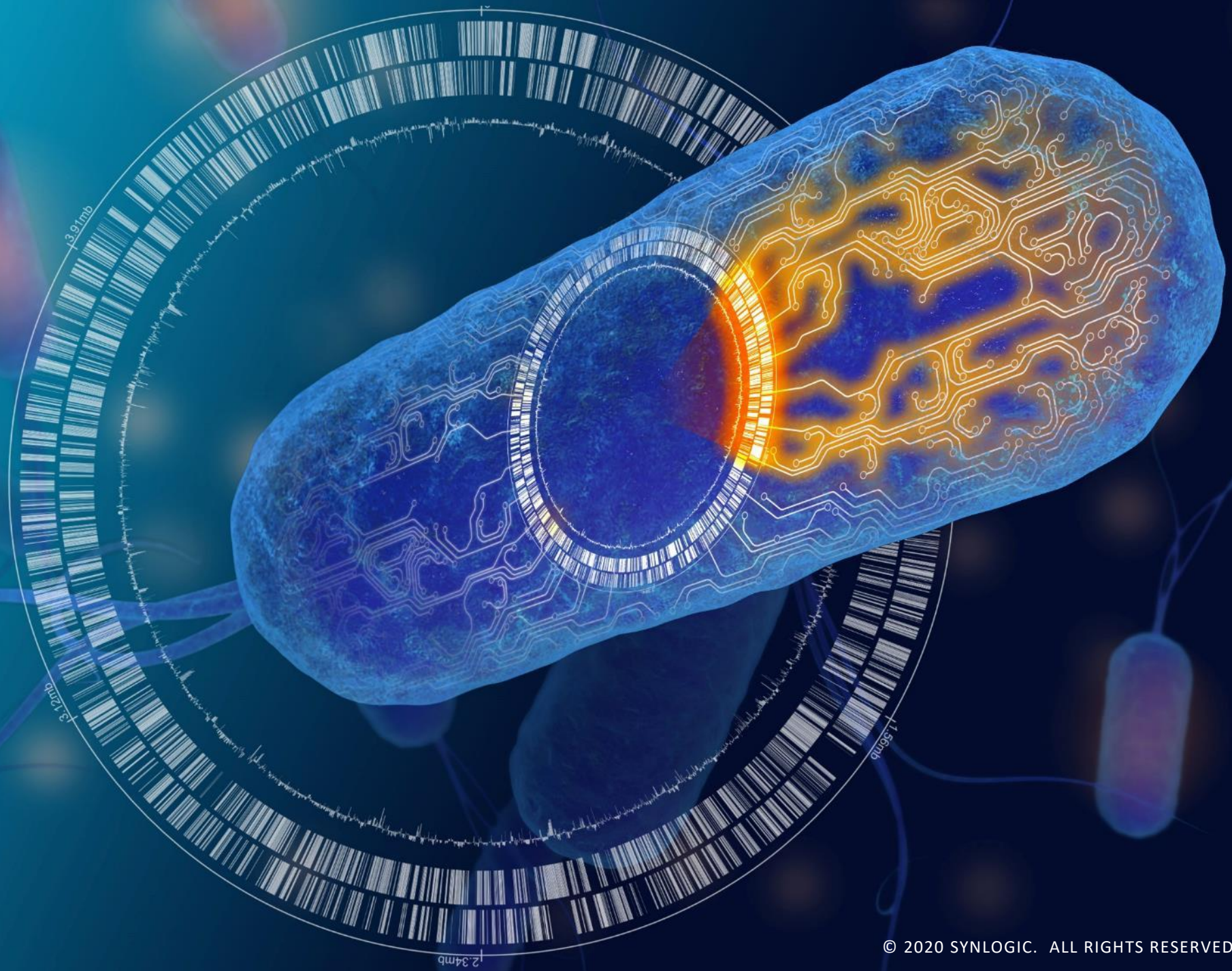
synlogic

Designed For Life

Corporate Presentation
September 2020



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 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.

Synthetic Biotic™ Medicines Designed For Life

Bringing The Transformative Potential Of Synthetic Biology To Medicine

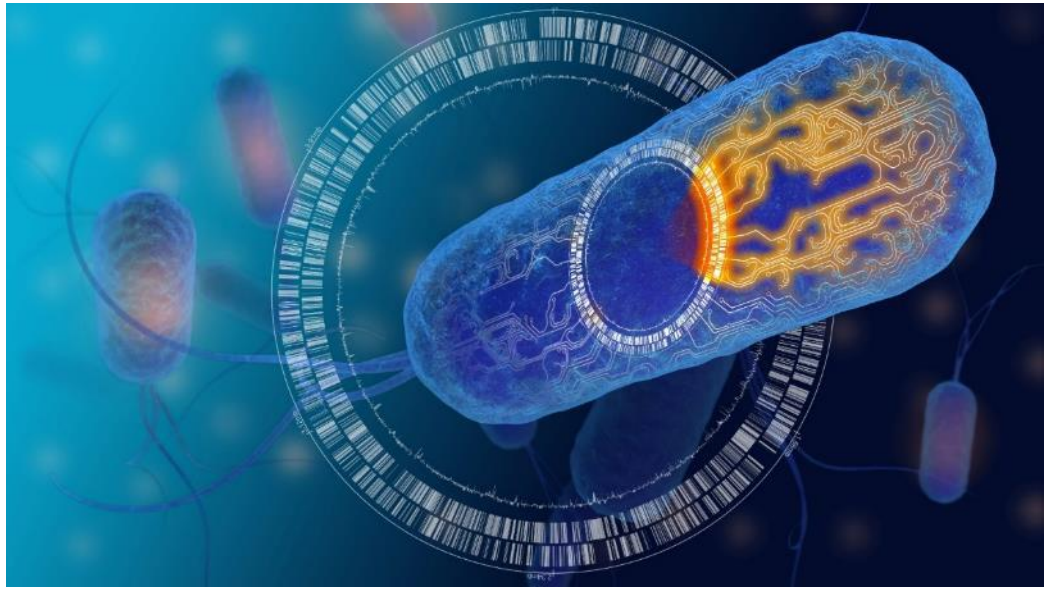
Corporate Overview

- **The premier Synthetic Biology** platform to **engineer bacterial Synthetic Biotic medicines** that benefit patients in new ways
- **Team**, **technology** and **portfolio** to succeed
- **Core focus:** Rapidly progressing **metabolic programs**
  - **SYNB1618 PKU** Phase 2 *synPheny* FPI expected late 2020
  - Advanced IND for **SYNB8802 in Enteric Hyperoxaluria**: FIH expected early 2021
- **Partnership Opportunities:** I**mmunomodulation** in immunology and oncology
  - **SYNB1891** monotherapy continues to enroll: data expected late 2020
- Strong cash position

