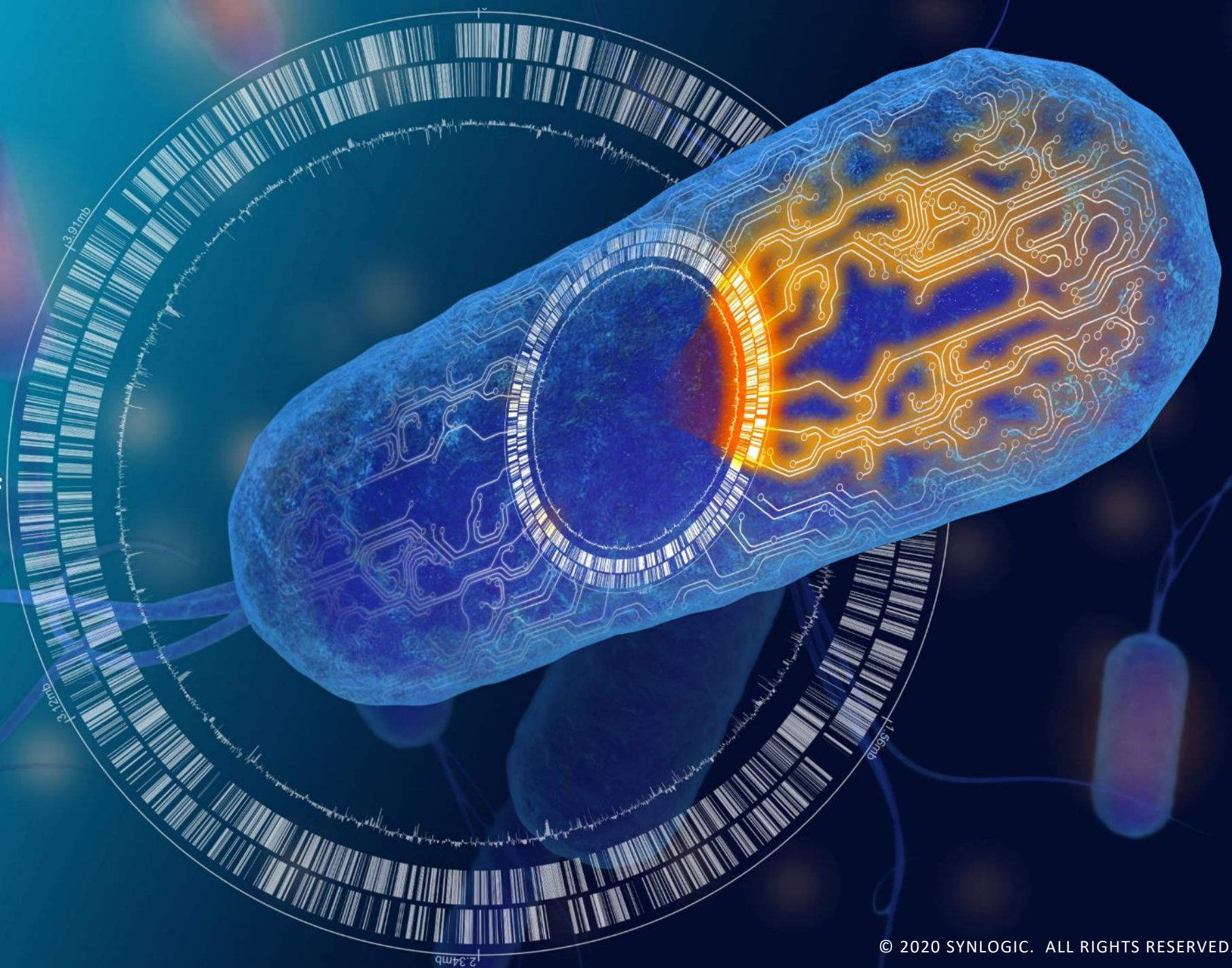


# synlogic

**Bringing the  
Transformative Power of  
Synthetic Biology to  
Medicine**

Corporate Presentation  
November 2020



# Forward Looking Statements

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This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this presentation regarding strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. In addition, when or if used in this presentation, the words “may,” “could,” “should,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “plan,” “predict” and similar expressions and their variants may identify forward-looking statements. Examples of forward-looking statements include, but are not limited to, the approach we are taking to discover and develop novel therapeutics using synthetic biology; statements regarding the potential of our platform to develop therapeutics to address a wide range of diseases, including: metabolic diseases, inflammatory and immune disorders, and cancer; the future clinical development of Synthetic Biotic medicines; the potential of our technology to treat phenylketonuria and cancer; the expected timing of our anticipated clinical trial initiations and availability of clinical data; the benefit of orphan drug and fast track status; the adequacy of our capital to support our future operations and our ability to successfully initiate and complete clinical trials; the results of our collaborations; and the difficulty in predicting the time and cost of development of our product candidates. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: the uncertainties inherent in the preclinical development process; our ability to protect our intellectual property rights; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading “Risk Factors” in our filings with the SEC. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in our quarterly report on Form 10-Q filed with the SEC on May 8, 2020, and in any subsequent filings we make with the SEC. The forward-looking statements contained in this presentation reflect our current views with respect to future events. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our view as of any date subsequent to the date hereof.



# Recent Progress: Execution Across the Portfolio

## Metabolic Programs

Rapidly progressed **metabolic programs**

- **SYNB1618 in PKU** Phase 2  
*SynPheny-1* study initiated
- IND for **SYNB8802 in Enteric Hyperoxaluria** opened and Phase 1 study initiated

## Immunomodulation

**Immunomodulation** in immunology and oncology

- **SYNB1891** monotherapy continues to enroll: study update expected late 2020

Advanced exploratory work in IBD

**We are the premier Synthetic Biology platform engineering bacterial Synthetic Biotic medicines**

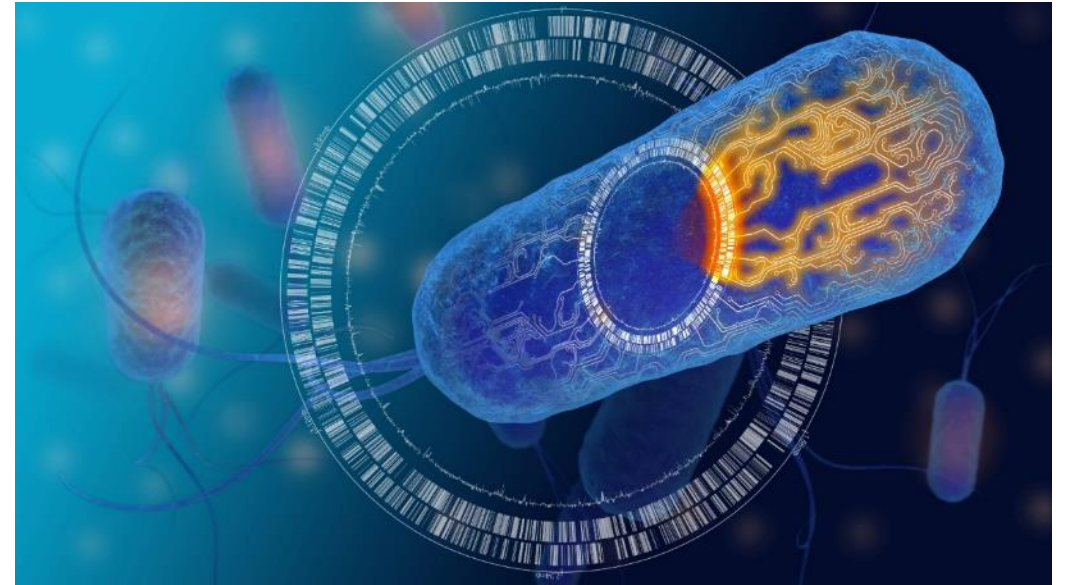
# A New Class of Medicines

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Bacteria and Humans Co-Evolved and Co-Exist



We Rationally Design Bacteria  
To Provide Clinical Benefit



**The Result is Synthetic Biotic Medicines with Potent and Programmable Therapeutic Effects**

# Building a Diverse Portfolio of Synthetic Biotic Medicines

Platform for Clinical Benefit Across Multiple Disease States



## Validated Biological Targets

Where a Synthetic Biotic medicine is uniquely positioned to impact patients



## Enabling Engine Core Differentiating Capabilities

Synthetic Biology  
Internal + Ginkgo



Manufacturing of live  
Synthetic Biotics

Regulatory, Translational  
& Clinical Dev.



## Internal Focus: Metabolic Programs

Consumption of toxic metabolites from  
the GI tract

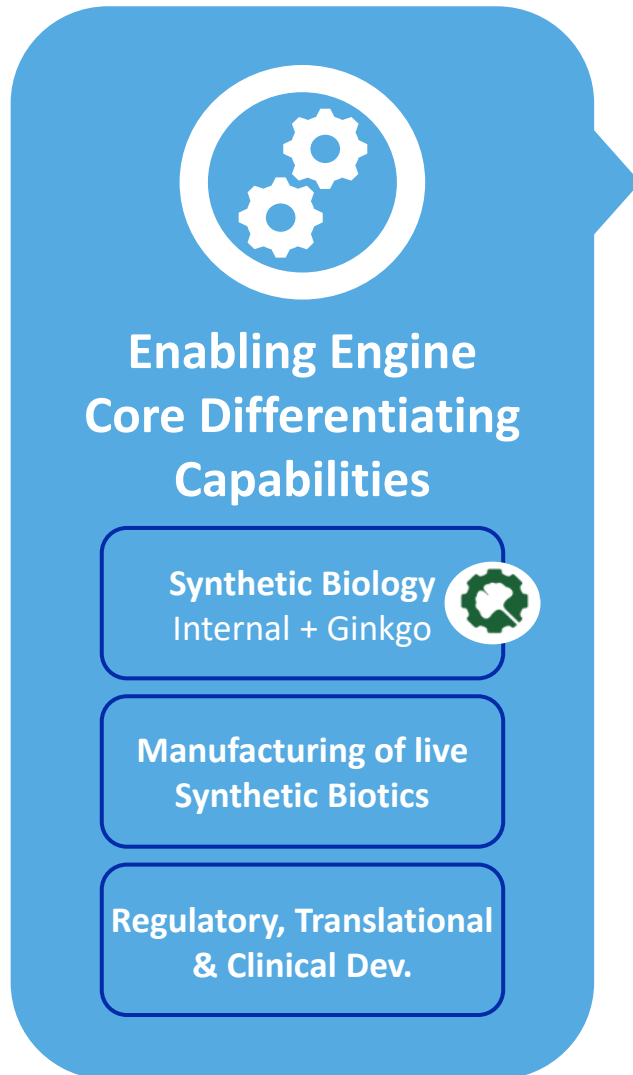


## External & Collaboration Focus: Immunomodulation

Immunology and oncology: Leveraging  
the ability of bacteria to **interact** with  
the immune system

