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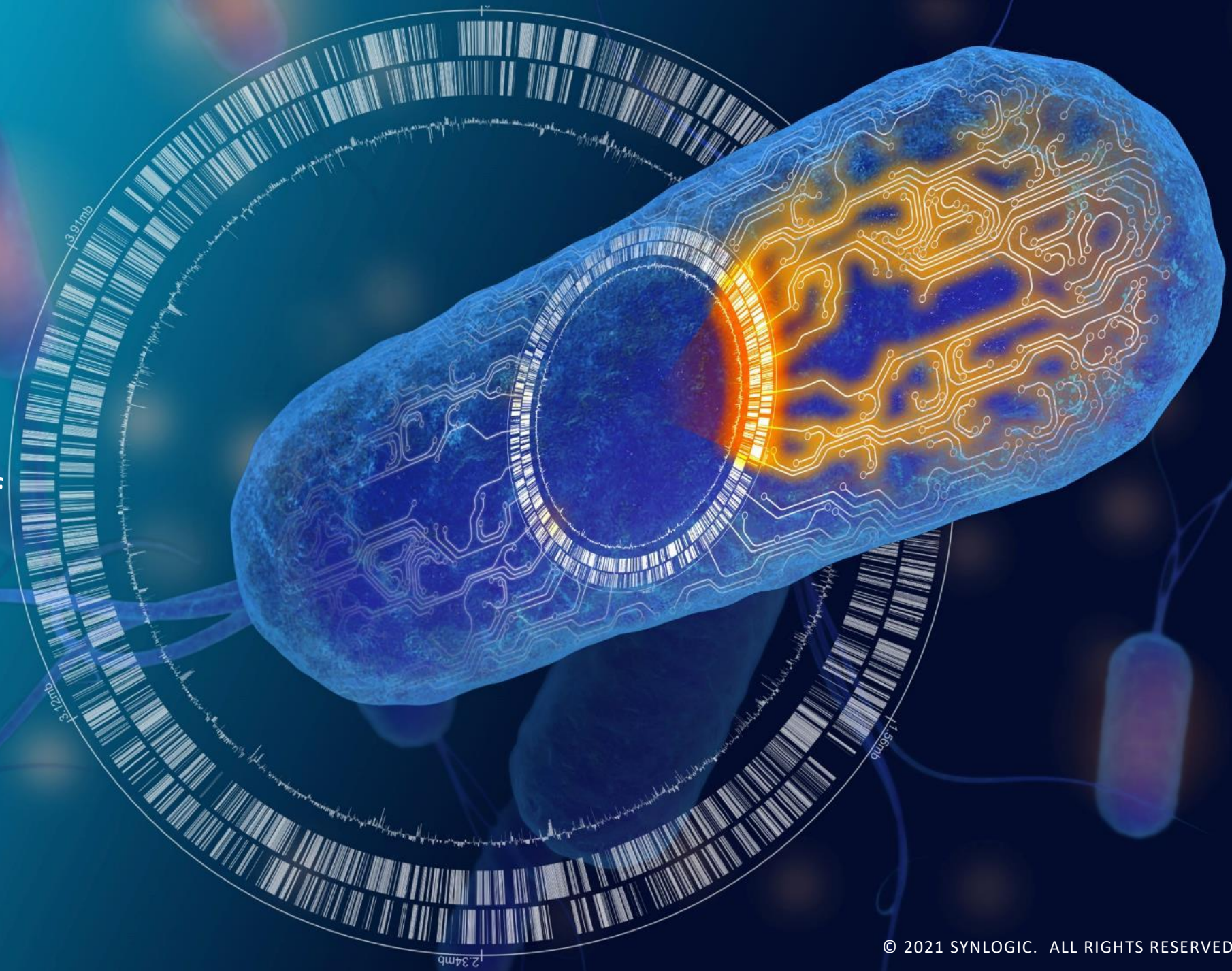
Bringing the Transformative Power of Synthetic Biology to Medicine

Corporate Presentation
February 2021



Forward Looking Statements

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 November 5, 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.

Clinical PoC Data Expected Across Multiple Programs in 2021

Metabolic Programs: Two PoC Opportunities

SYNB1618 in PKU

- Proof of mechanism demonstrated in Phase 1 HV with solid oral approach
- Phase 2 SynPheny-1 study data expected mid-year

SYNB8802 in Enteric Hyperoxaluria

- Phase 1A (dietary hyperoxaluria induced in healthy volunteers) ongoing
- Phase 1B (patient) data expected mid-year

Immunomodulation

SYNB1891 in Solid Tumors

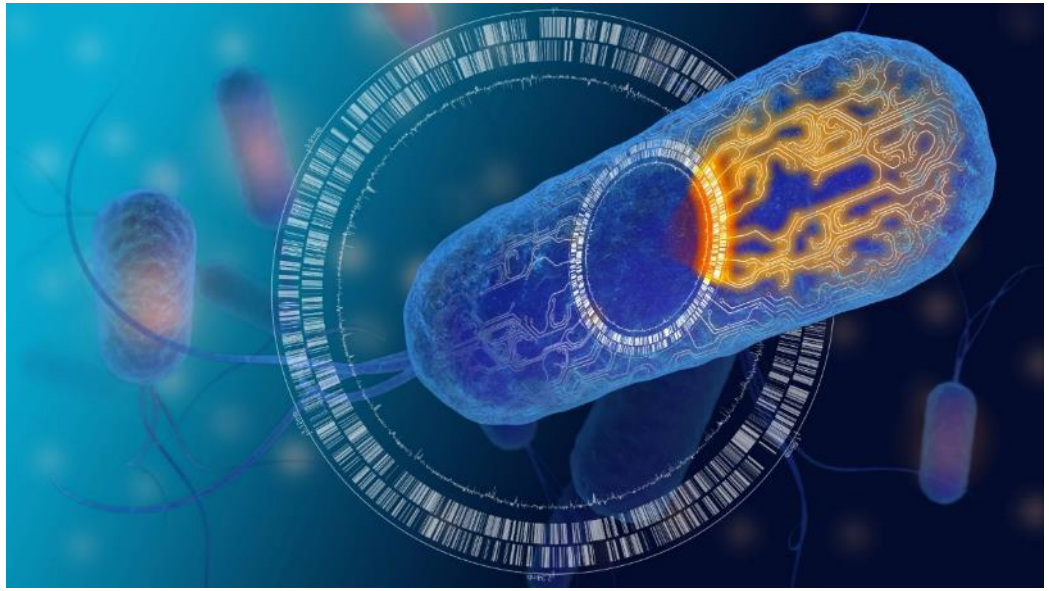
- Monotherapy demonstrated target engagement, meaningful pharmaco-dynamic effects, good safety
- Combination with anti-PD1 and continued dose escalation ongoing

2021 Data With Potential To Demonstrate Clinical Benefit of the Synthetic Biotic Platform

A New Class of Medicines

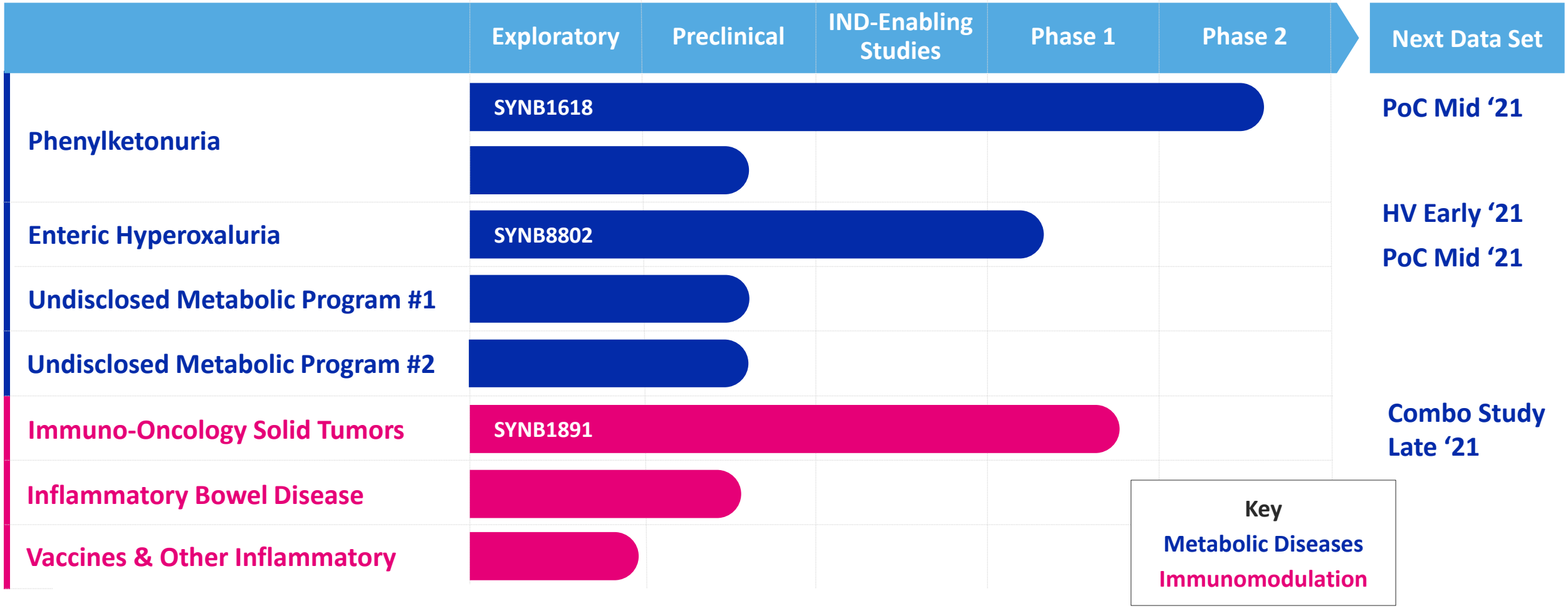
Bacteria and Humans Co-Evolved and Co-Exist

We Rationally Design Bacteria
To Provide Clinical Benefit



Enabling Engine of Synthetic Biology, Manufacturing and Translational Capabilities Provides Creates Multiple Product Opportunities

Robust Pipeline With Meaningful Catalysts



Why Metabolic Diseases For Synthetic Biotic Medicines?