Synthetic Biotic Medicines: A New Class of Medicines

Bacteria and Humans Co-Evolved and Co-Exist

We Rationally Design Bacteria
To Provide Clinical Benefit



The Result Is Therapeutic Bacteria With Potent And Programmable Therapeutic Effects

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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

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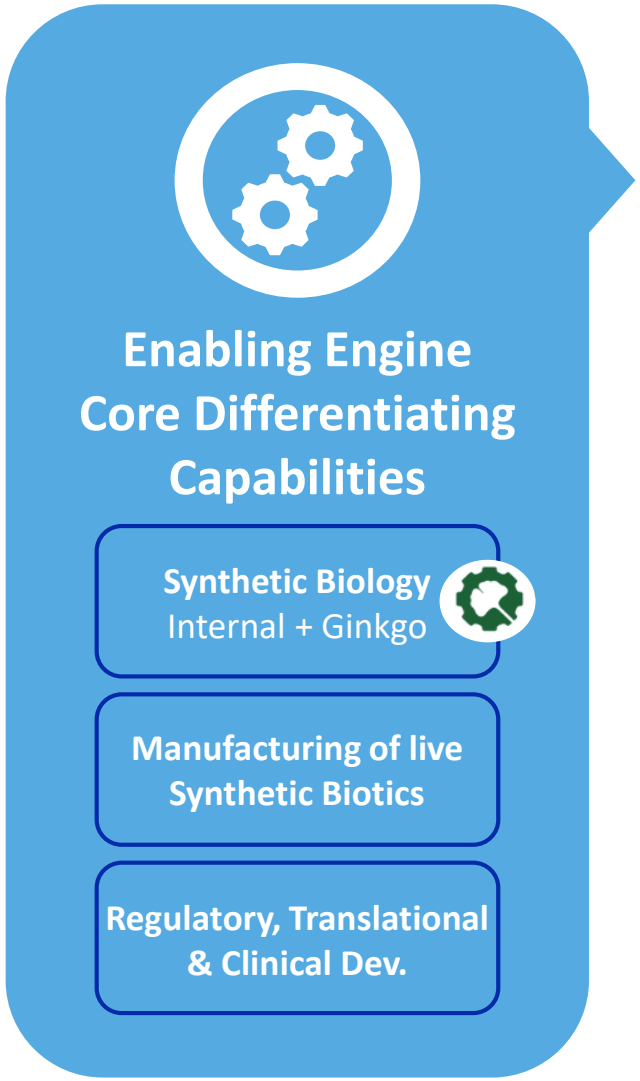
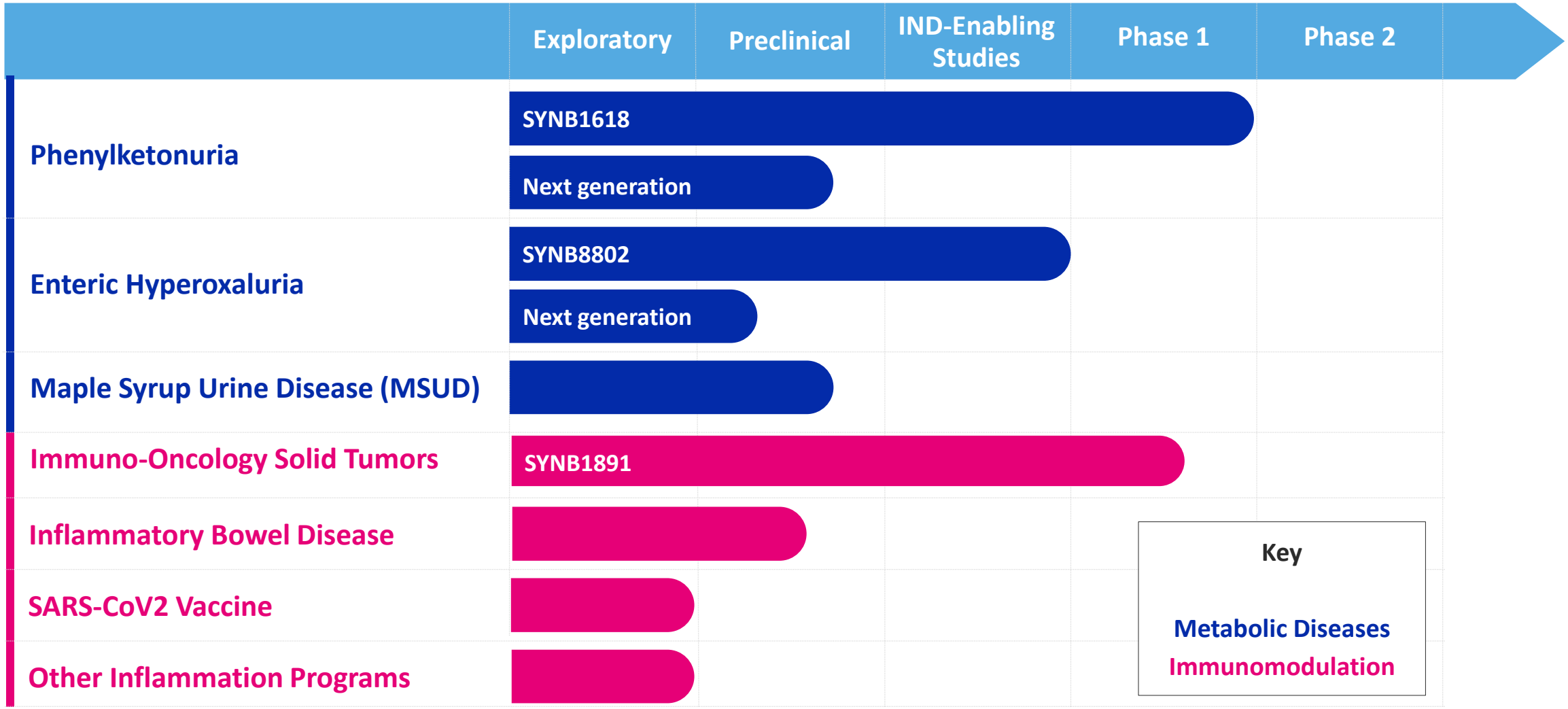
Enabling Engine



- **Clinical Evidence**
  - **>200 humans dosed** with Synthetic Biotic medicines
  - **3 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

Pipeline



Upcoming Milestones

Synlogic Entering Data Rich Period In The Clinic

	Expected Milestone	2020 early	2020 mid	2020 late	2021 early	2021 mid	2021 late
SYNB1618 PKU	Initiate Ph.2 study in PKU patients						
	Ph.2 Phe-lowering read-out						
SYNB8802 HOX	Initiate IND-enabling studies	initiated					
	Initiate Ph.1 study in HV and Patients						
	Ph.1 Patient Read-out						
SYNB1891 I/O	Ph.1 Monotherapy read-out						
	Initiate Ph.1 combination study arm						
	Ph.1 Combination therapy read-out						

