Targeted GI Delivery of Orally Administered Cells and Proteins for Microbiome-Based Therapeutics

Contact: Gerard Honig PhD, Director
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Overview

• Biotechnology startup developing drug delivery solutions to realize the therapeutic potential of the microbiome

• Drug delivery & formulation technology for controlled release of orally administered therapeutics for local action in the GI tract

• SHP-01 for *C. difficile*: Towards an ultra-targeted microbiome-sparing antimicrobial for gastrointestinal infection

• New funding opportunity for IBD product development
Drug delivery solutions to realize the therapeutic potential of the microbiome

Novel microbe-derived proteins

Novel microbiome organisms

Validated biologic therapeutics

Targeted oral drug delivery
Formulation platform for targeted oral delivery of proteins & cells

Small molecules
Probiotic bacteria

Anaerobic bacteria
Recombinant proteins

Standard enteric formulations

Standard capsule

Loss of therapeutic activity

Proprietary oral biologics delivery platform
Formulation platform for targeted oral delivery of proteins & cells

- Microencapsulated hydrogel phase retains proteins & cells in native hydrated state
- Stabilized macroemulsions confer stability & controlled release
- Scalable, cost-effective manufacturing
- Preserves activity of sensitive biologics
- Stable product formulation
- GRAS composition with option to integrate add't'l validated chemistries
Multi-stage delivery system for delivery of proteins & cells to the lower GI tract

Enteric coating protects cargo

Enteric layer erodes

Muco-adhesive layer swells & erodes

Time release lipid matrix adheres to GI wall & erodes

Phosphate triggered Hydrogel release of API

pH3
Stomach (~1hr)

Small Intestine (~2hrs)

Colon (~8-12hrs)

pH8
Compatibility with large molecule & cell-based therapeutics
Targeted & tunable delivery of protein in simulated GI transit

- **Formulation A**
- **Formulation B**
- **Formulation C**

![Graph showing the hydrolysis of substrate molecules over time in different parts of the GI tract for three formulations.](image)
Non-invasive *in vivo* imaging of oral formulations in GI tract by microCT

- Noninvasive tracking of capsule location in GI tract *in vivo* using sphere tracer

- Visualization of capsule matrix integrity due to differential density
Imaging delivery of fluorescently labeled protein therapeutic to the colon

Delivery is colon-specific; protein not observed in small intestine

Labelled protein (SHP-01, yellow) accumulates specifically in the cecum and proximal colon

- Protein cargo labelled with long-wavelength fluorescent dyes
- Combined with quantitative PK
- Label any protein or bacterial strain with fluorophores
Oral drug delivery for proteins & cells: Competitive landscape

- Tunable controlled release
- Compatibility with diverse cargo

Logos of companies: assembly biosciences, SYMBIOTIC HEALTH, CAPSUGEL, Catalent, avaxia BILOGICS, SYNEXON® synlogic, SERES THERAPEUTICS™, entrega
C. difficile infection: Disease of the microbiome

DEADLY DIARRHEA:
C. DIFFICILE CAUSES IMMENSE SUFFERING, DEATH

IMPACT

- Antibiotics kill microbiome bacteria, leading to C. difficile
- 400% increase since 1993; $4B excess US medical cost
- Unmet medical need: Protracted & recurrent infections
SHP-01: Ultra-targeted lysin enzyme antimicrobial for *C. difficile* infection

- Phage-derived lysin engineered to cleave cell wall
- Undetectable acquired resistance
- Clear regulatory precedents
- Licensed from Rockefeller University

Bacterial Cell Wall

Cytoplasm

Lysin rapidly kills *C. difficile* in infected GI tract

* Significant (400-fold) decrease

SHP-01 kills diverse *C. difficile* strains while sparing microbiome bacteria

Symbiotic Health Team

Management, Staff & Advisors

**Founder & President:** Gerard Honig PhD

**Chief Technology Officer:** Noel Goddard PhD
  
  Biomaterials & genomics expert & serial entrepreneur

**Founder & VP Clinical:** Bruce Hirsch MD
  
  Infectious disease medicine innovator

**Selected Advisors:**

Vincent Fischetti PhD: Professor, Rockefeller University; leading antimicrobial inventor

Larry Miller MD: Chief of Gastroenterology, Northwell Health; functional GI innovator

Directors

Steve Winick & Leo Guthart, Topspin Partners
  
  Leading biotechnology portfolio & exits (Immune Design, NGM, Aragon, Seragon)

Katy Stein PhD: Frmr FDA Division Chief & SVP, Macrogenics; bacterial products expert

Funding & Partners

The Rockefeller University

Stony Brook University Center for Biotechnology
Crohn’s & Colitis Foundation
Entrepreneurial Investing Initiative

Contact: Gerard Honig PhD, Manager
entrepreneurship@crohnscolitisfoundation.org
• Up to $500K per project per year for product discovery & development
• Accelerator resources
• Must address unmet need in IBD
• All technologies considered
• Companies preferred

Apply by July 21!
http://www.crohnscolitisfoundation.org/science-and-professionals/

Contact: Gerard Honig PhD, Manager
entrepreneurship@crohnscolitisfoundation.org
Oral delivery of biologics: Challenges & opportunities

- Since 2011, biologic therapeutics are \( \geq 30\% \) of new FDA approvals.
- In 2015, 1,367 biologic therapeutic INDs were filed.
- Of the >240 biologics approved, only 5 are oral formulations.

The majority of commercial delivery technologies are devoted to protecting the cargo as it passages through the stomach or improving drug absorption in the small intestine.

Our delivery technology is tunable, allowing release in the small intestine or lower GI tract, making it uniquely suited for delivery of peptides, proteins, and organisms into the colonic microbiome.
## Symbiotic Health
### Product Development Pipeline

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<thead>
<tr>
<th></th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Clinical</th>
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<tbody>
<tr>
<td><strong>1st gen delivery platform</strong></td>
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<tr>
<td><strong>2nd gen delivery platform</strong></td>
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<td>SHP-01 for acute &amp; recurrent <em>Cdiff</em></td>
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<td><strong>Monoclonal Antibodies for IBD</strong></td>
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*Hirsch et al, *BMC ID* 2015. Superseded by 2\textsuperscript{nd} gen platform.

**Integrated into current therapeutic product candidates.
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<th>Current &amp; Future <em>C. difficile</em> Therapy: SHP-01 Competitive Differentiation</th>
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<tr>
<td><strong>Antibiotics</strong></td>
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<td>Acute or recurrent label</td>
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<tr>
<td>Microbiome sparing</td>
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<td>Undetectable resistance</td>
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<td>Synergistic w/ standard-of-care</td>
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<td>Stable oral formulation</td>
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Recurrent *C. difficile* infection

>60% risk of relapse

**SHP-01:** Potential Clinical Benefits & Synergies for Recurrent Infection

- Standard antibiotics
- Suppression of acute infection
- Reduced risk of relapse

**Microbiome Transplantation**

**Defined Probiotics**

- Potential to accelerate resolution & reduce relapse