# Enabling Engine: Driver for Success

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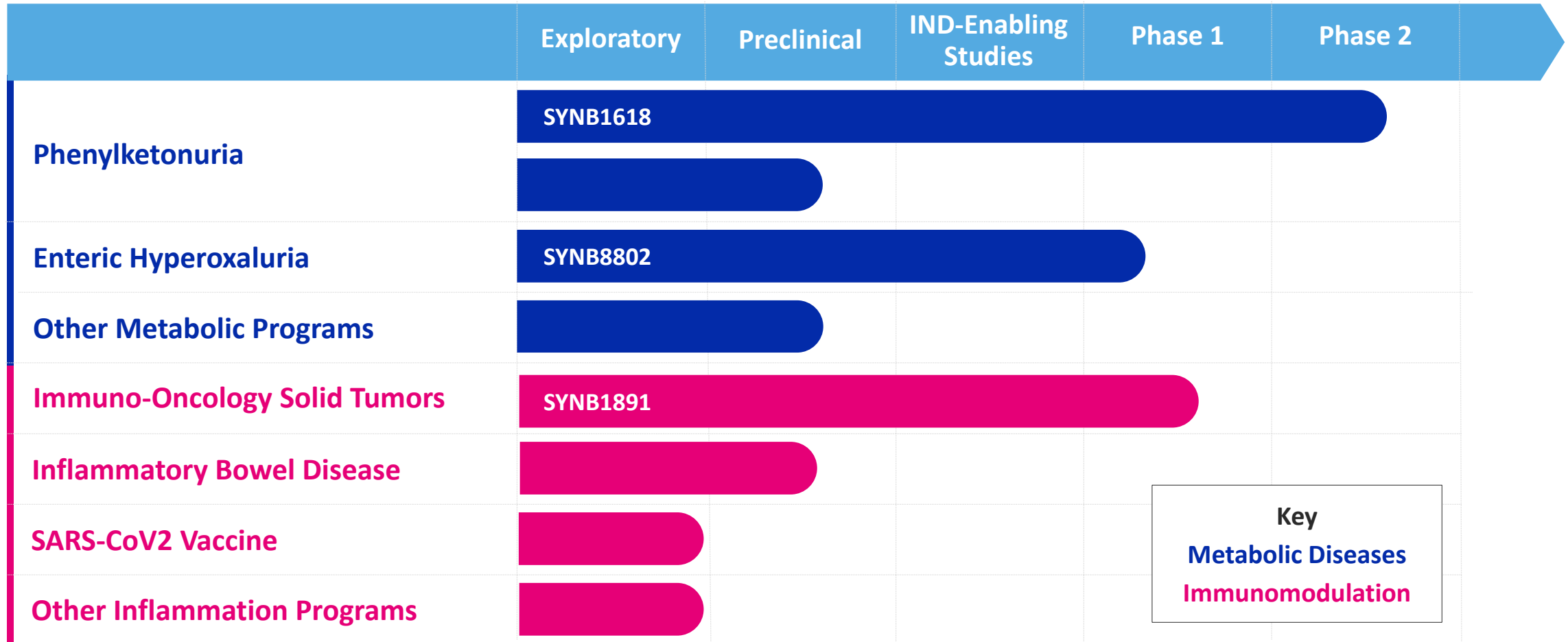
- **Clinical Evidence**

- **>200 humans dosed** with Synthetic Biotic medicines
- **4 INDs opened** with the U.S. FDA
- **Supportive regulatory feedback** from global agencies
- **Safe** (>100 years of human experience) probiotic bacterial chassis

- **Core Technology**

- **Deep synthetic biology expertise** with Ginkgo Bioworks collaboration
- **Modular and reusable synthetic biology components** enable iterative, efficient platform learning
- **Internal process development and GMP manufacturing** capabilities

# Robust Pipeline



# Synlogic Entering Data Rich Period in the Clinic

Expected Milestone		2020			2021		
		early	mid	late	early	mid	late
<b>SYNB1618 PKU</b>	Initiate Ph.2 study in PKU patients			initiated			
	Ph.2 Phe-lowering read-out						
<b>SYNB8802 HOX</b>	Initiate IND-enabling studies	completed					
	Initiate Ph.1 study in HV and patients			initiated			
	Ph.1 patient read-out						
<b>SYNB1891 I/O</b>	Ph.1 Monotherapy interim update						
	Initiate Ph.1 combination study arm						
	Ph.1 combination therapy read-out						

**Significant Clinical Readouts within our Current Cash Window**



# Why Metabolic Diseases For Synthetic Biotic Medicines?

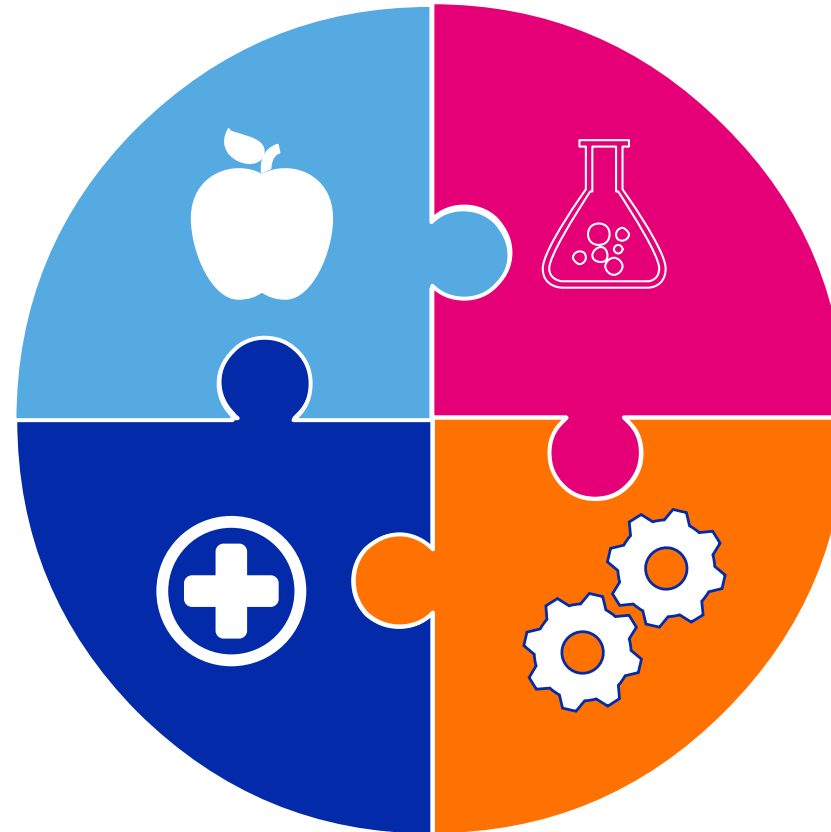
## Validated Biology

Diseases with known pathophysiology

Dietary intervention provides support for GI-based approach

## Unmet Medical Need

Across both inherited and acquired metabolic diseases



## Platform Proof of Mechanism

PKU program demonstrated we can consume toxic metabolites in the GI tract

Subsequent programs build on experience

## Unique Advantage of SYNBI

Bacteria act catalytically

Contain multiple enzyme pathways

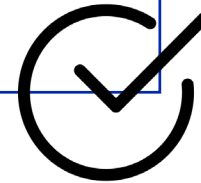
Are protected from digestion within the GI tract

# Phenylketonuria (PKU)

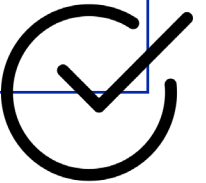
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**Emerging treatment  
options will continue to  
leave many patients  
behind**

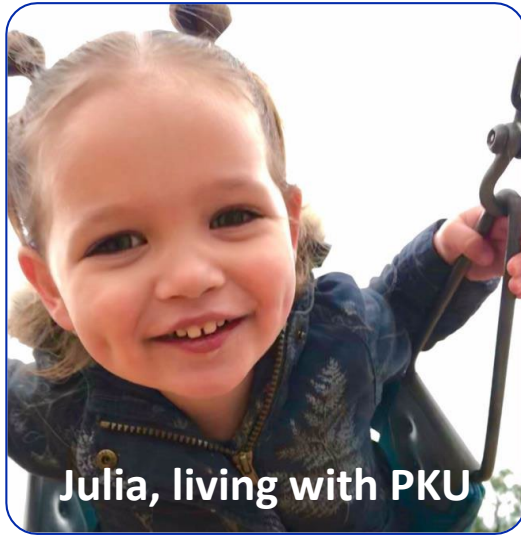
**SYNB1618 demonstrates  
potential to lower Phe in  
PKU patients**



**Phase 2 Phe-lowering  
trial initiated**



# Synlogic's Approach to Phenylketonuria (PKU)



## Synthetic Biotic Mechanism of Action

Consume Phe in the GI Tract



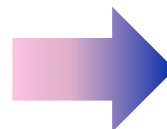
Reduce Phe in the blood

## PKU Program Status

SYNB1618 was able to consume Phe in healthy volunteers

Synlogic has initiated a Phase 2 Study in PKU patients (SynPheny-1)