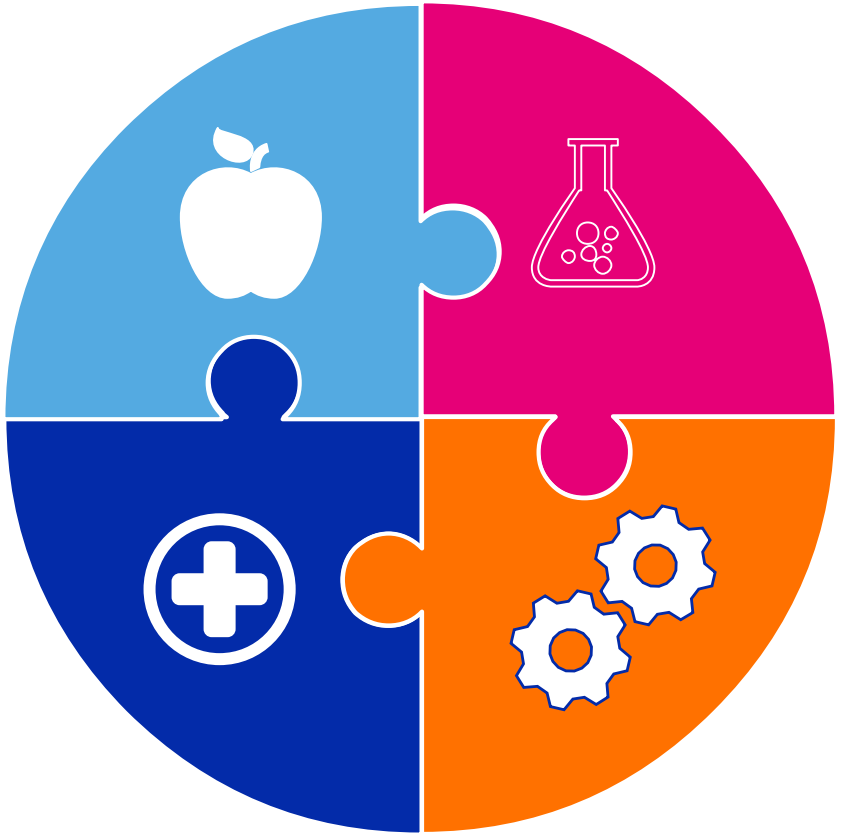
Significant Clinical Readouts Within Our Current Cash Window

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 SYNB
Bacteria act catalytically

Contain multiple enzyme pathways

Are protected from digestion within the GI tract

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Phenylketonuria (PKU)

Meaningful Opportunity To Improve Patient Lives

Emerging treatment options will continue to leave many patients behind

SYNB1618 demonstrates potential to lower Phe in PKU patients

Phase 2 Phe-lowering trial starting in 2H 2020

Next generation strain in development

Phenylketonuria (PKU)

Julia, living with PKU

Why PKU?

Biology well-understood Inability to break down phenylalanine (Phe) results in toxic levels in the brain leading to cognitive impairment, convulsions and behavioral problems

⬇ Phe in GI tract = ⬇ blood Phe = clinical benefit

High unmet need particularly for pediatric patients

~ 34,000 patients US + EU

Status

Solid oral formulation of SYNB1618 demonstrated good tolerability and activity in healthy volunteers

Enrolling Phase 2 SynPheny Study in PKU patients

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PKU Has Changed:
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.

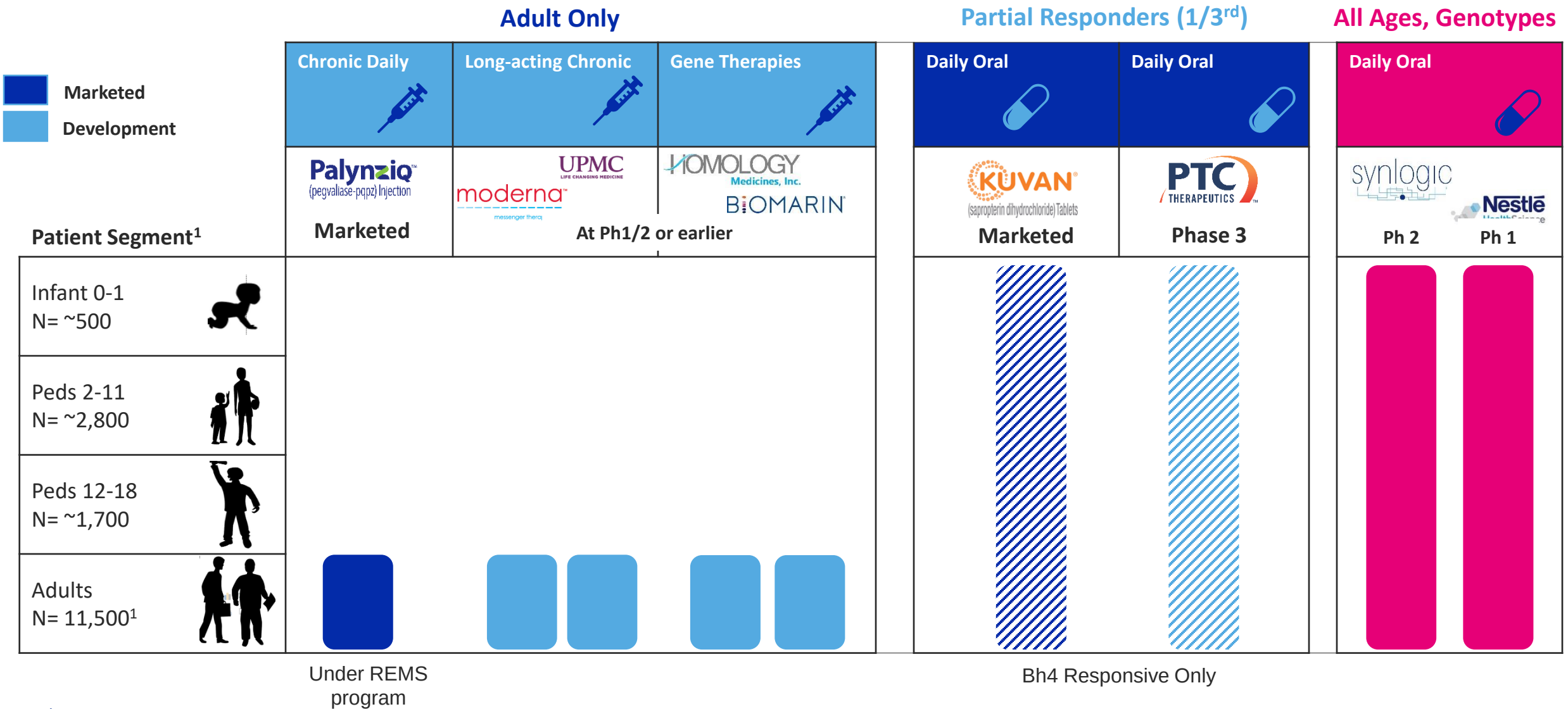
Early diagnosis and strict diet control enables better Phe management.