Validated Biology
Diseases with known pathophysiology

Dietary intervention validates GI 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

Unique Advantage of SYNB
Bacteria evolved to produce and consume metabolites

Contain multiple enzyme pathways

Protected from digestion in GI tract

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Synthetic Biotics Potential To Address PKU and Enteric Hyperoxaluria

	PKU	Enteric Hyperoxaluria
Validated Biology	• Lower Phe intake = • lower Phe levels, improves outcomes	• Lower Oxalate intake = • lower urinary Oxalate, improves outcomes
Platform Proof of Mechanism	• SYNB1618 consumes Phe and produces TCA biomarker in HV	• SYNB8802 consumes Oxalate in multiple preclinical models
Unmet Medical Need	• Many patients unable to control Phe • Low BH4 oral therapy response rates	• High kidney disease risk • No effective interventions or treatments
Unique Advantage of SYNB	• Only modality able to consume Phe in the GI tract, before it can cause damage	• Only modality able to consume Oxalate throughout GI tract, including colon

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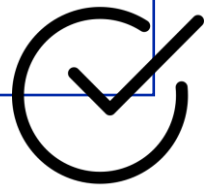
Phenylketonuria (PKU)

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)


Julia, living with PKU

synpheny
LIVING IN HARMONY WITH 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 Stuggle to Maintain Blood Phe within Target Range

SYNB1618 is Uniquely Positioned to Address Needs Across Ages and Genotypes

Marketed
Development

Bh4 Responsive Only

Patient Segment[1]	Chronic Daily	Gene Therapies	Daily Oral	Daily Oral	SYNB1618
	Palynziq (pegvaliase-pqpz) Injection	HOMOLOGY Medicines, Inc. / BIOMARIN	KUVAN (sapropterin dihydrochloride) Tablets	PTC THERAPEUTICS	synlogic
	Marketed	Phase 1/2	Marketed	Phase 3	Phase 2
Infant 0-1 N= ~500					
Peds 2-11 N= ~2,800					
Peds 12-16 N= ~1,200					
Adults & 16+ N= 13,000[1]					

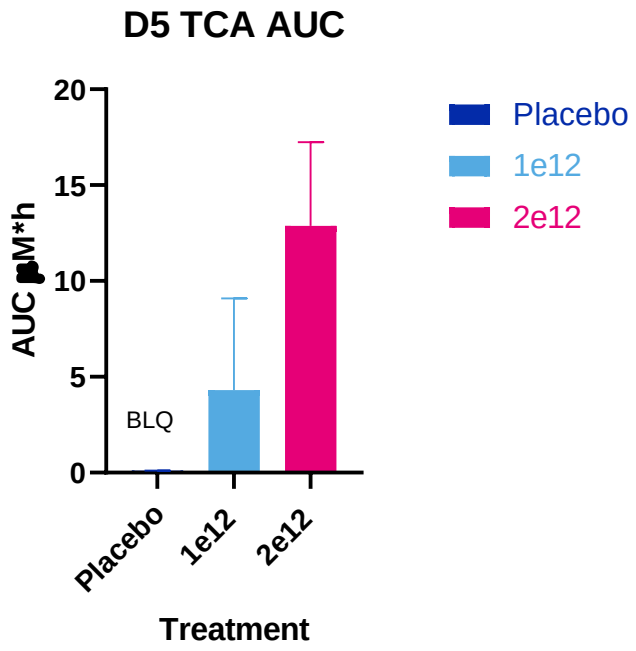
Under REMS, adults only

- Mechanism does not depend on genotype
- Appropriate for pediatrics and adults
- Benign safety profile, no systemic exposure
- Oral administration

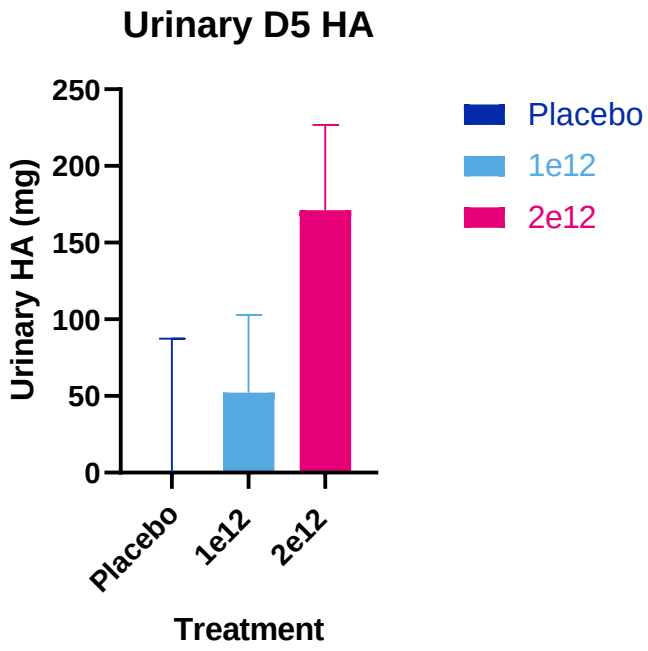
1. *Includes 7,500 "lost to follow up"*

SYNB1618 In The Clinic: D5 Tracer Data in Healthy Volunteers

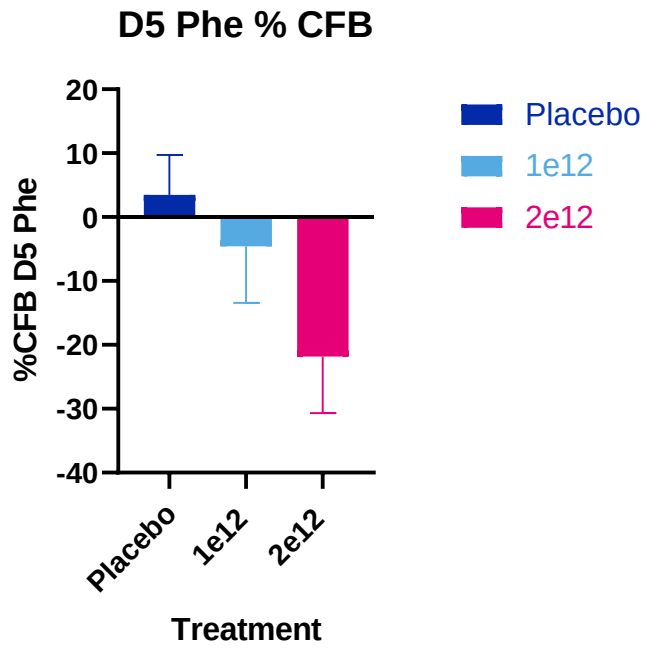
D5 Phe Converted to D5 TCA



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

SynPheny-1 Phase 2 Proof of Concept Study in PKU

- **Demonstrate Phe Lowering in PKU Patients (N = 12)**
  - Plasma Phe lowering in fasted state at 1 x 10^{12} live cells over 7 days
  - Post meal D5-Phe AUC lowering at 2 x 10^{12} live cells (**not impacted** by diet)
- **Validate PD Model**
  - Understand relationship of strain specific biomarkers with plasma Phe lowering
- **Safety and Tolerability**

SynPheny-1 Potentially Demonstrates Multiple Clinically Relevant Outcomes

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LIVING IN HARMONY WITH PKU

Reduction in labelled plasma Phe after a meal challenge, not influenced by diet

Reduction in fasting plasma Phe (on treatment relative to baseline, holding diet steady)

Consistency in response: Responder population or consistent response across subjects

Learning Opportunities in current SynPheny-1 study

Study powered for 20% reduction in labelled plasma Phe, providing clinically meaningful endpoint for patients without other treatment options