# Living with PKU: Parents Expect Their Children to Achieve Their Full Potential



**Prospect of severe mental disability and institutionalization.**

**Parents wanted PKU child to avoid institutionalized care before adulthood.**

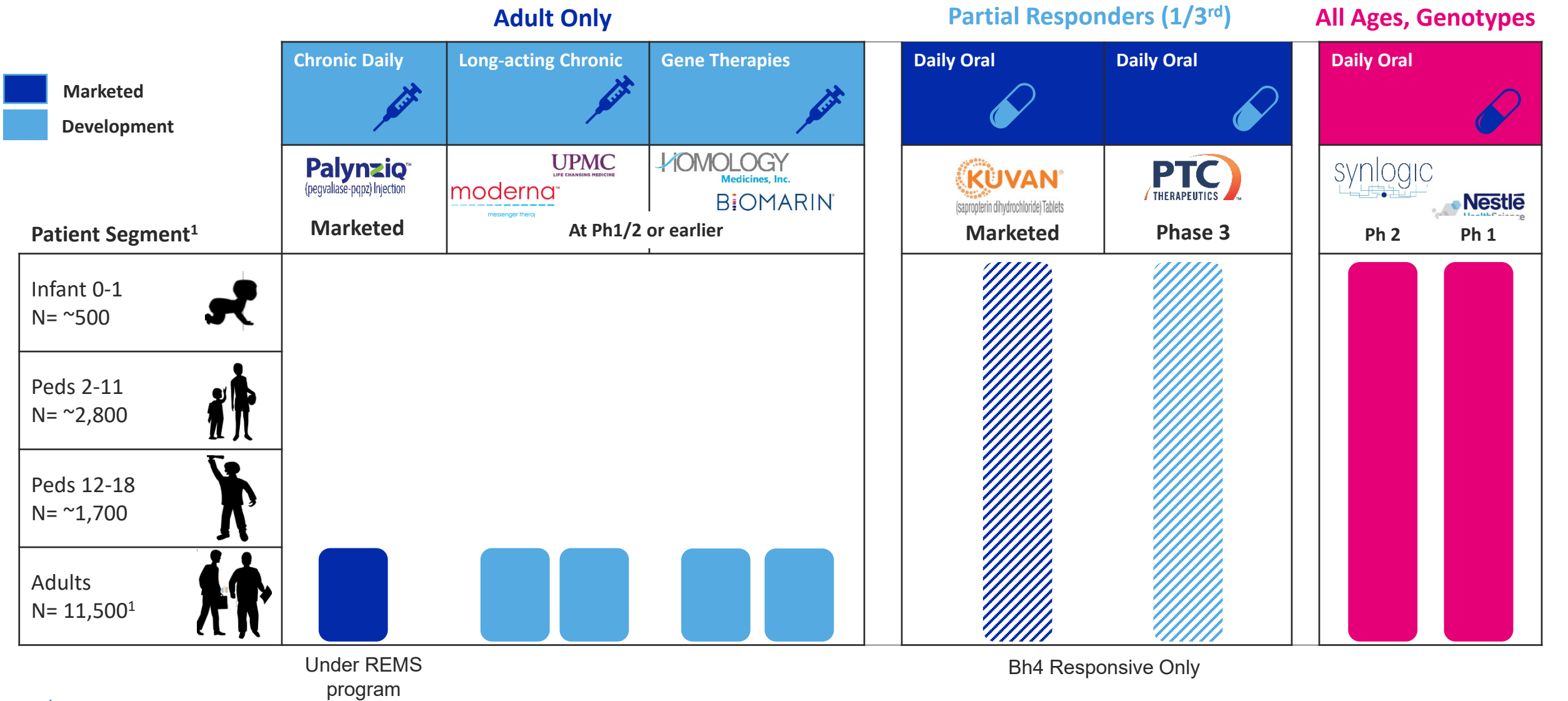
**Early diagnosis and strict diet control enables better Phe management.**

**Parents expect PKU child to achieve full potential, college attendance, self-support.**

**Reality: 25% – 65% of Patients Still Struggle to Maintain Blood Phe within Target Range**



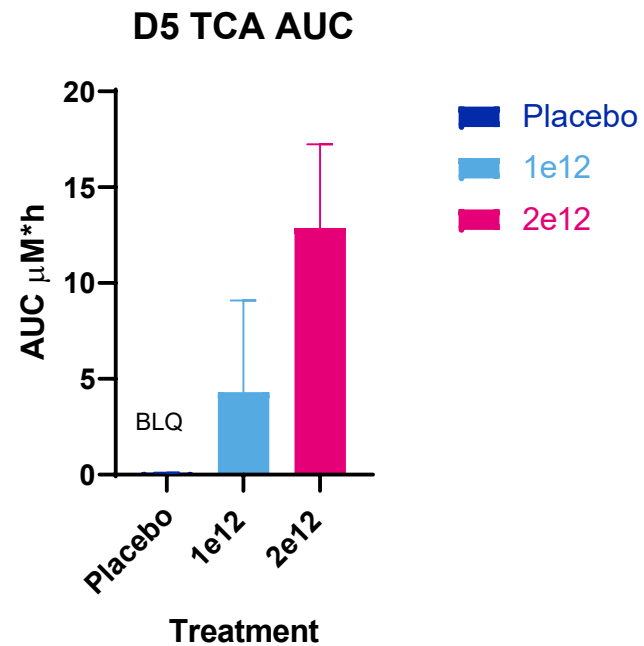
# SYNB1618 is Uniquely Positioned to Address Needs Across Ages and Genotypes



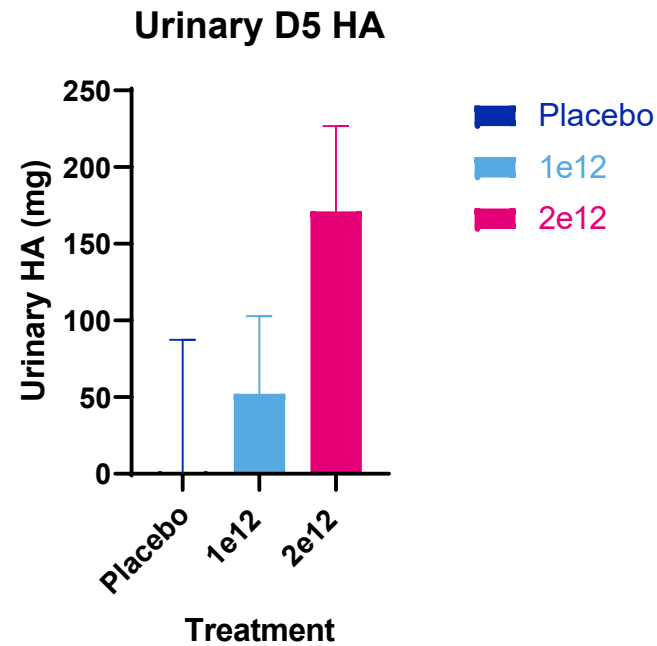
1. Includes 7,500 "lost to follow up" adult patients

# SYNB1618 In The Clinic: D5 Tracer Data in Healthy Volunteers

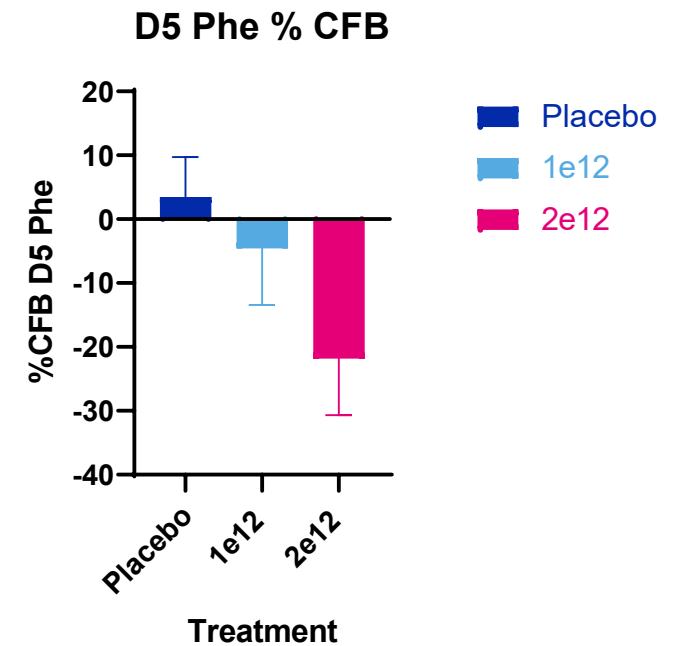
## D5 Phe Converted to D5 TCA



## D5 TCA Converted to D5 HA



## Plasma D5 Phe Blunted



Data are means and 90% CI

**SYNB1618 Mechanism Confirmed: Accessed D5 Phe Tracer in Gut & Lowered Plasma D5 Phe**

# Phe Modeling from Urinary HA Levels in HV Solid Oral Bridging Study



## Inputs

Strain Activity

Metabolite  
Consumption  
Requirements<sup>1</sup>

Bridging Study  
Biomarker Read-outs<sup>2</sup>

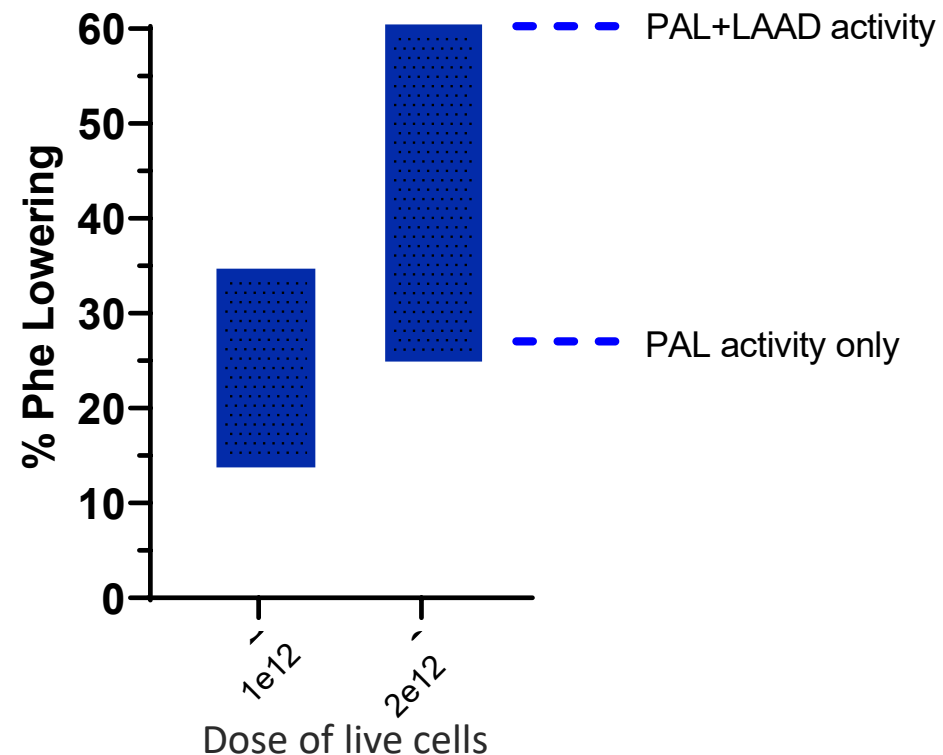


## In Silico Model

Proprietary Synlogic  
Simulation Models

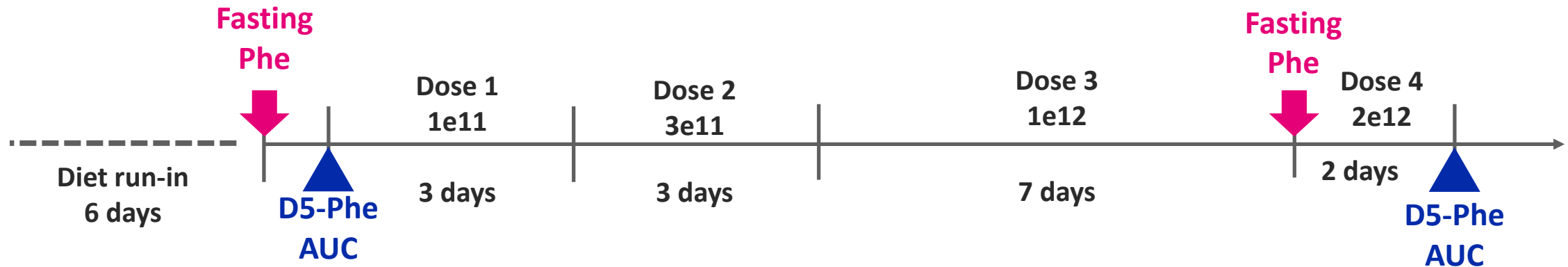


## Outputs: Phe Lowering Potential



Modeling Predicts SYN1618 Activity in Target Range

# SynPheny-1 Phase 2 Proof of Concept Study in PKU



- **Demonstrate Phe Lowering in PKU Patients**

- Plasma Phe lowering in fasted state at  $1 \times 10^{12}$  live cells over 7 days
- Post meal D5-Phe AUC lowering at  $2 \times 10^{12}$  live cells (**not impacted** by diet)