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 Differentiation

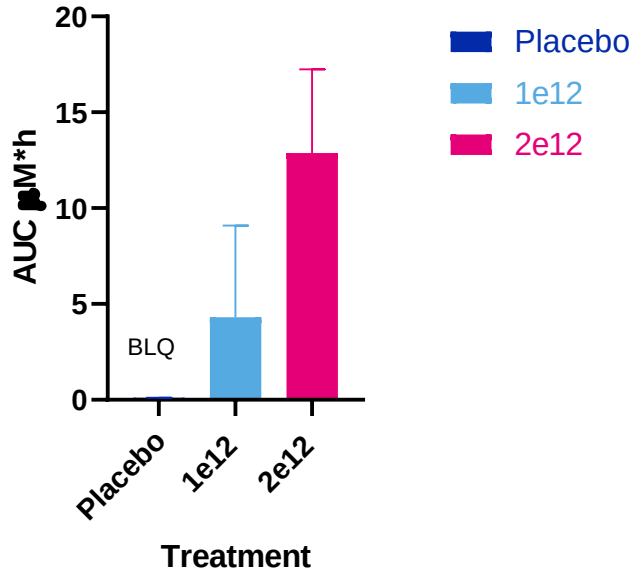
SYNB1618 uniquely positioned to address needs across ages and genotypes



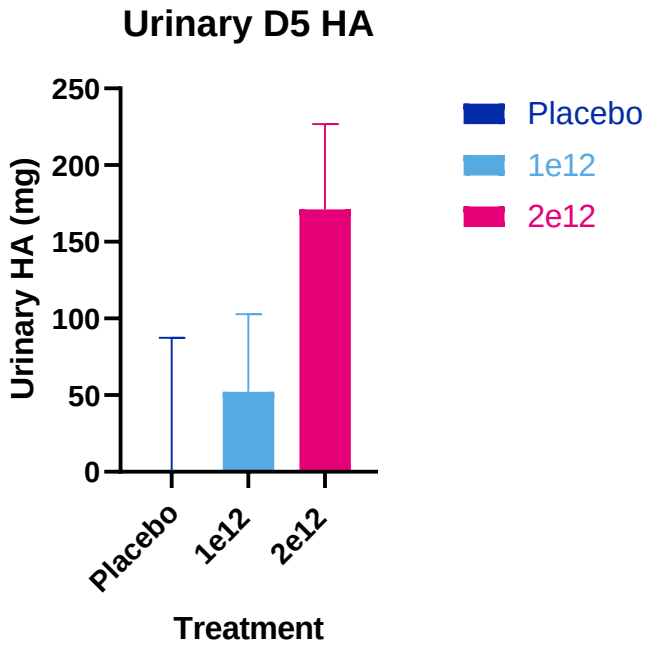
1. *Includes 7,500 "lost to follow up" adult patients*

SYNB1618 In The Clinic: D5 Tracer Data in Healthy Volunteers

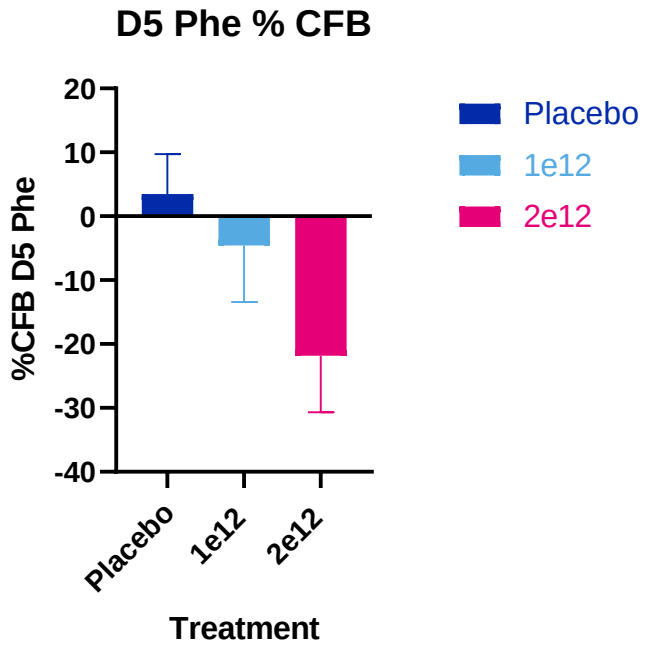
D5 Phe Converted to D5 TCA



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

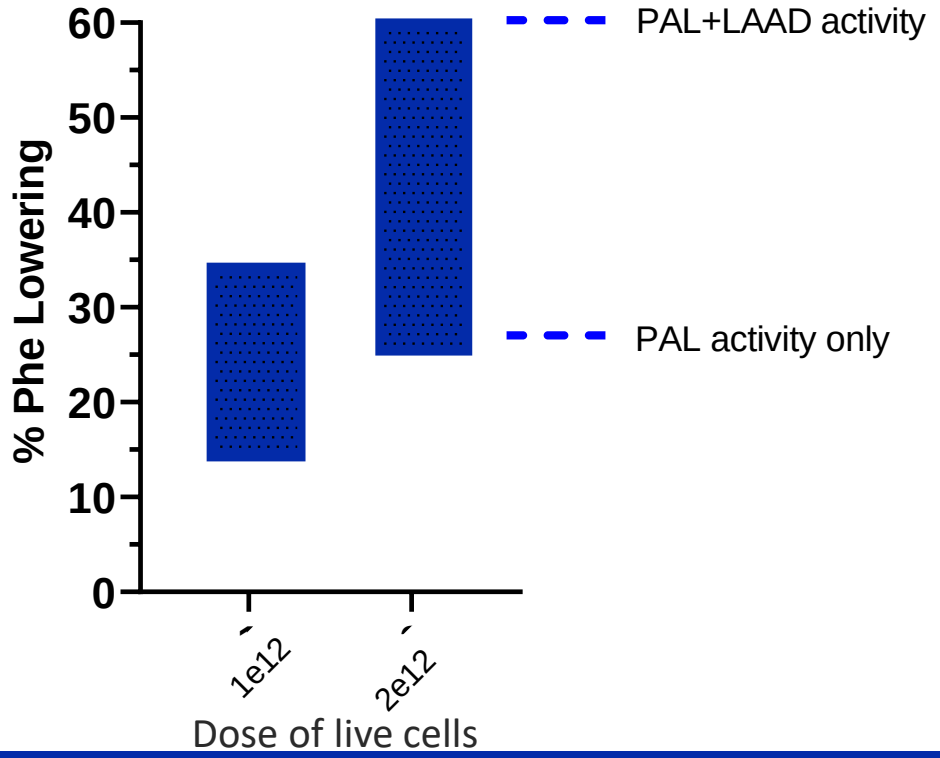
Metabolite Consumption Requirements[1]