Patient-Centered Clinical Trial Design & Execution

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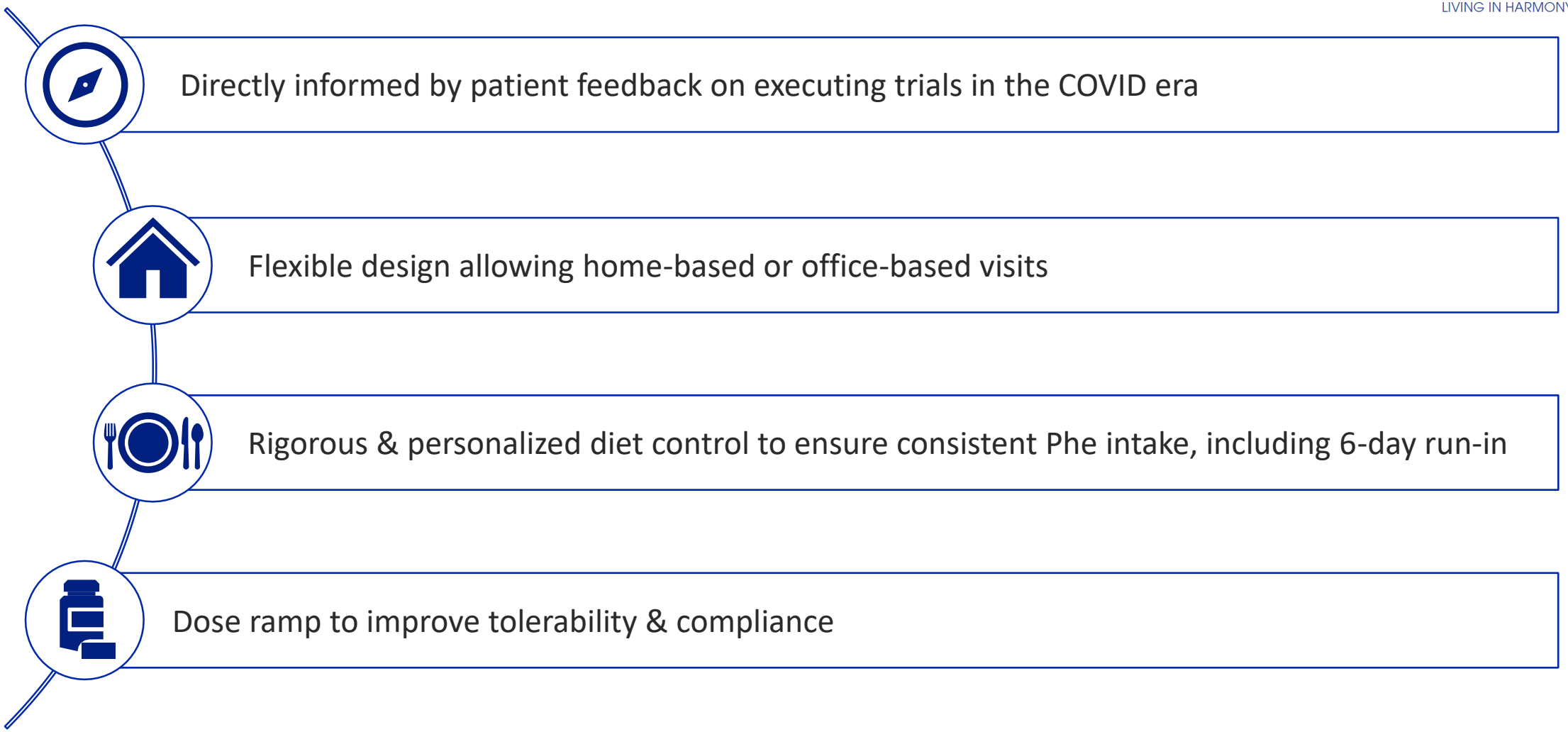
LIVING IN HARMONY WITH PKU



- 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

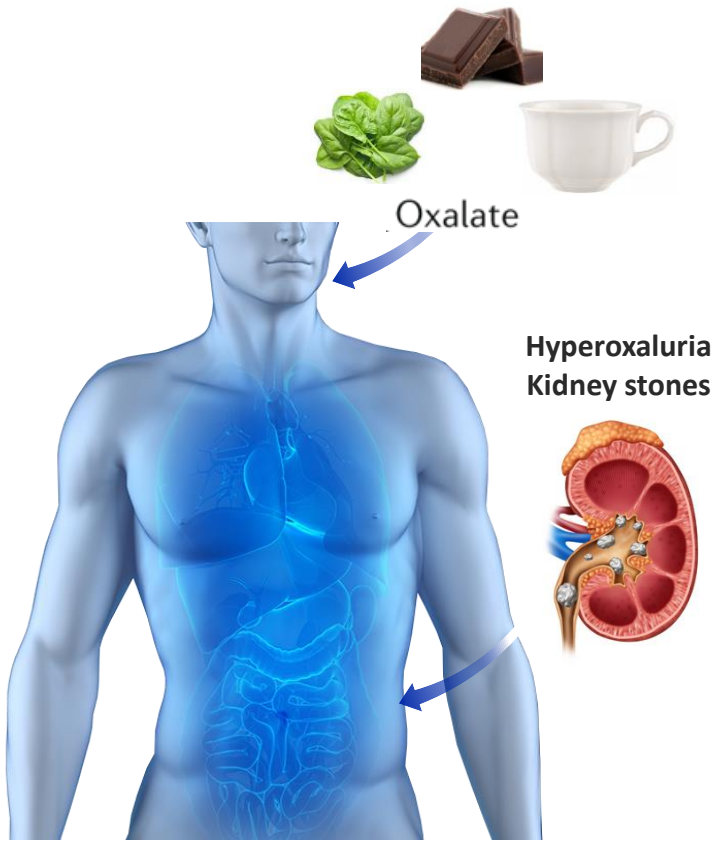
Enteric Hyperoxaluria results in significant kidney damage with no available treatment options

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
Pathology	Family of autosomal recessive monogenic disorders in which liver enzyme deficiency results in endogenous oxalate overproduction	Pathogenic hyperabsorption of dietary oxalate, often accompanies underlying bowel disease or bariatric surgery
Urinary Oxalate Levels	90 – 500 mg / 24 hrs (up to 10x normal)	45 – 130 mg / 24 hrs (up to 3x normal)
Onset	Pediatric	Adult
Key Players	Dicerna pharmaceuticals; Alnylam PHARMACEUTICALS	Allena PHARMACEUTICALS; synlogic
U.S. Epidemiology	~5,000 – 8,000	~200,000 – 250,000
Clinical Consequences	• Limited ability to manage with diet • Nephrocalcinosis • Recurrent, chronic kidney stones • Impaired renal function • Systemic Oxalosis	• Limited ability to manage with diet • Nephrocalcinosis • Recurrent, chronic kidney stones • Impaired renal function • Systemic Oxalosis

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

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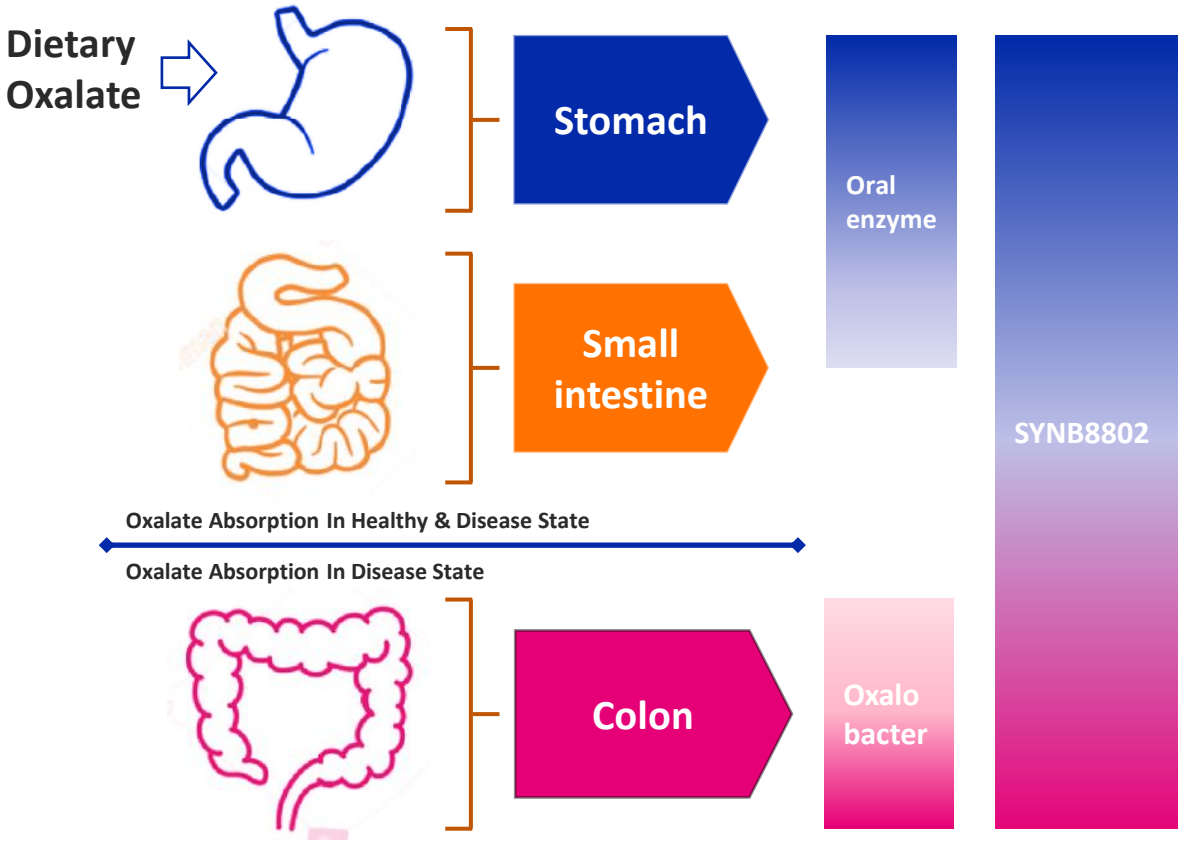
Nazzal et al. Nephrol Dial Transplant 2016

