


Unpublished

Model peptide (~5 kDa) with multi-fold bioabsorption compared to reported data through GI exposure

Summary

- Syntis Bio has a proven platform technology, SYNT, that can be utilized in multiple ways to advance a wide range of therapeutics forward clinically.
- Syntis Bio can fine tune the delivery of SYNT to the optimal region of the gastrointestinal tract by utilization of a wide range of controlled release polymers.
- The Syntis team has developed in vivo, ex vivo, and in vitro testing methodologies to optimize SYNT formulations and release profiles.
- Syntis Bio has multiple programs in early phase development and is eager to entertain discussions with potential partners (info@syntis.bio).



Syntis Bio

Thank you