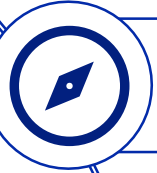
- **Validate PD Model**

- Understand relationship of strain specific biomarkers with plasma Phe lowering

- **Safety and Tolerability**



# Patient-Centered Clinical Trial Design & Execution



Directly informed by patient feedback on executing trials in the COVID era



Flexible design allowing home-based or office-based visits



Rigorous & personalized diet control to ensure consistent Phe intake, including 6-day run-in



Dose ramp to improve tolerability & compliance

# Enteric Hyperoxaluria

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**Enteric Hyperoxaluria  
results in significant  
kidney damage with no  
available treatment  
options**

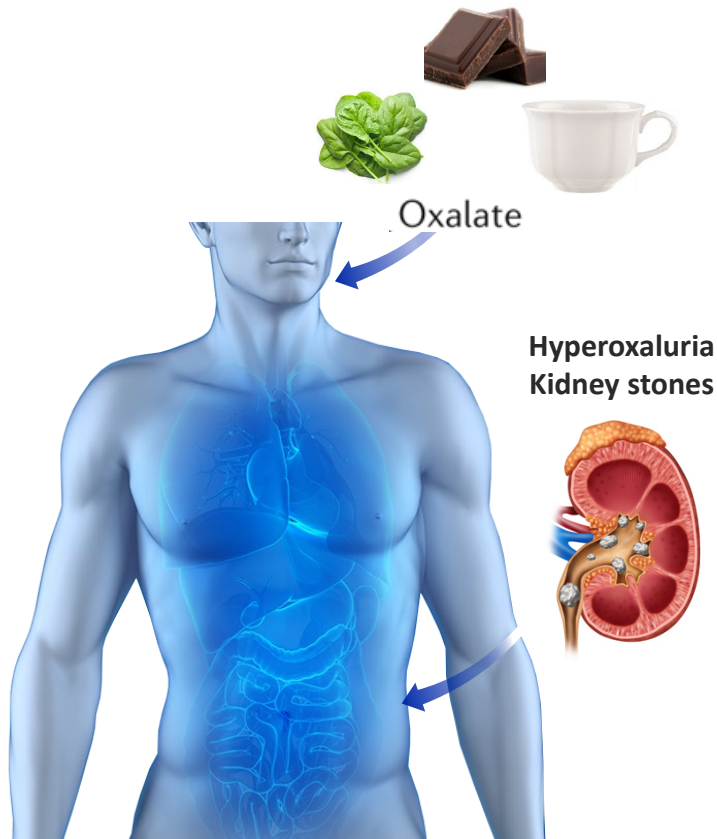
**SYNB8802 has the potential  
to meaningfully lower  
urinary oxalate levels**

**SYNB8802 Phase 1 clinical  
study initiated ahead of  
schedule**



# Synlogic's Approach to Enteric Hyperoxaluria

## Dietary Sources of Oxalate



## Synthetic Biotic Mechanism of Action

Consume Oxalate in the GI Tract







Reduce Oxalate in the urine

## Enteric Hyperoxaluria Program Status

SYNB8802 was able to consume oxalate in multiple animal models

Synlogic has initiated a Phase 1 Study in healthy volunteers

# Hyperoxaluria: Primary vs. Enteric

	Primary Hyperoxaluria	Enteric Hyperoxaluria
<b>Pathology</b>	Family of autosomal recessive monogenic disorders in which liver enzyme deficiency results in endogenous oxalate overproduction	Pathogenic hyperabsorption of dietary oxalate, often accompanies bowel disease or bariatric surgery
<b>Urinary Oxalate Levels</b>	90 – 500 mg / 24 hrs (up to 10x normal)	45 – 130 mg / 24 hrs (up to 3x normal)
<b>Onset</b>	Pediatric	Adult
<b>Clinical Mgmt</b>	Limited nutrition options; nephrocalcinosis; dialysis; transplant; pyridoxine	Limited nutrition options; treatment of kidney stones as they occur; nephrocalcinosis; dialysis
<b>U.S. Epidemiology</b>	~5,000 – 8,000	200,000 – 250,000
<b>Key Players</b>	 	 



# Enteric Hyperoxaluria Case Studies: An Important Cause of Renal Failure

## 33-Year-Old Female with Crohn's

- 33 yo woman with Crohn's requiring bowel resection resulting in severe hyperoxaluria (135 mg/day)
- Clinical course punctuated by:
  - Recurrent kidney stones
  - Progressive renal failure
  - Hemodialysis
  - Renal transplant x 1
  - Recurrent renal failure
  - Hemodialysis
  - Renal transplant x 2

## 48-Year-Old Male with Crohn's

- 48 yo man with Crohn's requiring 2 bowel resections with severe hyperoxaluria (110 mg/day)
- Clinical course punctuated by:
  - Recurrent kidney stones
  - Nephrocalcinosis
  - Progressive renal failure
  - Hemodialysis
  - Renal transplant

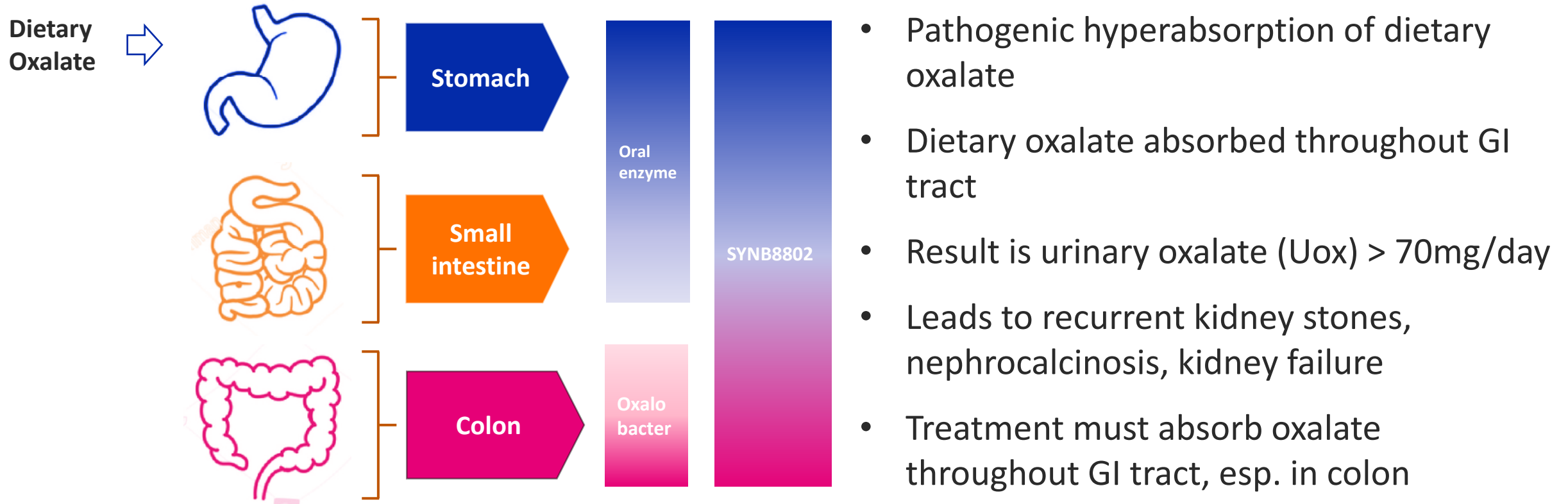
## 47-Year-Old Female with Crohn's

- 47 yo woman with Crohn's requiring extensive bowel resections with severe hyperoxaluria (114 mg/day)
- Clinical course punctuated by:
  - Recurrent kidney stones
  - Recurrent obstructive nephropathy
  - Progressive renal failure
  - Bilateral nephrectomies due to stone-related infections
  - Hemodialysis
  - Renal transplant
  - Recurrent renal failure

**Urinary oxalate levels remains markedly elevated in all patients, despite aggressive medical regimen**

# Enteric Hyperoxaluria Disease Pathogenesis

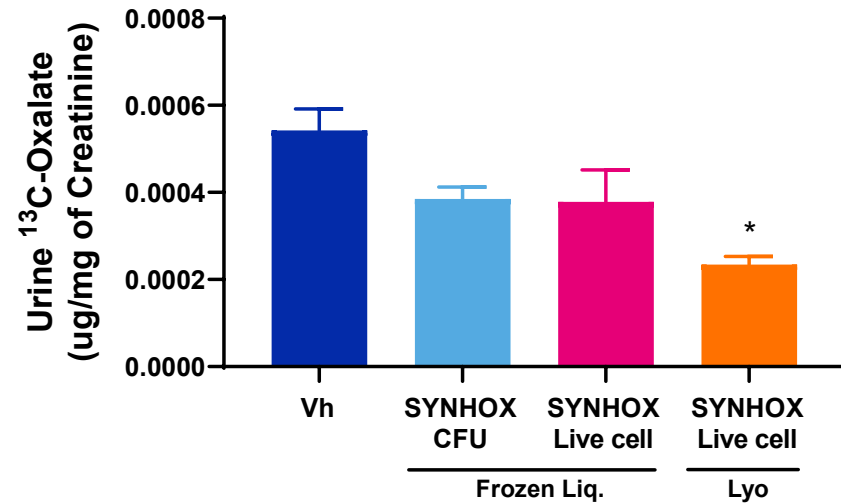
GI Based Therapies Have Demonstrated Lowering of Systemic Oxalate