Enteric Hyperoxaluria Disease Pathogenesis

GI Based Therapies Have Demonstrated Lowering of Systemic Oxalate

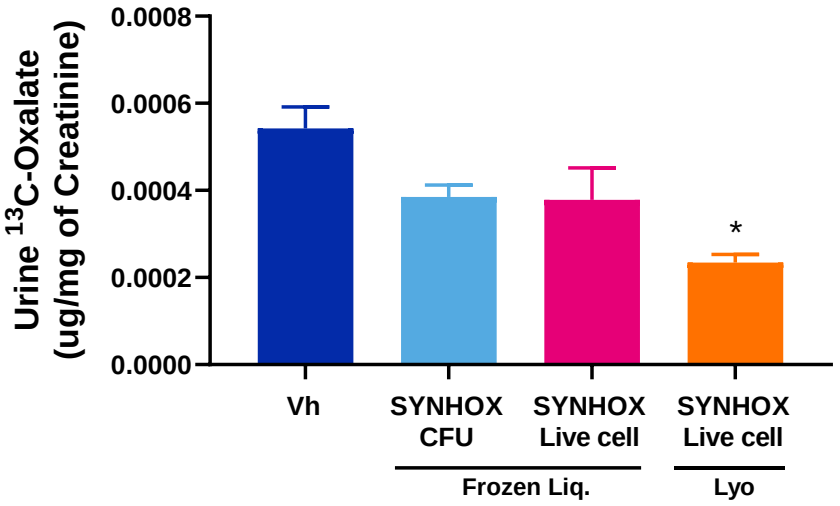


- Pathogenic hyperabsorption of dietary oxalate
- Healthy people absorb ~10% of dietary oxalate, mostly via stomach and small intestine
- Patients absorb ~20-30% of dietary oxalate, though entire GI tract including colon
- Optimal treatment would absorb oxalate throughout GI tract, esp. in colon

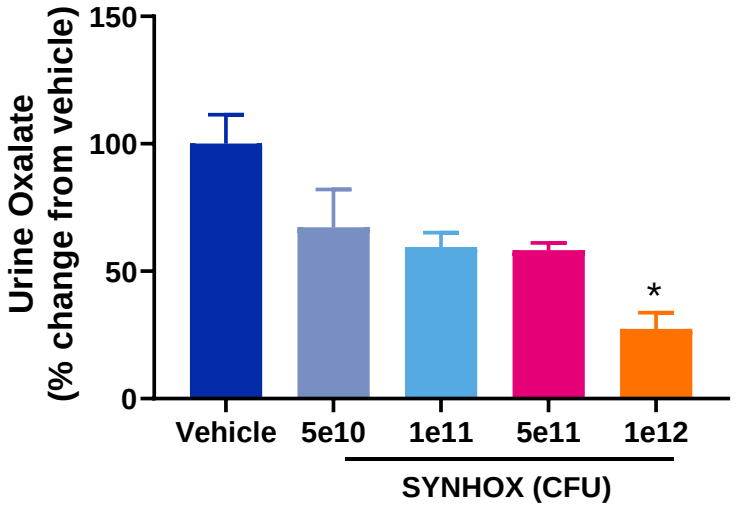
Intestinal Degradation of Oxalate Throughout GI Tract Could Enhance Oxalate Lowering

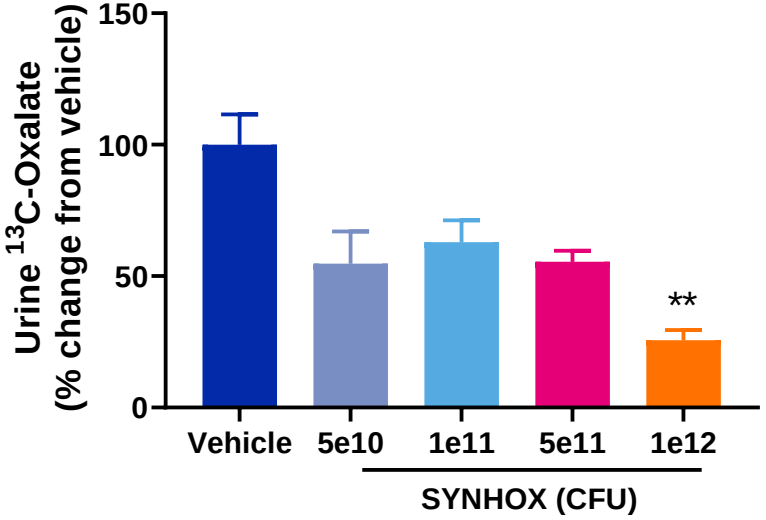
SYN-HOX Attenuates Urinary Oxalate Increase

SYN-HOX Consumes ^{13}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

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* $p < 0.05$, ** $p < 0.01$ versus vehicle

Enteric Hyperoxaluria: Phase 1 Design Provides PoC Opportunity

Phase 1A

Dietary Hyperoxaluria (Healthy Volunteers)

Multiple Ascending Dose

- High oxalate & low calcium diet run-in
- Induce dietary hyperoxaluria
- *Primary:* Safety & tolerability
- *Secondary:* Microbial kinetics of strain
- *Exploratory:* Change in plasma and urine biomarkers

Phase 1B

Enteric Hyperoxaluria Patients

Cross-over

- TID dosing
- N = 20 patients (Roux-en Y gastric bypass, UOx >70 mg/day)
- *Primary:* Change in Urinary Oxalate
- *Secondary:*
  - Microbial kinetics of strain
  - Safety and tolerability

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

SYNB8802 Phase 1 Will Inform Multiple Clinical Development Opportunities

Potential for urinary oxalate lowering in dietary hyperoxaluria (HV) model

Potential for urinary oxalate lowering in enteric hyperoxaluria patient population (Roux-n-Y)

Degree of colonic activity of SYNB8802 and potential for less frequent dosing

Learning Opportunities in two-part Phase 1 Study

Potential to demonstrate meaningful urinary oxalate lowering in patients with active disease

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 SYNB

Targeted efficacy and improved safety

Multiple effectors from single strain delivered to site of disease

Immunomodulation & Immuno-Oncology

Synthetic Biotics can be engineered for immune activation or regulation, with application to immuno-oncology

SYNB1891 + checkpoint inhibitors have potential for improved efficacy relative to other STING approaches

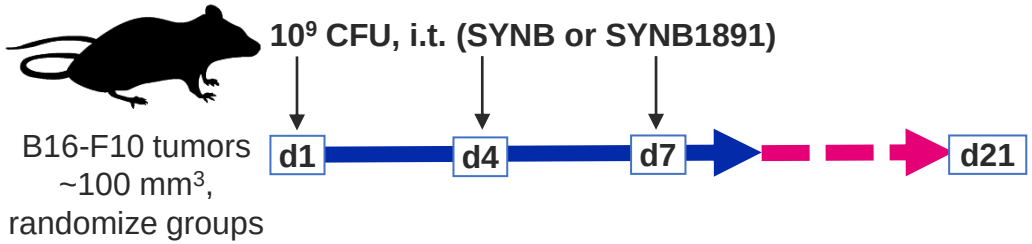
SYNB1891 as monotherapy demonstrated target engagement and meaningful pharmacodynamic effects