Bridging Study Biomarker Read-outs[2]

In Silico Model

Proprietary Synlogic Simulation Models

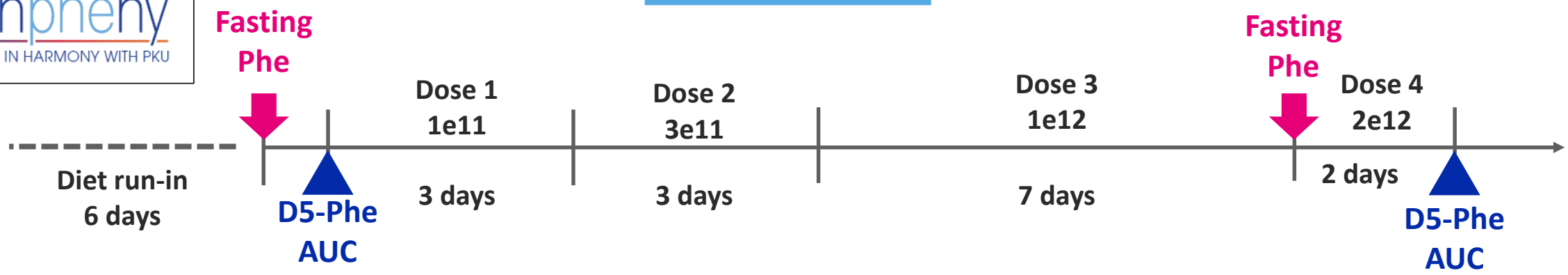
Outputs: Phe Lowering Potential



Modeling Predicts SYNB1618 Activity In Target Range

1. Kaufman S. 1999 PNAS V96:3160-3164
2. Denny W et al 2019, SSIEM conference

SynPheny Phase 2 Study in PKU



Study Goals

- **Demonstrate Phe Lowering in PKU Patients**
  - 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**

Execution

- **Flexible design** allowing home-based or office-based visits
- Informed by **direct patient feedback** on executing trials in the COVID era
- **Dose ramp** to improve tolerability
- **Strict diet control** to ensure consistent Phe intake, including 6-day run-in

Enteric Hyperoxaluria

Our Next Step To Synthetic Biotic Medicines

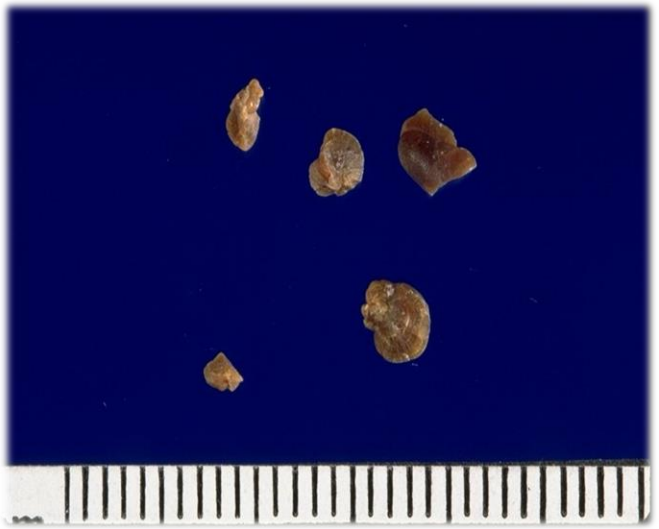
High unmet medical need with no available therapeutic options

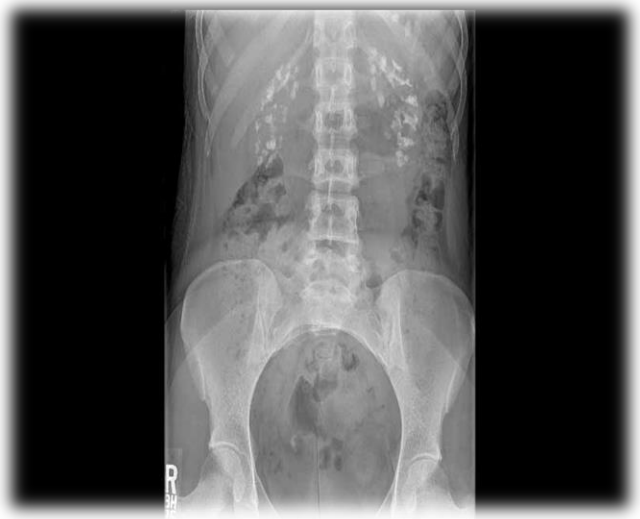
Efficient clinical development: PoC achievable in Phase 1b

SYNB8802 has potential to meaningfully reduce urinary oxalate levels

Enteric Hyperoxaluria

Our Next Step To Synthetic Biotic Medicines





Why Enteric Hyperoxaluria?

Biology well-understood: Inability to metabolize oxalate in the gut, leading to high levels of urinary oxalate and increased risk of kidney stones; progressing to chronic kidney disease

Frequent complication of inflammatory bowel diseases, ileal resection and Roux-en-Y gastric bypass

↓ urinary oxalate = ↓ stone risk = clinical benefit for patient

No treatment options for 200,000 - 250,000 US patients

Status

Rapid preclinical development: project initiation to development candidate in <10 months. IND-enabling studies ongoing

Potential initiation of health volunteer studies in early 2021

Potential initiation of Roux-en-Y patient study in early 2021

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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 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
Clinical Mgmt	Limited nutrition options; nephrocalcinosis; dialysis; transplant; pyridoxine	Limited nutrition options; treatment of kidney stones as they occur; nephrocalcinosis; dialysis
U.S. Epidemiology	~5,000 – 8,000	200,000 – 250,000
Key Players	Dicerna pharmaceuticals; Alnylam PHARMACEUTICALS	Allena PHARMACEUTICALS; synlogic