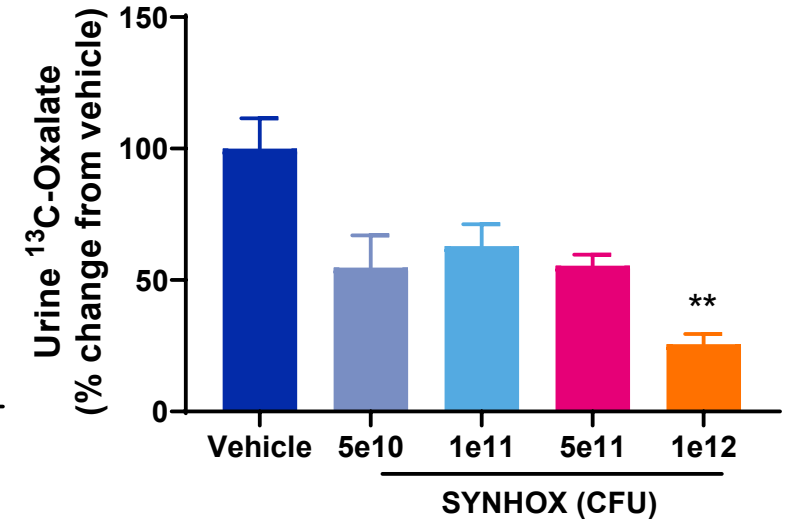
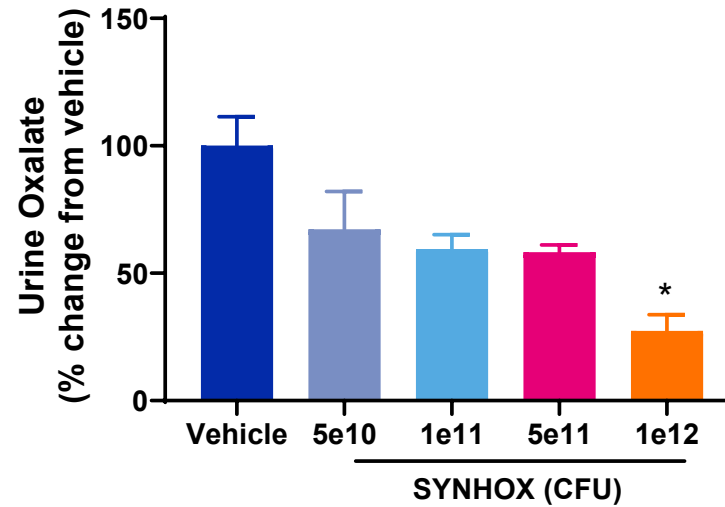
Intestinal Degradation of Oxalate Throughout GI Tract Could Enhance Oxalate Lowering

# SYN-HOX Attenuates Urinary Oxalate Increase

## SYN-HOX Consumes $^{13}\text{C}$ -Oxalate in Mice

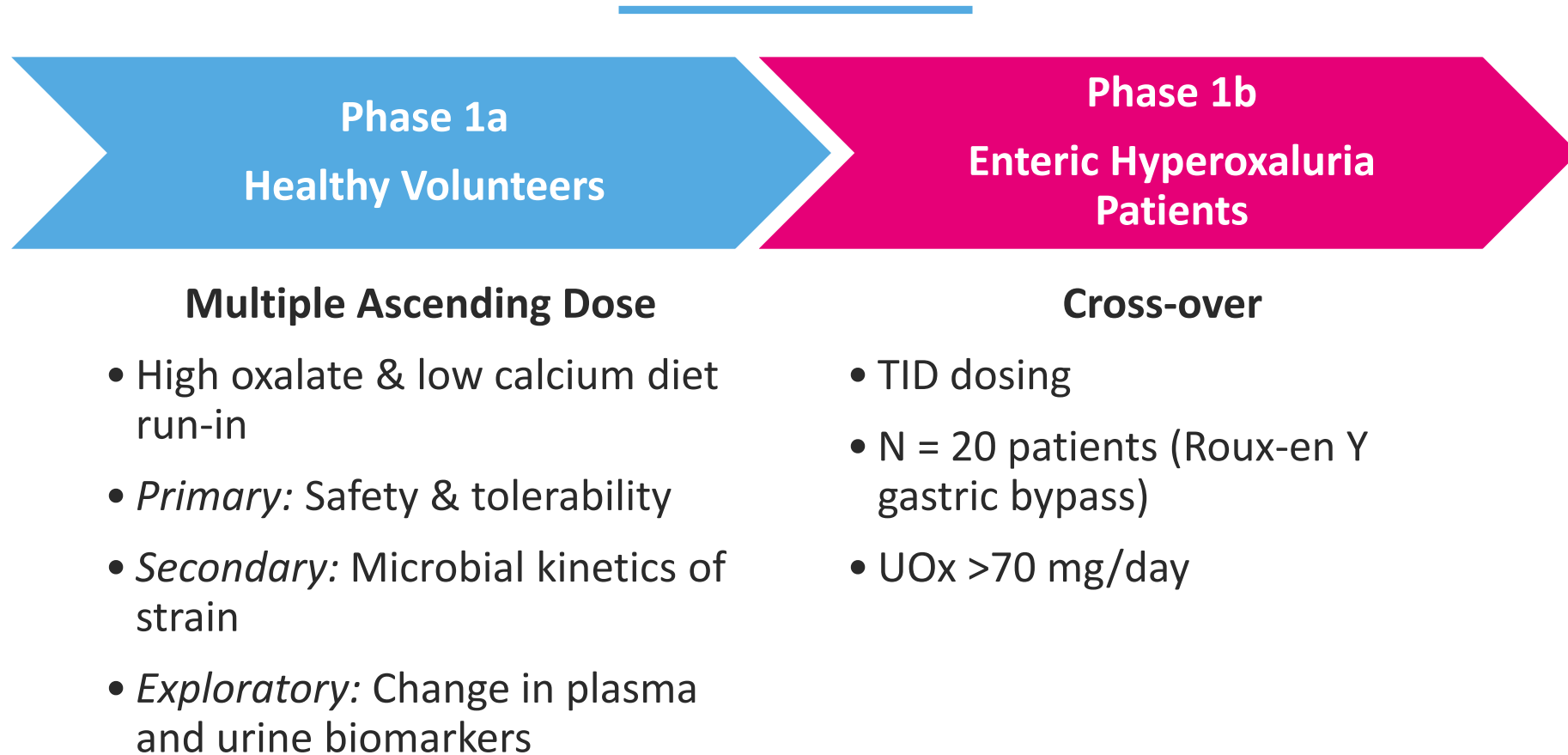


## SYN-HOX Attenuates Urinary Oxalate Increase In NHPs



## SYN-HOX Consumes Oral Load of Oxalate in Mouse and Non-Human Primate Models

# Enteric Hyperoxaluria: Phase 1 Design Provides PoC Opportunity



**Roux-en-Y Gastric Bypass Population Provides Opportunity to Demonstrate Urinary Oxalate Lowering in Disease State**



# Why Diseases of Immune System Regulation For Synthetic Biotic Medicines?

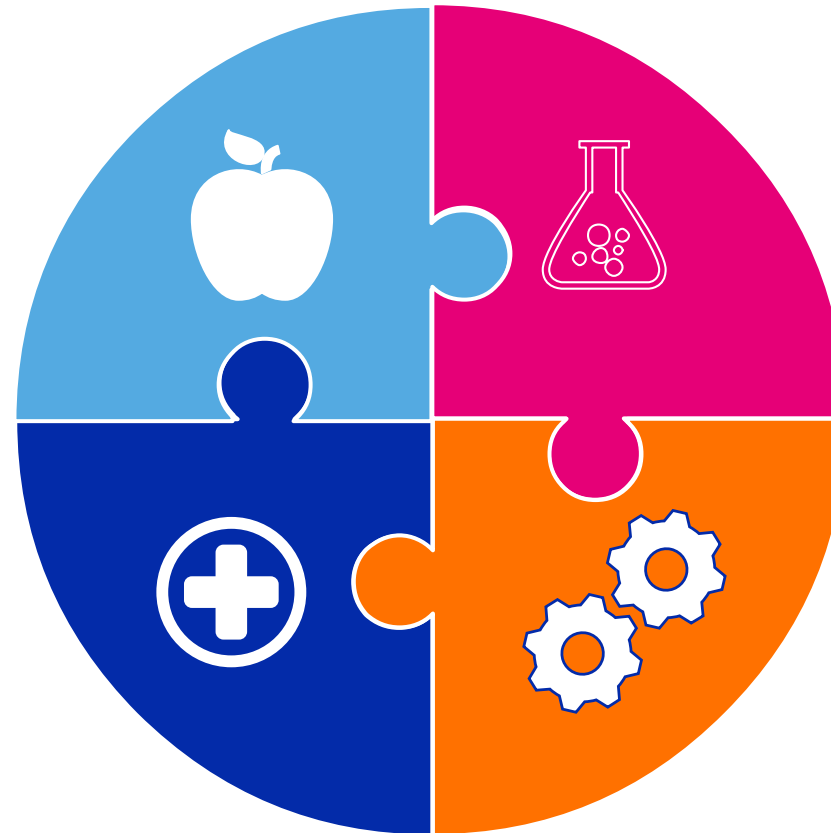
## Cross-talk Between Bacteria and Immune System

Immune system has evolved to recognize bacteria

Bacteria have evolved mechanisms to control the immune response

## Unmet Medical Need

Growing need for novel treatments for immunological diseases and cancer



## Platform

Preclinical POC for both immune stimulation and immunoregulation

Can produce immune mediators (small molecules, peptides, human cytokines)