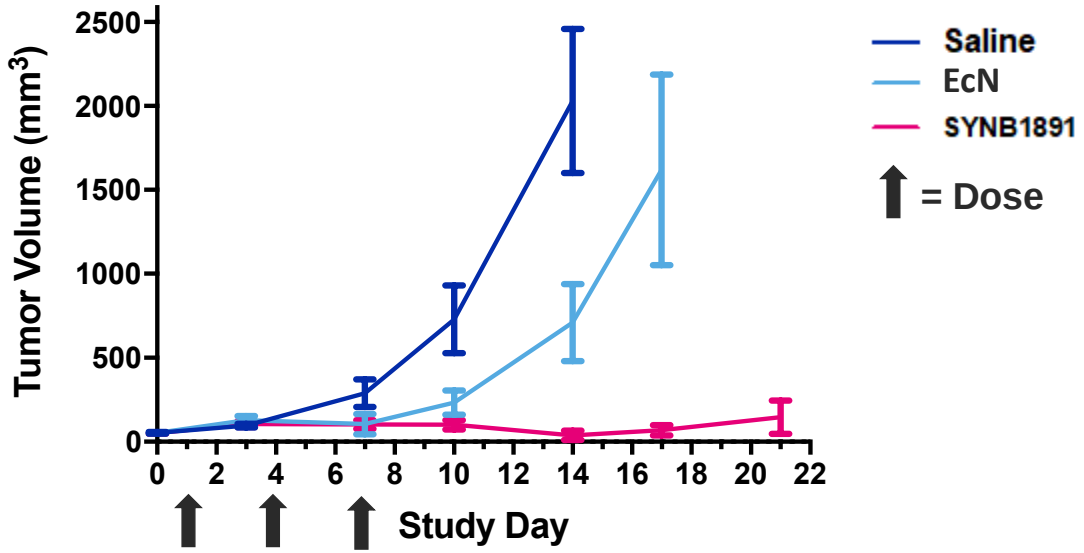
Phase 1 in combination with Tecentriq initiated:

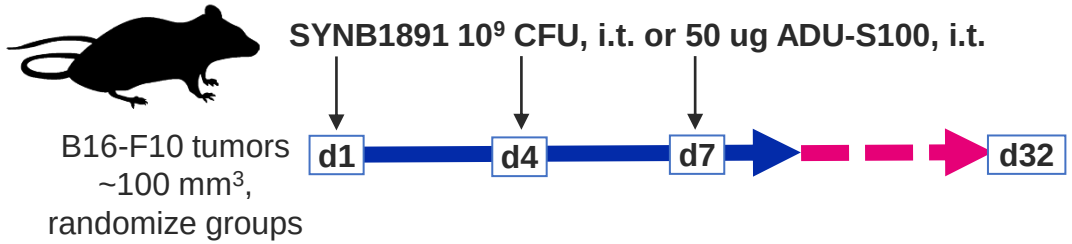
Data will be available in 2021

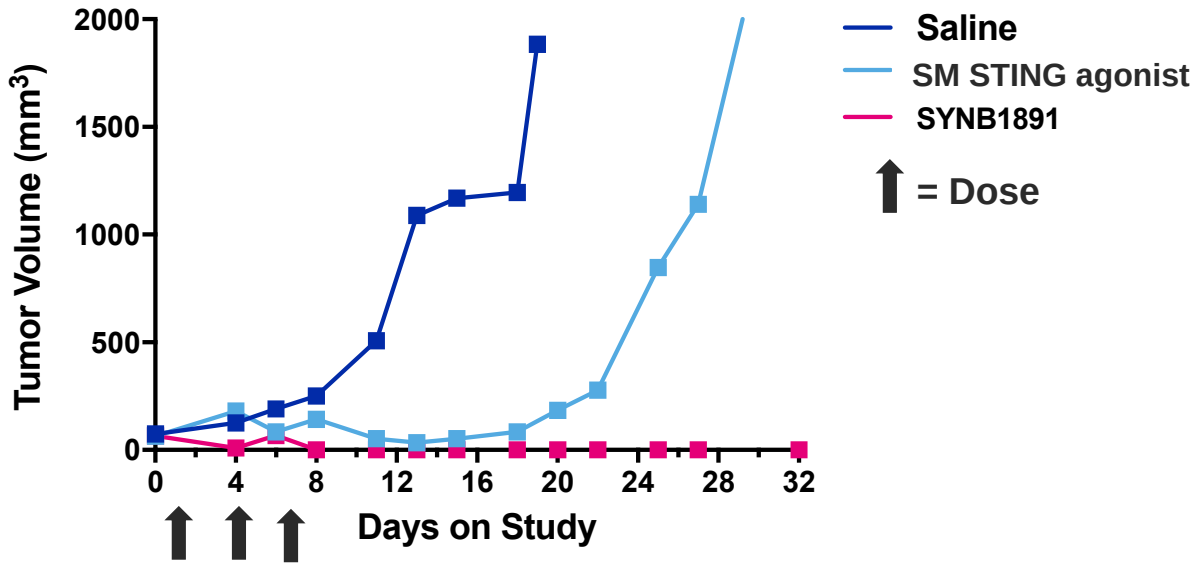
SYNB1891 Induces Potent Anti-tumoral Effects