Enteric Hyperoxaluria Case Studies: An Important Cause of Renal Failure

33-Year-Old Female with Crohn's	48-Year-Old Male with Crohn's	47-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 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 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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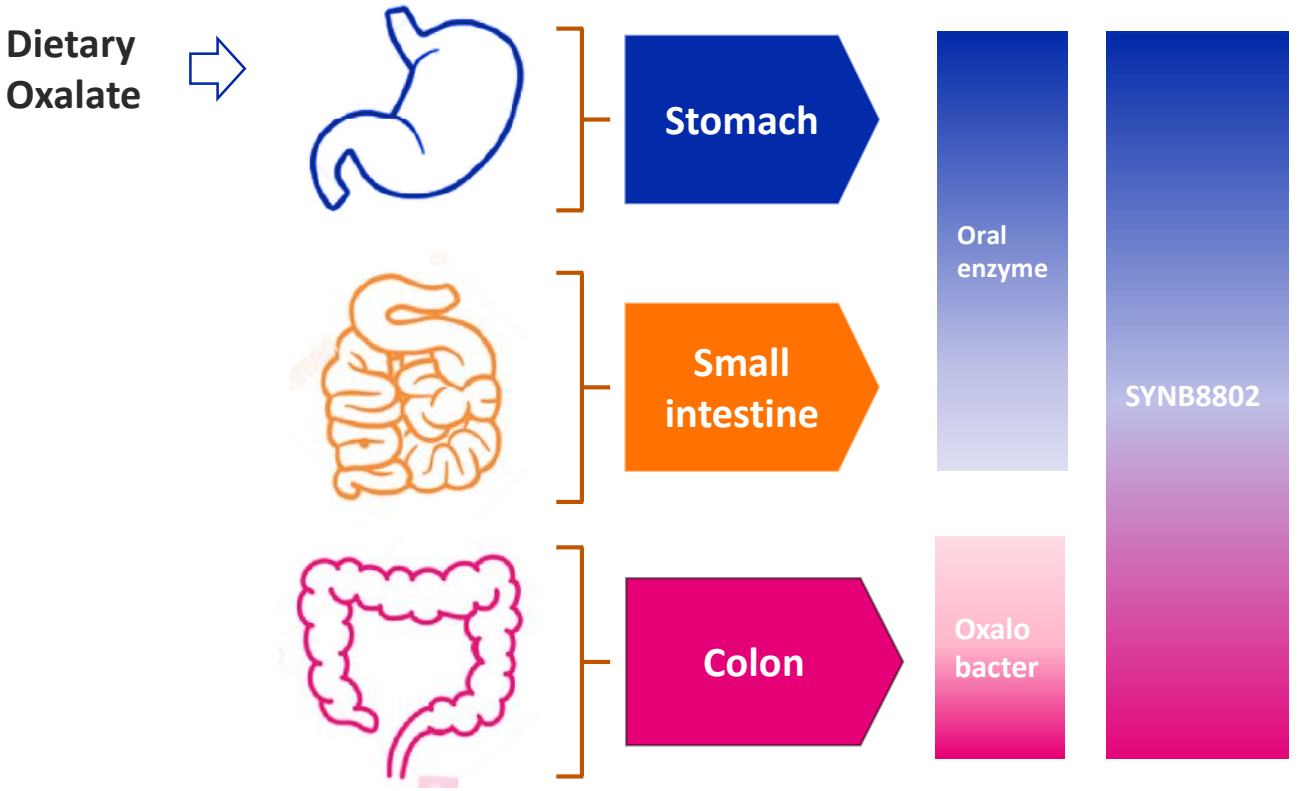
Nazzal et al. Nephrol Dial Transplant 2016

Enteric Hyperoxaluria Disease Pathogenesis

GI Based Therapies Have Demonstrated Lowering of Systemic Oxalate

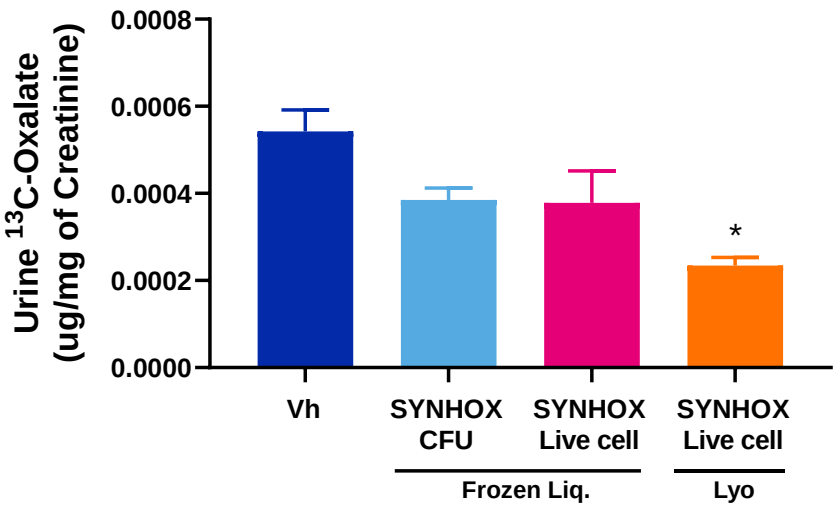


- Pathogenic hyperabsorption of dietary oxalate
- Dietary oxalate absorbed throughout GI tract
- Result is urinary Oxalate (Uox) > 70mg/day
- Leads to recurrent kidney stones, nephrocalcinosis, kidney failure
- Treatment must absorb oxalate throughout GI tract, esp. in colon

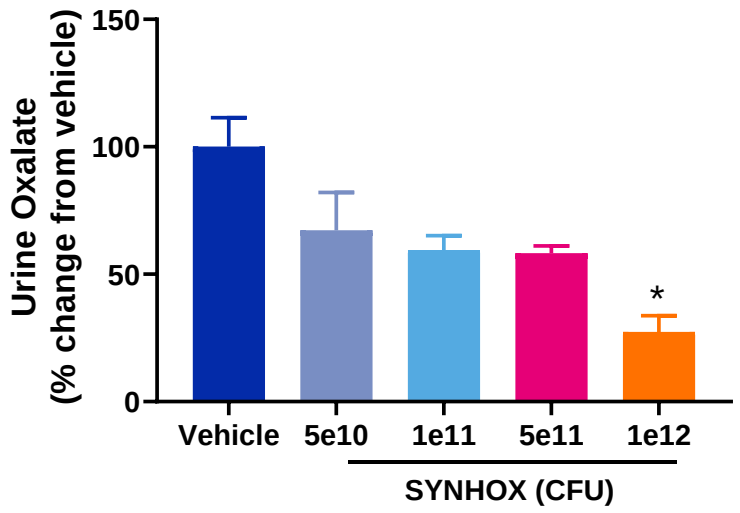
Intestinal Degradation of Oxalate Throughout GI Tract Could Enhance Oxalate Lowering