## Unique Advantage of SYN B

Targeted efficacy and improved safety

Multiple effectors from single Tx strain delivered to site of disease

# Immunomodulation & Immuno-Oncology

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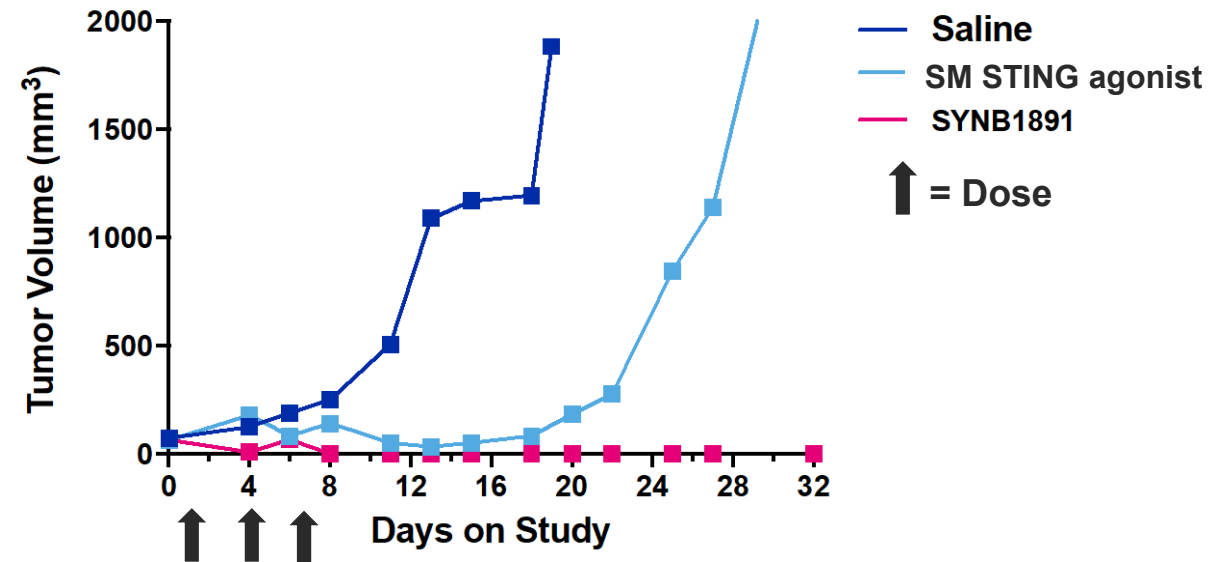
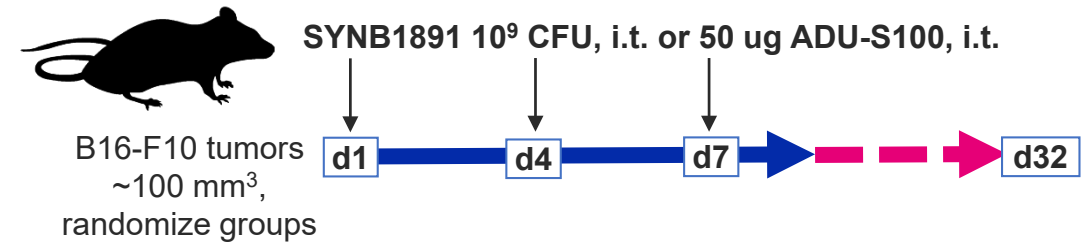
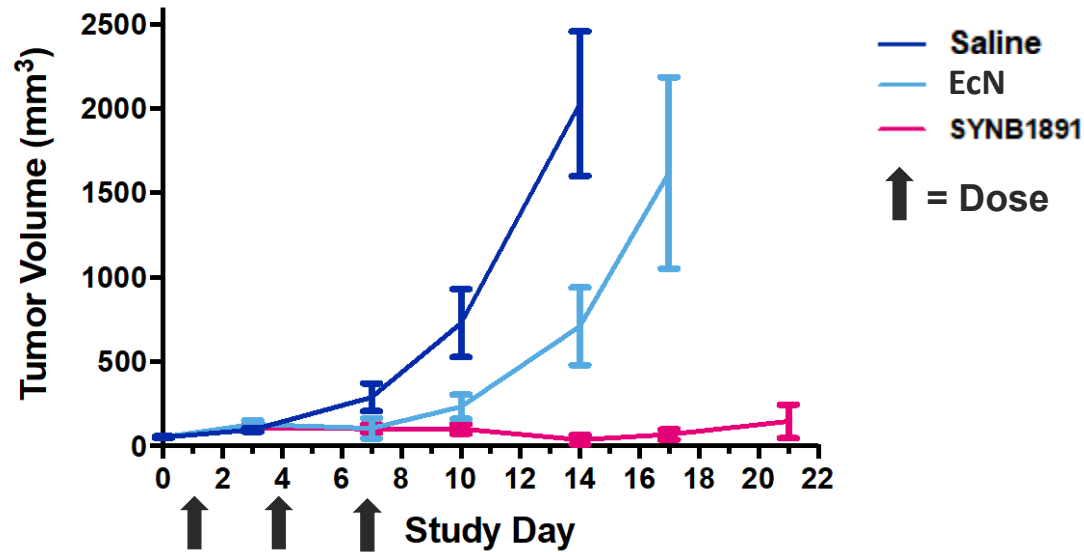
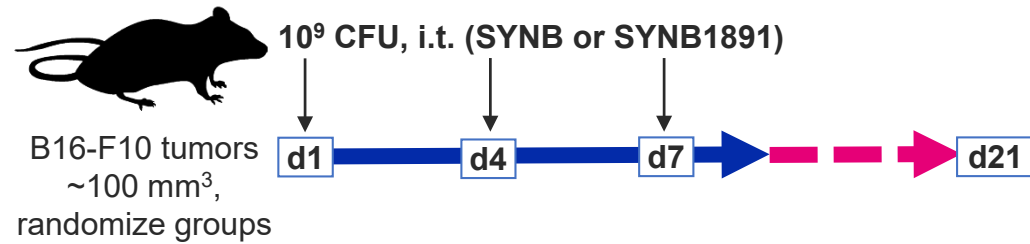
**Synthetic Biotics can  
be engineered for  
immune activation or  
regulation**

**SYNB1891 will provide  
clinical data in 2020  
from a monotherapy  
cohort**

**SYNB1891 has  
potential for improved  
efficacy relative to  
other STING  
approaches**

# SYNB1891 Induces Potent Anti-tumoral Effects

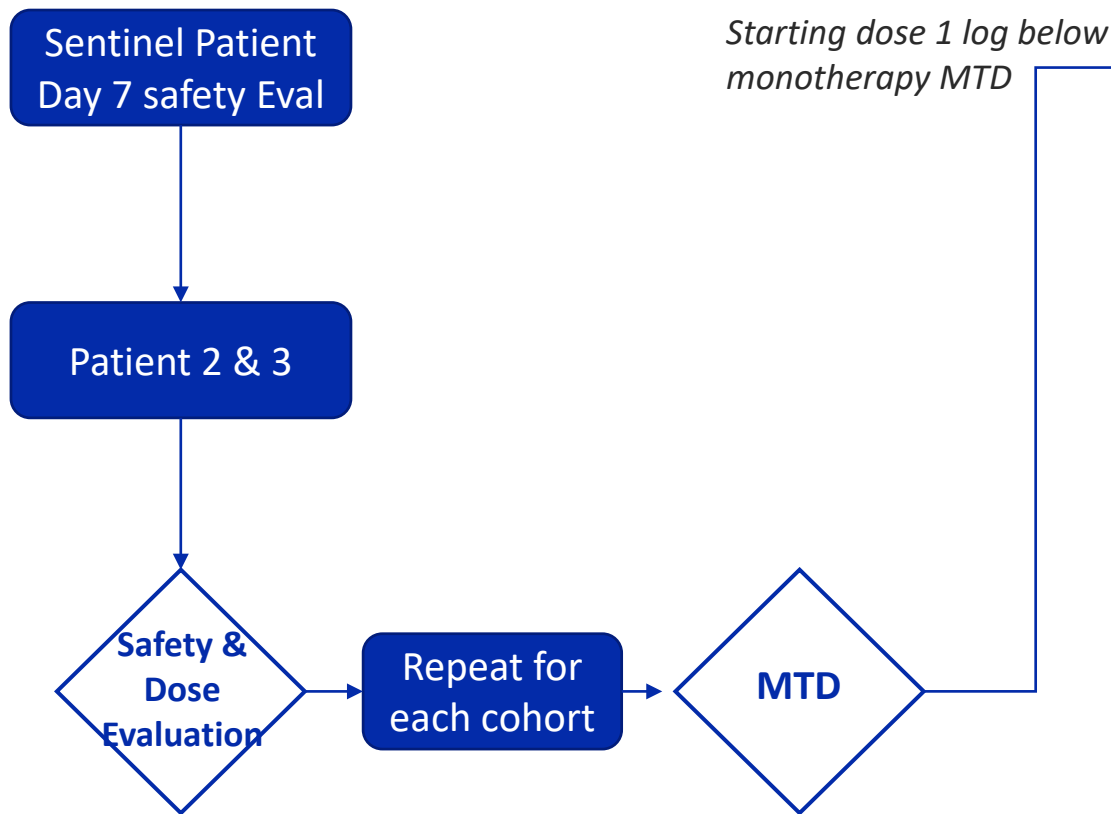
Effects Superior to 'Naked' STING Agonist in Animal Model of Cold Tumor



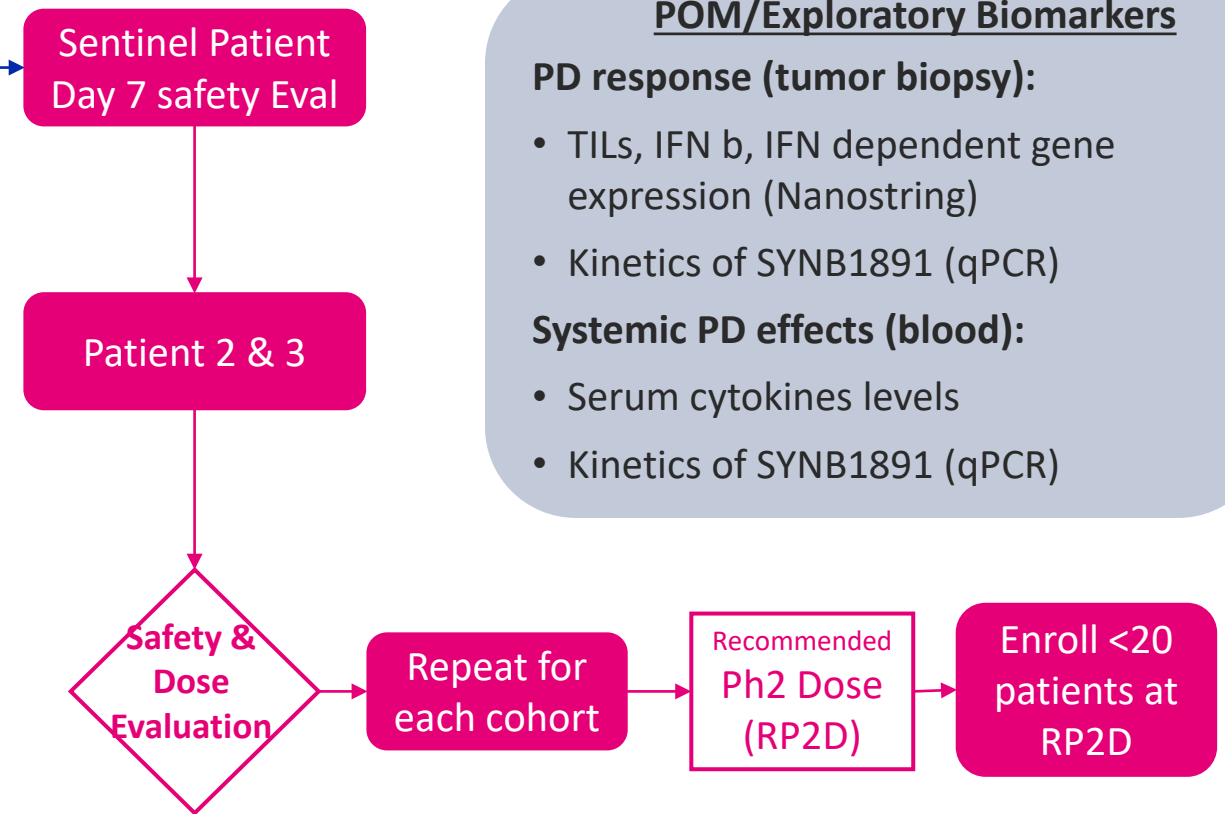
# SYNB1891-CP-001 Study Design: Multidose Tolerability, IT Mono and Combo