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





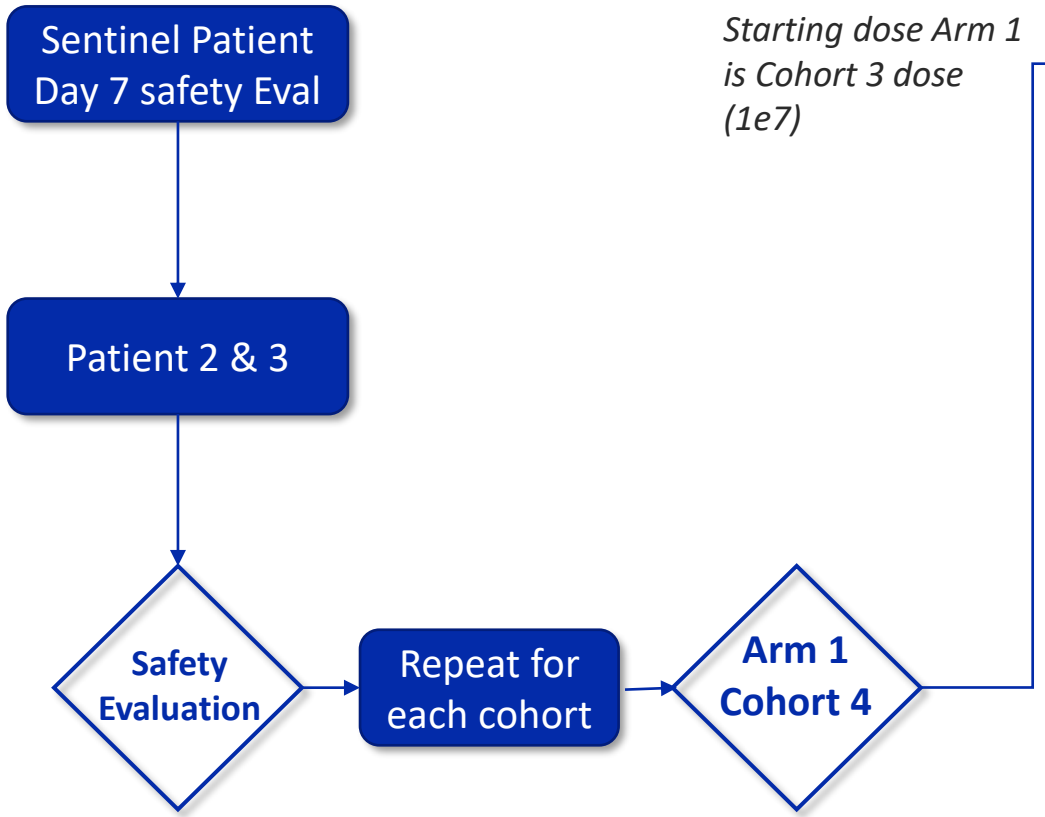




SYNB1891-CP-001 Study Design: Multidose Tolerability, IT Mono and Combo

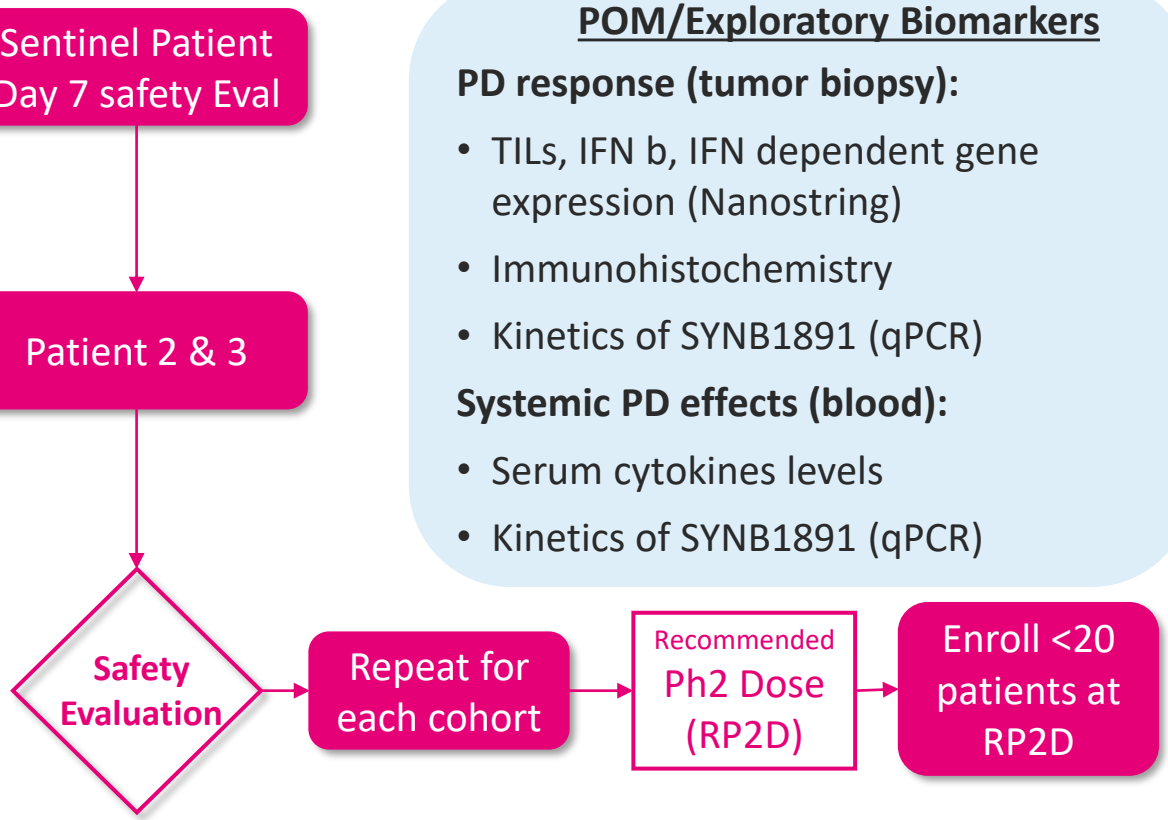
Proof of mechanism: exploratory biomarkers in advanced solid tumors or lymphomas

Arm 1: Monotherapy Cohorts



Starting dose Arm 1 is Cohort 3 dose (1e7)

Arm 2: Combination Cohorts - Atezolizumab



POM/Exploratory Biomarkers

PD response (tumor biopsy):

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

Systemic PD effects (blood):

- Serum cytokines levels
- Kinetics of SYNB1891 (qPCR)

SYNB1891 Advanced Into Combo. Therapy Arm of Ph. 1 With Tecentriq

- SYNB1891 is **safe and well-tolerated** as an intratumoral injection with no dose limiting toxicities or infections to date
- SYNB1891 **demonstrates target engagement** as assessed by upregulation of IFN-stimulated genes and T-cells
- SYNB1891 demonstrates **meaningful pharmacodynamic effects** including systemic cytokine responses observed in two subjects
- Evidence of **durable stable disease** was observed in two patients
- **Monotherapy dose escalation will continue in parallel to combination dose** escalation of SYNB1891 with fixed dose of Atezolizumab (Tecentriq)
- Combination therapy **data will be available in H2 2021**

Synlogic Entering Data Rich Period in the Clinic

	Expected Milestone	2020	2021		
			early	mid	late
SYNB1618 PKU	Initiate Ph.2 study in PKU patients	initiated			
	Ph.2 Phe-lowering read-out				
SYNB8802 HOX	Initiate Ph.1A study in HV	initiated			
	Initiate Ph. 1B study in patients				
	Ph.1B patient read-out				
SYNB1891 I/O	Ph.1 Arm 1 Monotherapy interim update	completed			
	Initiate Ph.1 Arm 2 combination study		initiated		
	Ph.1 Arm 2 combination read-out				

Significant Clinical Readouts In 2021

3rd Quarter 2020 Summary Results

Balance Sheet (unaudited)	30 Sept 2020	30 June 2020
Cash, Cash Equivalents, and Short & Long Term Marketable Securities	$102.0 M	$109.1M

	Three Months Ended	
Statement of Operations (unaudited)	**30 Sept 2020**	**30 Sept 2019**
R&D Expenses	$10.5 M	$10.6 M
G&A Expenses	$3.0 M	$3.9 M
Net Loss	$(13.2 M)	$(13.3M)
Net loss per share – basic and diluted*	$(0.36)	$(0.39)
*Weighted Average Shares Outstanding**	*36.3 M*	*34.2 M*

Strong Cash Position with Runway into 2022

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* weighted average shares used in computing net loss per shares - basic and diluted

Synlogic Leadership

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

Board

Peter Barrett, *Chair*
Atlas Venture

Mike Burgess
Turnstone Biologics

Chau Khuong
Orbimed Advisors

Nick Leschly
Bluebird Bio

Ed Mathers
NEA

Richard Shea
Syndax

Michael Heffernan
Collegium

Patricia Hurter
Lyndra Therapeutics

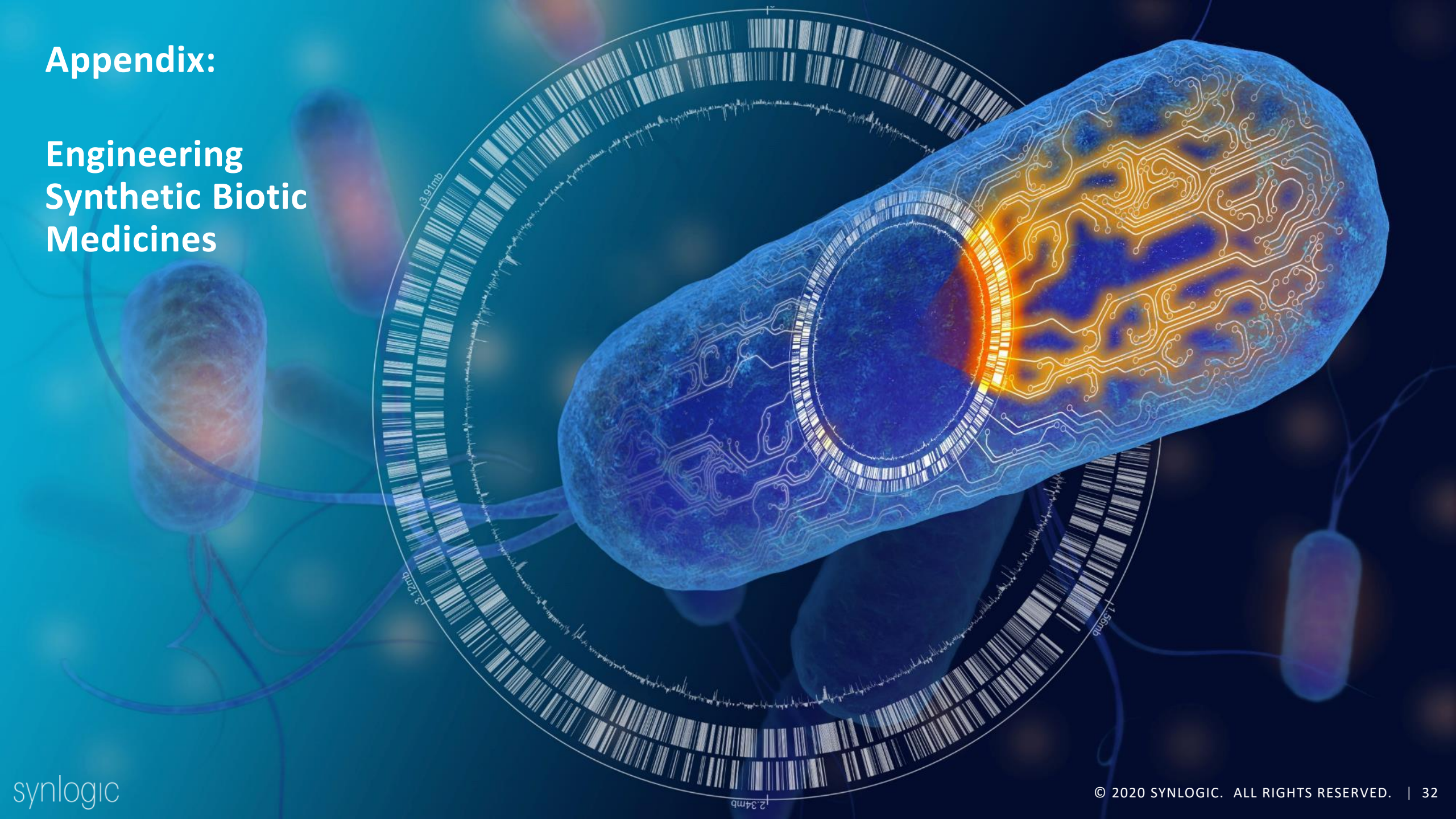
Lisa Kelly-Croswell
Boston Medical Center Health System

Collaborators

GINKGO BIOWORKS
THE ORGANISM COMPANY

Appendix:

Engineering Synthetic Biotic Medicines



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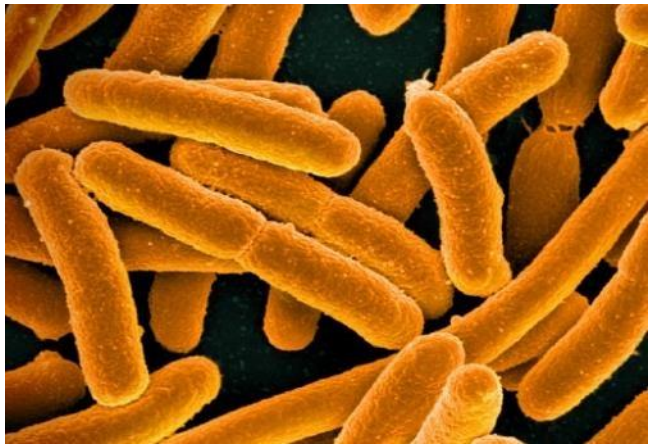
Synthetic Biotic Medicines: A New Class of Cellular Medicines

Cellular + **Programmable** = **Synthetic Biotic Medicine**

Bacterial Chassis
Non-pathogenic



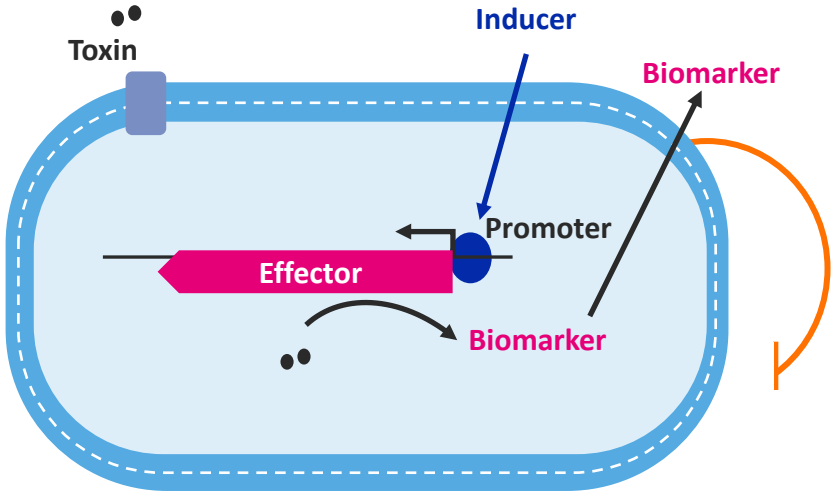
Synthetic Biology
Reusable Parts

Bacterial Chassis

Inducer-Promoter Switch

Effector Design

Safety Features



Reusable Parts Enable Rapid Iteration of Rationally Designed Prototypes

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Photo credit: NIH Image Gallery

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 in PKU and Enteric Hyperoxaluria

External & Collaboration Focus: Immunomodulation

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

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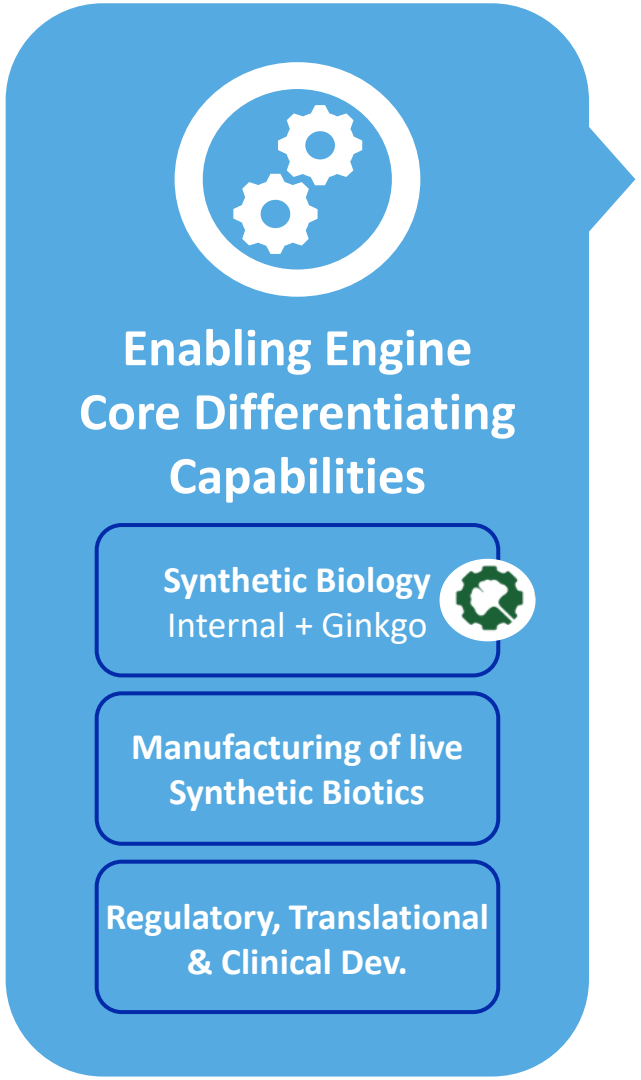
The Enabling Engine for Synthetic Biotic Medicines

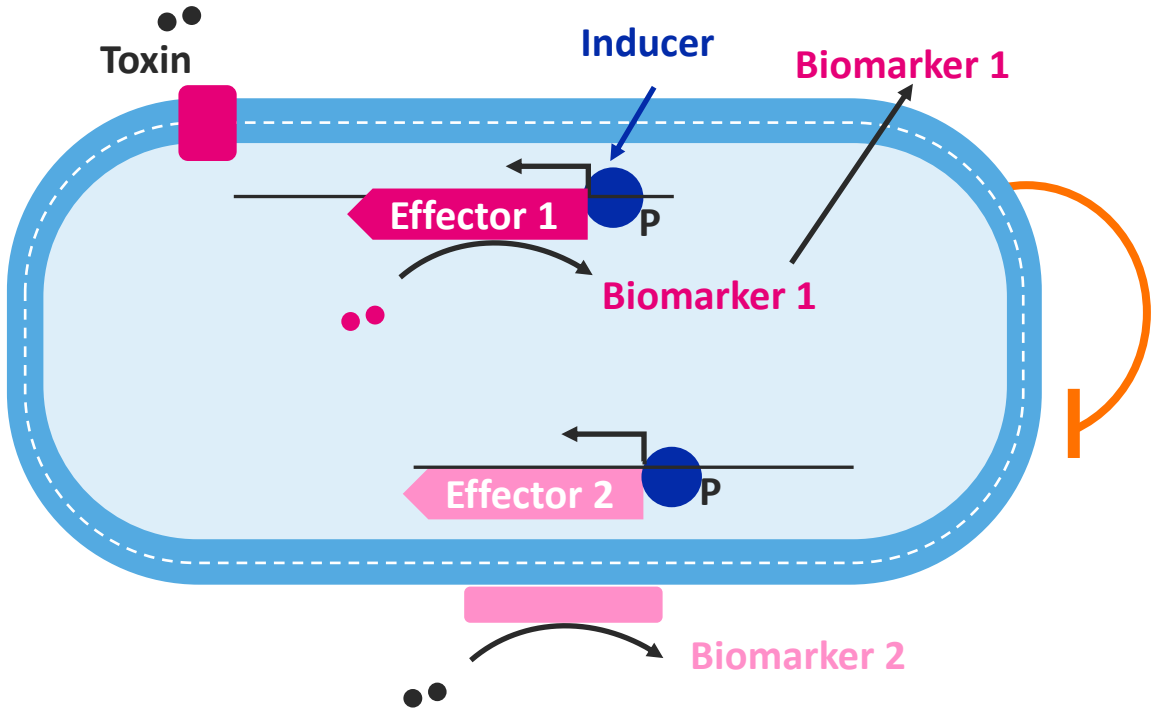


- **Clinical Evidence**
  - **>200 humans dosed** with Synthetic Biotic medicines
  - **4 INDs opened** with the U.S. FDA
  - **Supportive regulatory feedback** from global agencies
  - **Safe** (>100 years of human experience) probiotic bacterial chassis
- **Core Technology**
  - **Deep synthetic biology expertise** with Ginkgo Bioworks collaboration
  - **Modular and reusable synthetic biology components** enable iterative, efficient platform learning
  - **Internal process development and GMP manufacturing** capabilities