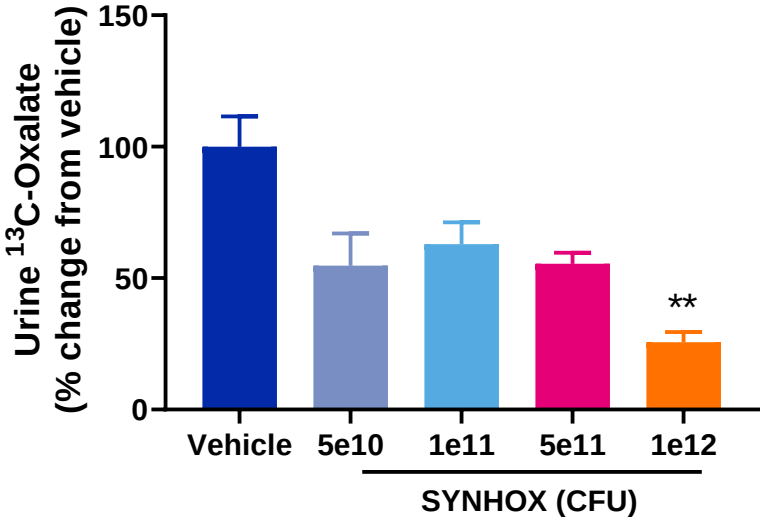
SYN-HOX Attenuates Urinary Oxalate Increase

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: Clinical Development Strategy

Phase 1a Healthy Volunteers

Multiple Ascending Doses

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

Phase 1b Gastric Bypass

Cross-over design

- TID dosing
- Approx. 20 hyperoxaluria patients (Roux-en Y gastric bypass)
- Uox >70 mg/day

Enables Rapid POC

Phase 2/3 Enteric hyperoxaluria

Parallel group design

Patients with:

- Gastric Bypass
- Inflammatory bowel disease
- Cystic Fibrosis
- Short bowel syndrome
- Biliary/pancreatic diseases

+Preserved renal function and stone disease

Initial Phase 1 Study in Both Healthy Volunteers (data early 2021)
& Roux-en-Y Gastric Bypass Population (data mid 2021)

Why Diseases of Immune System Regulation For Synthetic Biotic Medicines?

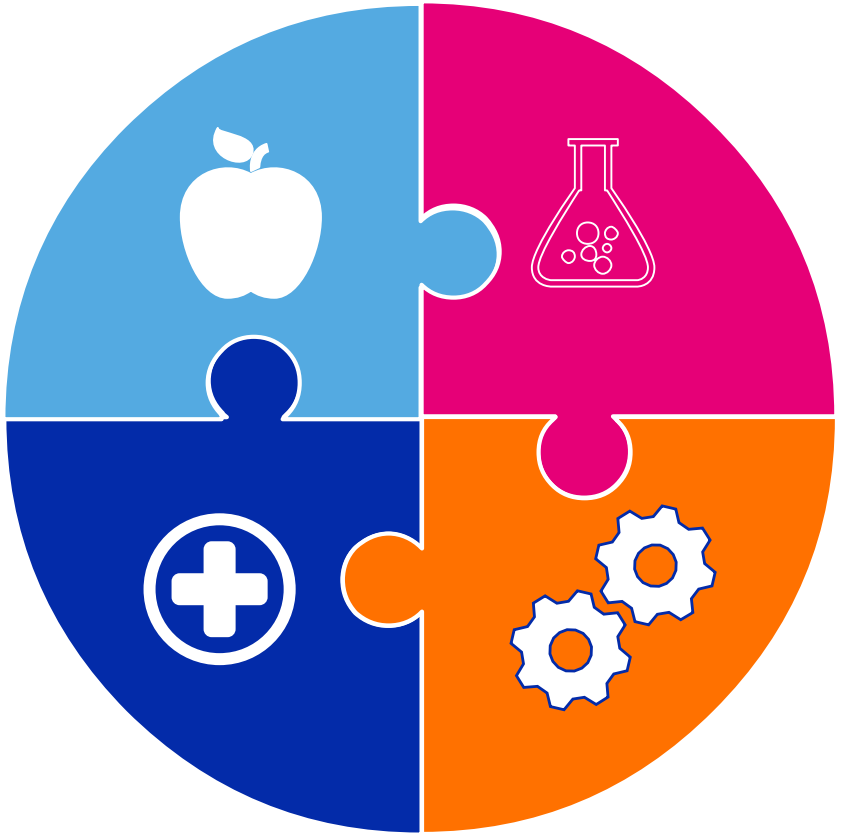
Cross-talk Between Bacteria and Immune System

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 Tx strain delivered to site of disease

Immunomodulation & Immuno-Oncology

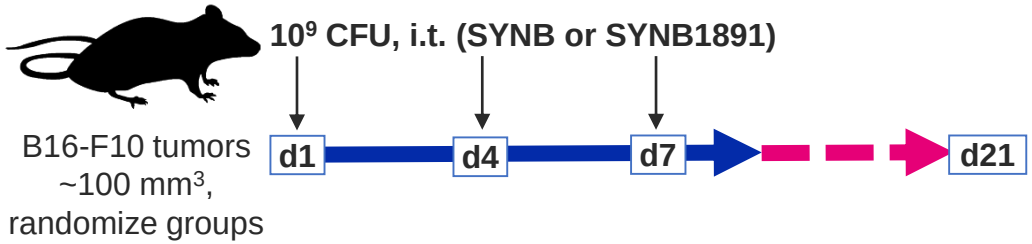
Synthetic Biotics can be engineered for immune activation or regulation

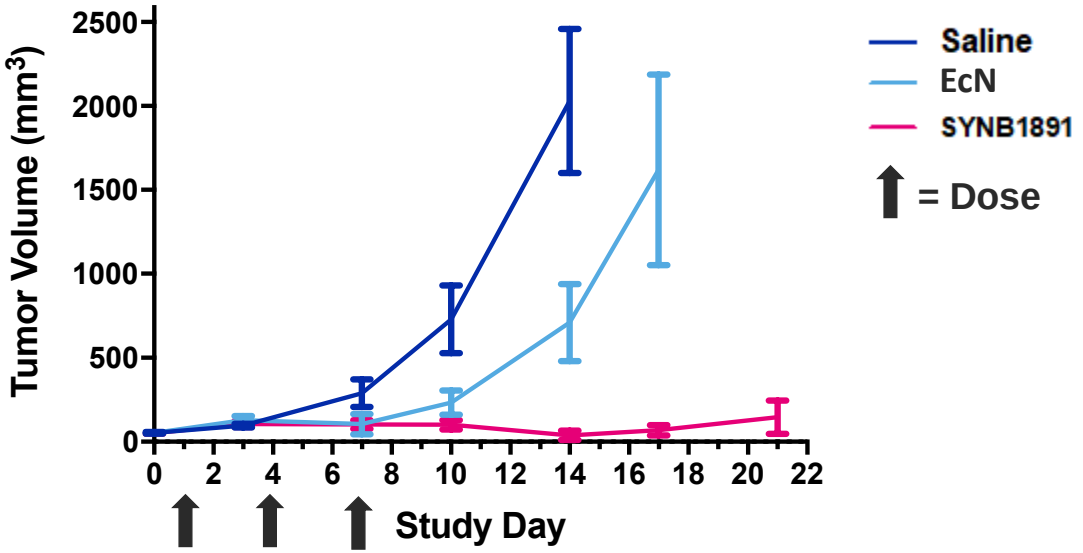
SYNB1891 will provide clinical data in 2020 from a monotherapy cohort