Proof of Mechanism: Exploratory Biomarkers in Advanced Solid Tumors or Lymphomas

## Arm 1: Monotherapy Cohorts



## Arm 2: Combination Cohorts - Atezolizumab



### POM/Exploratory Biomarkers

#### **PD response (tumor biopsy):**

- TILs, IFN b, IFN dependent gene expression (Nanostring)
- Kinetics of SYNB1891 (qPCR)

#### **Systemic PD effects (blood):**

- Serum cytokines levels
- Kinetics of SYNB1891 (qPCR)

# 3<sup>rd</sup> Quarter 2020 Summary Results

## Balance Sheet (unaudited)

Cash, Cash Equivalents, and Short & Long Term Marketable Securities

30 Sept 2020

\$102.0 M

30 June 2020

\$109.1M

## Statement of Operations (unaudited)

R&D Expenses

G&A Expenses

Net Loss

Net loss per share – basic and diluted\*

Weighted Average Shares Outstanding\*

## Three Months Ended

30 Sept 2020

\$10.5 M

\$3.0 M

\$(13.2 M)

\$(0.36)

36.3 M

30 Sept 2019

\$10.6 M

\$3.9 M

\$(13.3M)

\$(0.39)

34.2 M

**Strong Cash Position with Runway into 2022**

# Synlogic Leadership

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**Aoife Brennan, MB ChB**  
President & CEO



**Richard Riese, MD PhD**  
CMO



**Gregg Beloff, JD**  
Interim CFO



**Antoine Awad**  
COO



**Dave Hava, PhD**  
CSO



**Caroline Kurtz, PhD**  
Head of Product  
Development



**Daniel Rosan**  
Head of Corp. Finance &  
Investor Relations

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## Board

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**Peter Barrett, *Chair***  
Atlas Venture

**Ed Mathers**  
NEA

**Mike Burgess**  
Turnstone Biologics

**Richard Shea**  
Syndax Pharmaceuticals

**Chau Khuong**  
Orbimed Advisors

**Patricia Hurter**  
Lyndra Therapeutics

**Nick Leschly**  
Bluebird Bio

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## Collaborators

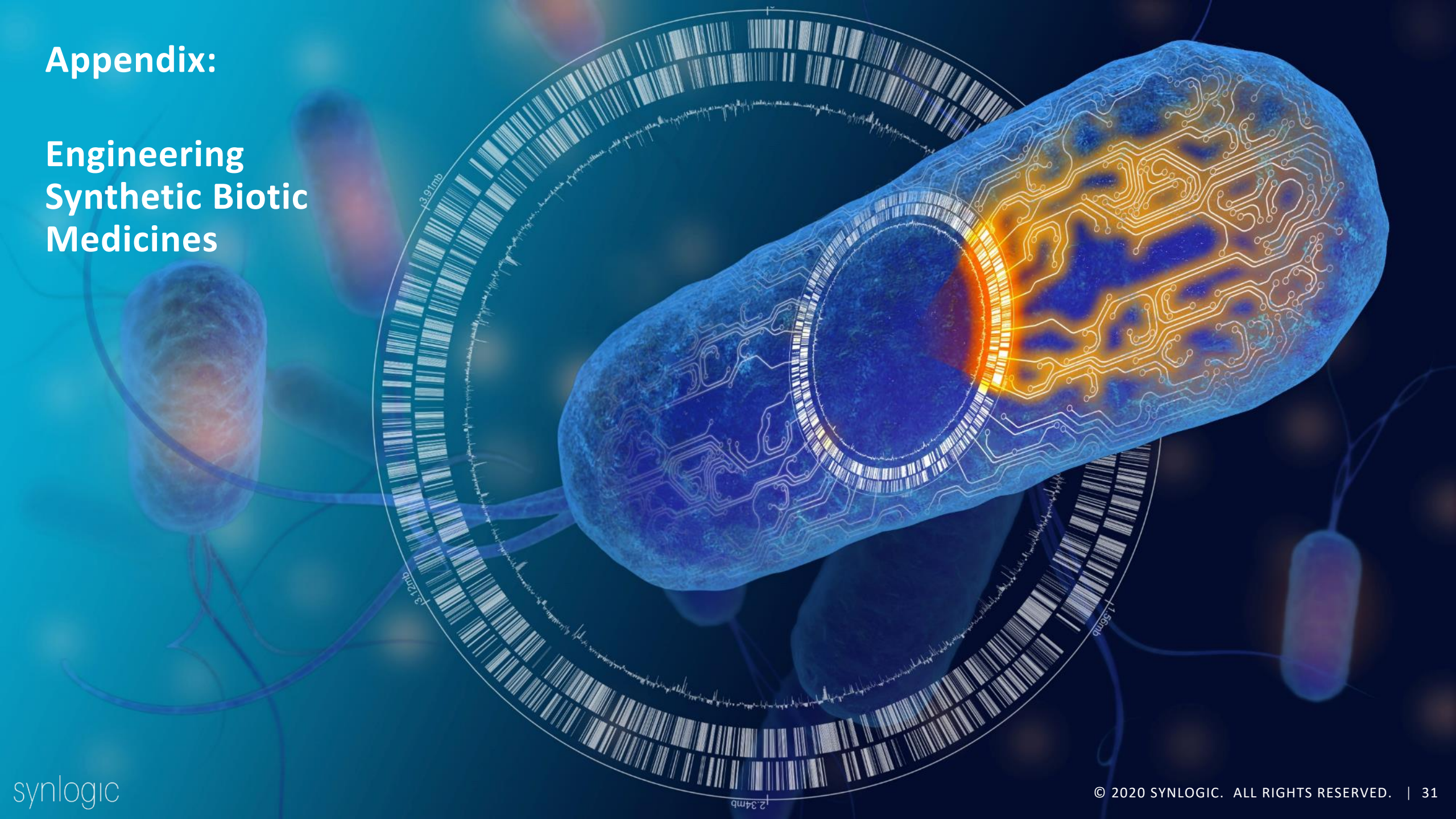
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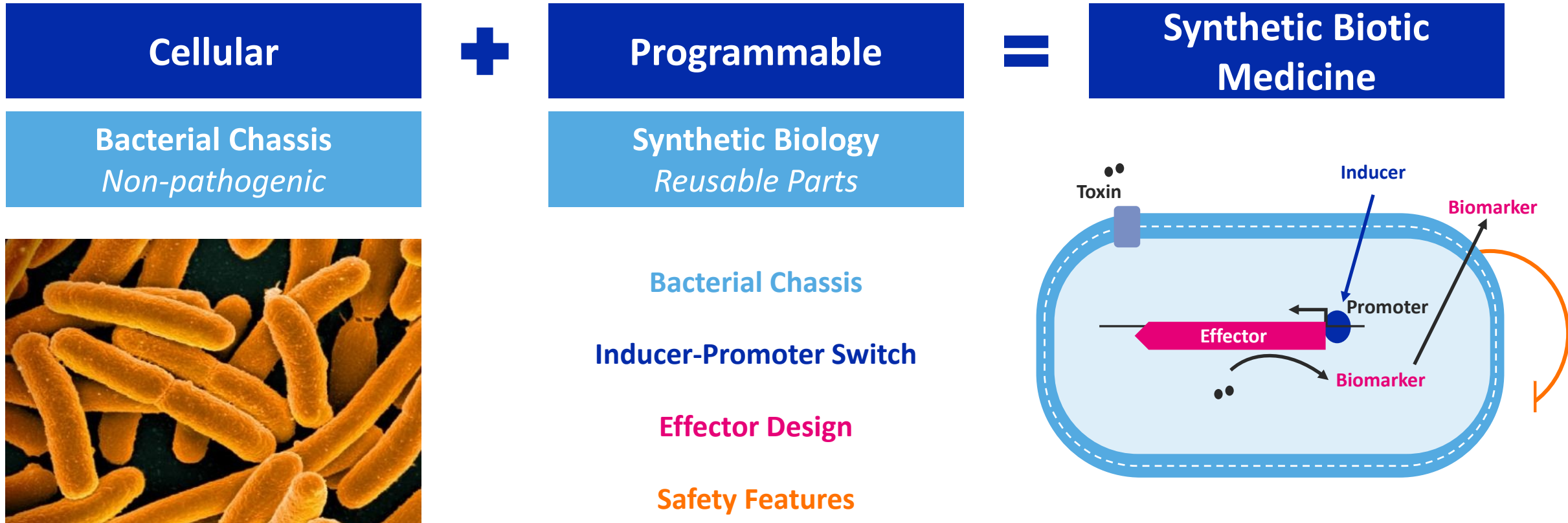
**Appendix:**