Library of Parts to Generate Prototypes

Synthetic Biology Library Rapidly Generates Drug Candidates

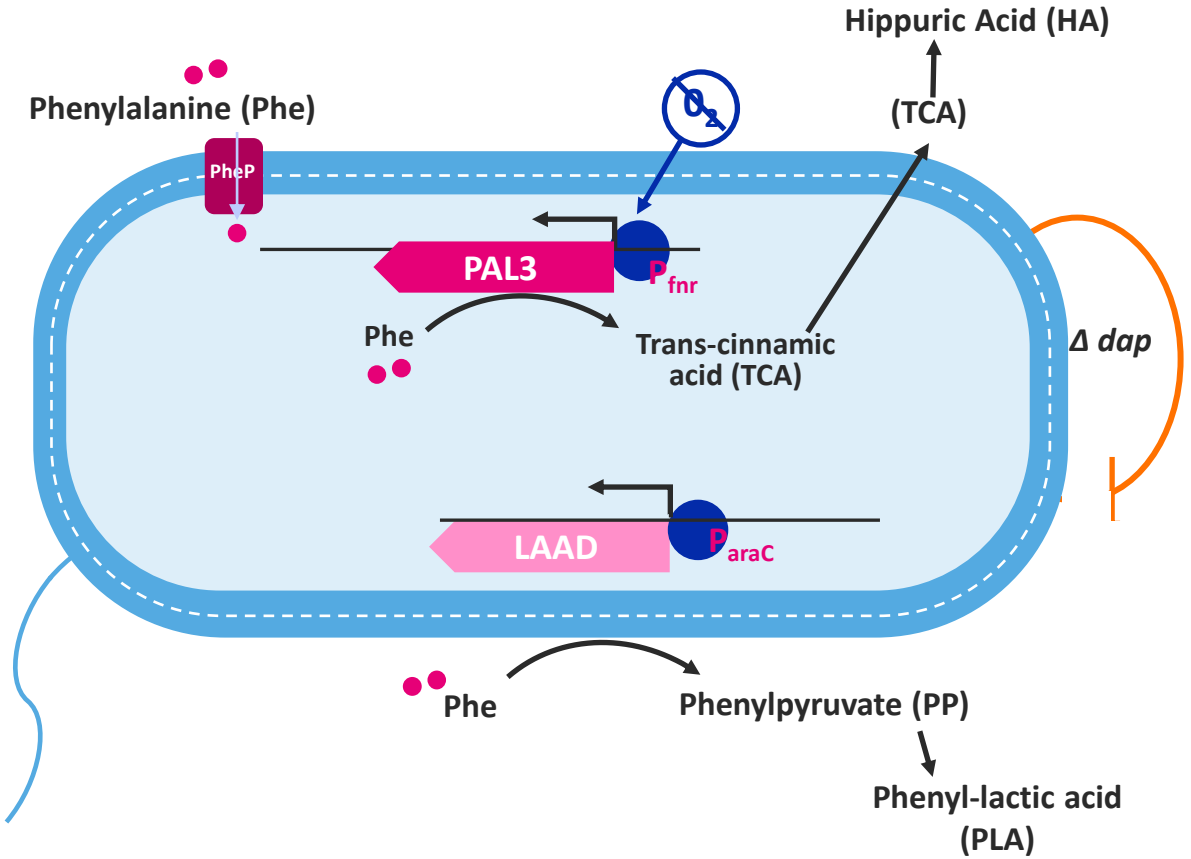
Component	*Benefit*
Bacterial Chassis	Probiotic: Decades of human use & safety data
Effector 1 **Effector 2** **….**	Proteins for activity: Can generate biomarkers
Switch	Inducer-promoter pair: Controls gene expression
Safety Features	Auxotrophies: Prevents growth within or external to the body



SYNB1618 Design

Built from Synthetic Library Specifically to Consume Phe

Component	Approach	Benefit
Bacterial Chassis	*E. coli* Nissle	Probiotic - decades of human use & safety data
Switches	FNR & AraC promoter	Promoters control expression during manufacturing and at site of action
Pump	*PheP*	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	*Δ dap*	Auxotrophy – requires diaminopimelic acid (DAP) to grow



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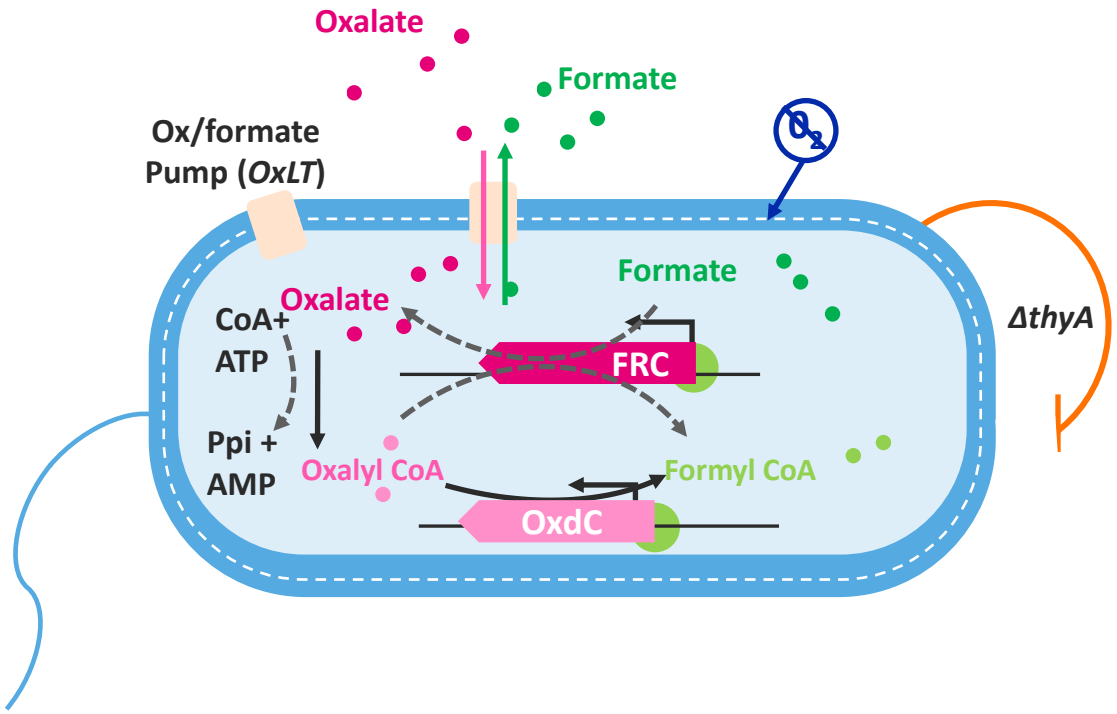
SYNB8802 Design

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

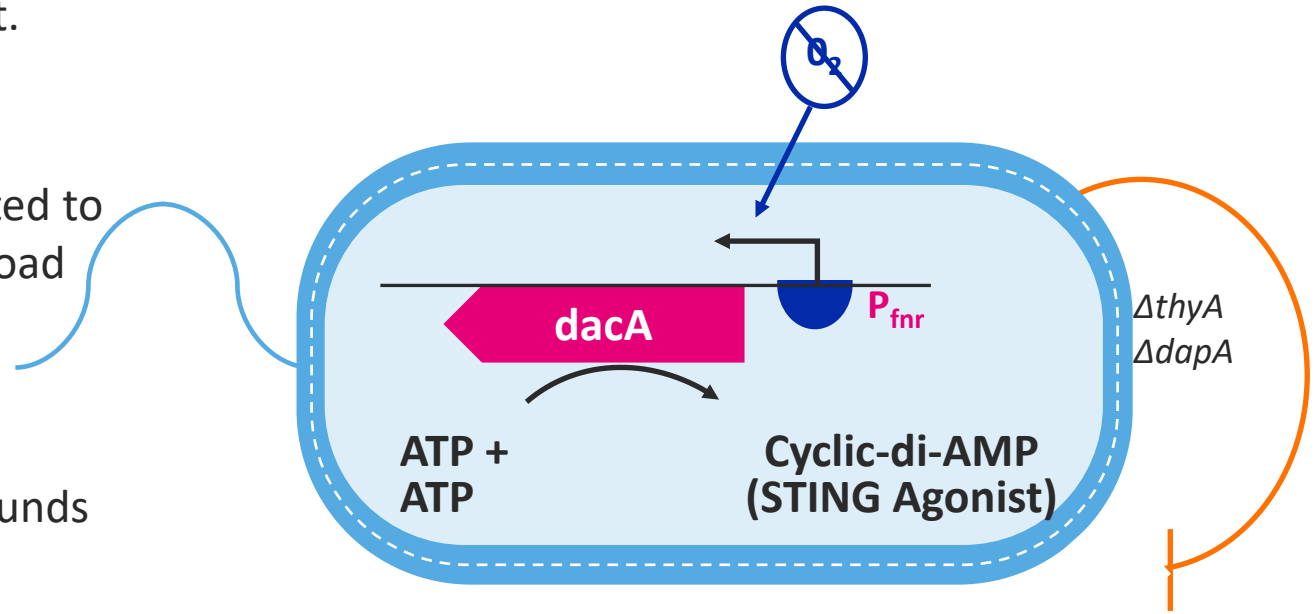
Component	Approach	Benefit
Bacterial Chassis	*E. coli* Nissle	Decades of human use
Switch	FNR promoter	Inducer-promoter pair
Pump	*OxLT*	Pumps oxalate in & formate out
Effector 1	*OxdC and associated components*	Catalyzes conversion of oxalate to formate
Safety Features	*Δ thyA*	Controls growth



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



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