**Engineering  
Synthetic Biotic  
Medicines**





# Synthetic Biotic Medicines: A New Class of Cellular Medicines

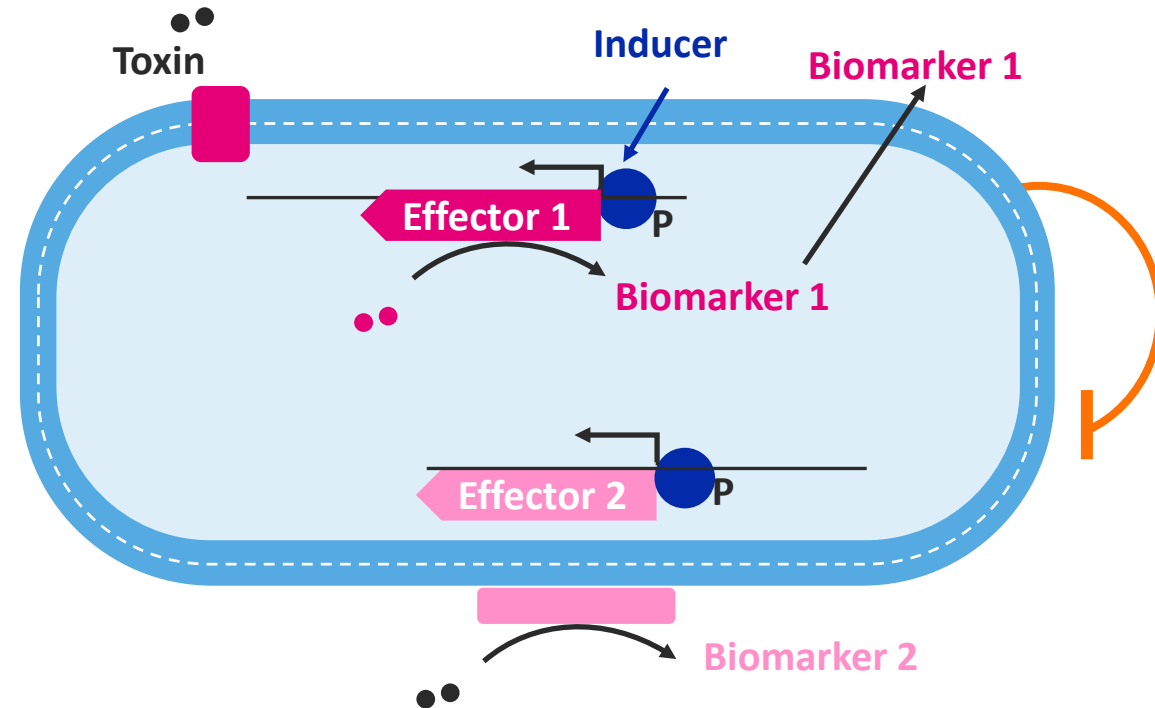


Reusable Parts Enable Rapid Iteration of Rationally Designed Prototypes

# Library of Parts to Generate Prototypes

Synthetic Biology Library Rapidly Generates Drug Candidates

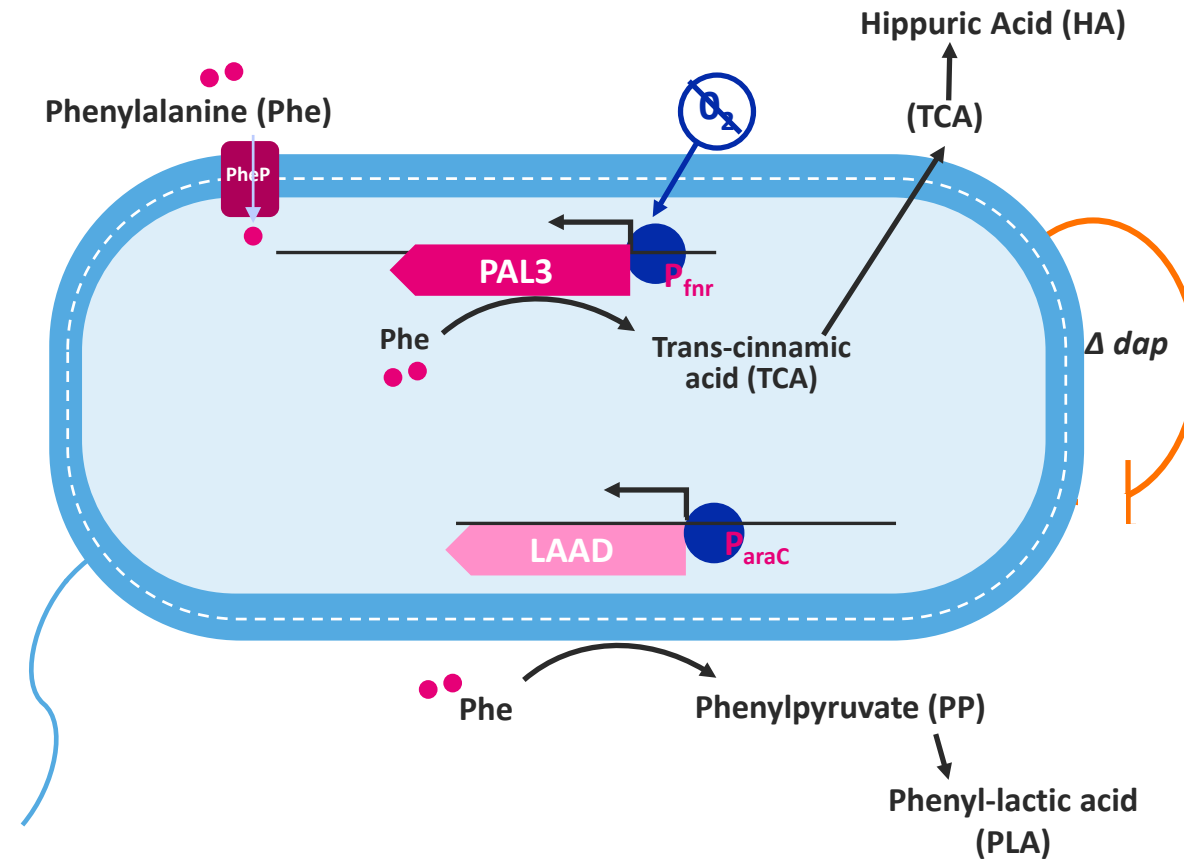
Component	Benefit
Bacterial Chassis	Probiotic: Decades of human use & safety data
Effector 1 Effector 2 ....	Proteins for activity: Can generate biomarkers
Switch	Inducer-promoter pair: Controls gene expression
Safety Features	Auxotrophies: Prevents growth within or external to the body



# SYNB1618 Design

Built from Synthetic Library Specifically to Consume Phe

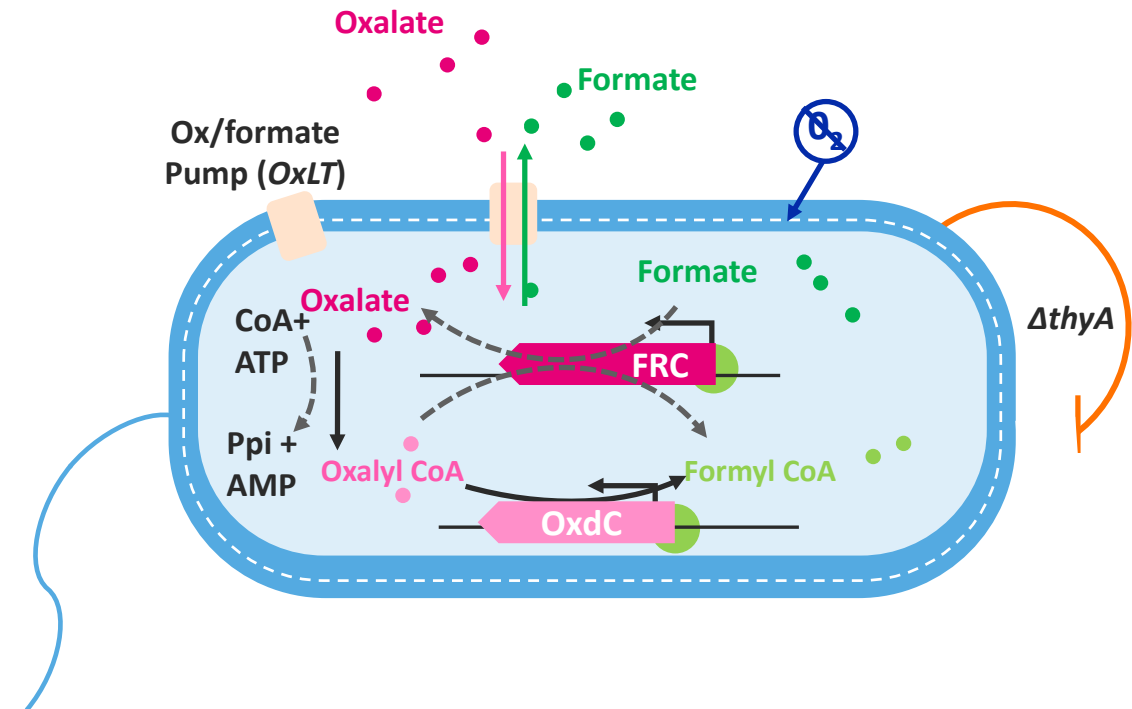
Component	Approach	Benefit
Bacterial Chassis	<i>E. coli</i> Nissle	Probiotic - decades of human use & safety data
Switches	FNR & AraC promoter	Promoters control expression during manufacturing and at site of action
Pump	<i>PheP</i>	Pumps Phe into cell
Effector 1	PAL3 Enzyme	Degrades Phe to TCA (measurable biomarker of activity)
Effector 2	LAAD Enzyme	Alt. Phe-consuming pathway
Safety Features	$\Delta dap$	Auxotrophy – requires diaminopimelic acid (DAP) to grow



# 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



# SYNB1891 Design

Leveraging the Ability of Bacteria to Interact with the Immune System to Turn a Cold Tumor Hot

## Component

## Benefit

### Bacterial Chassis

Targeting to antigen presenting cells in the tumor microenvironment.  
Innate immune activation

### Switch

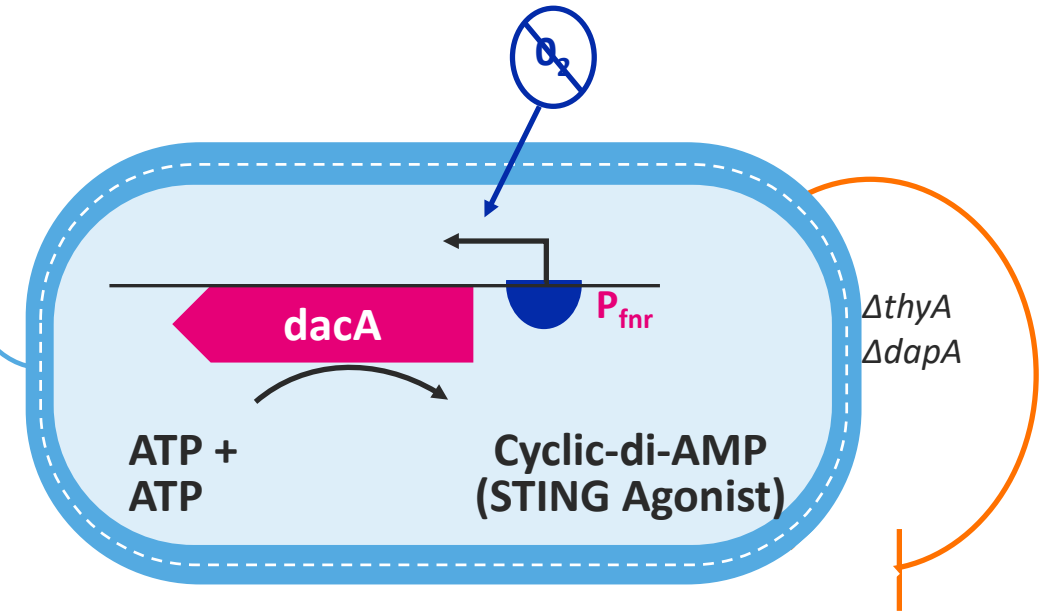
STING-agonist production restricted to hypoxic TME for sustained payload delivery

### Effector: STING Agonist

Innate immune activator compounds with chassis effect

### Safety Features

Dual auxotrophies inhibit bacterial proliferation outside of tumor





# synlogic

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EMAIL: [INFO@SYNLOGICTX.COM](mailto:INFO@SYNLOGICTX.COM)

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