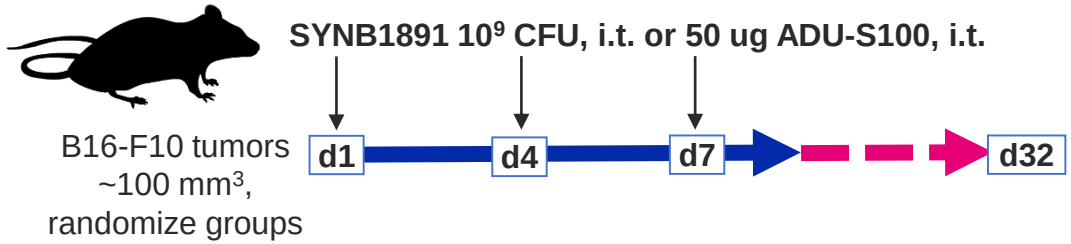
SYNB1891 has potential for improved efficacy relative to other STING approaches

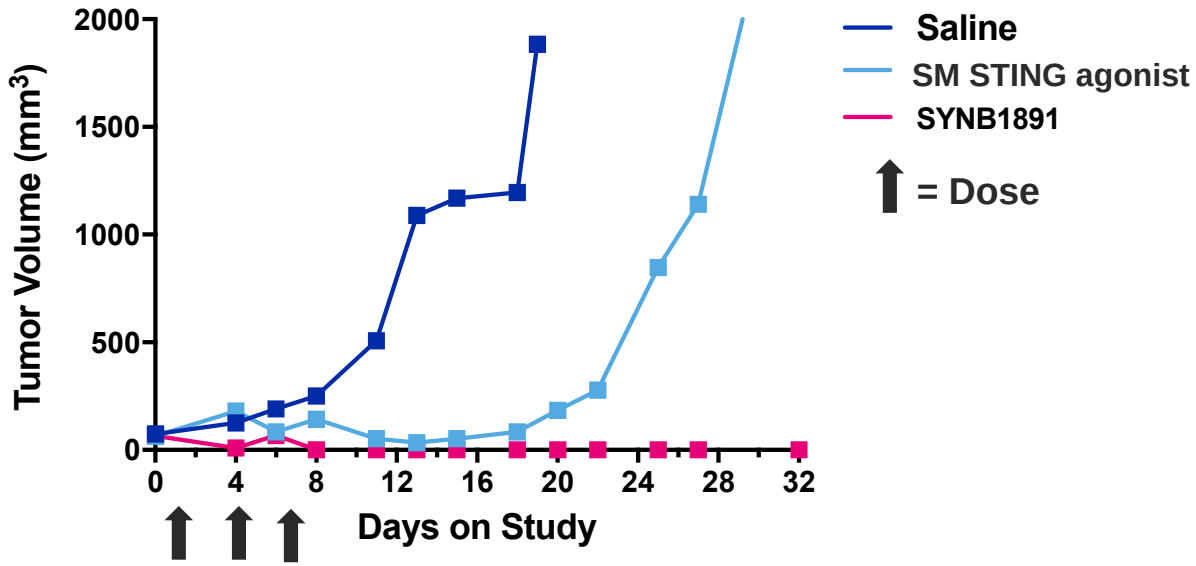
SYNB1891 Induces Potent Anti-tumoral Effects

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





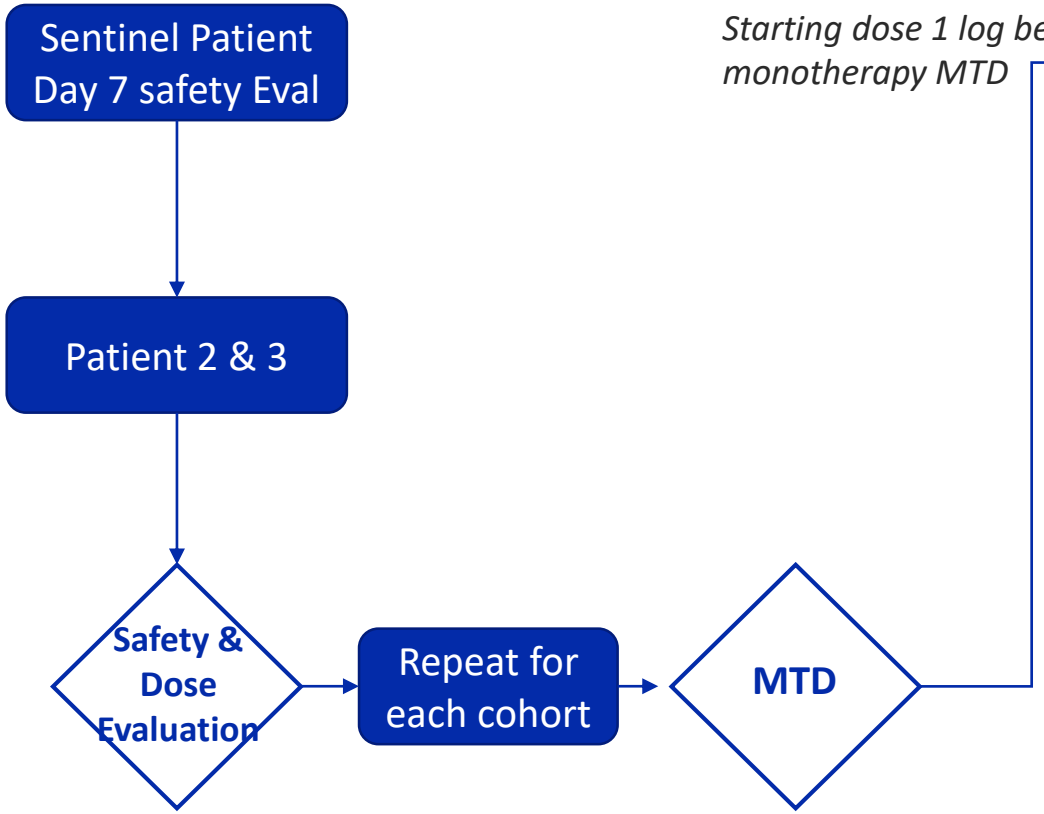




SYNB1891-CP-001 Study Design: Multidose Tolerability, IT Mono and Combo

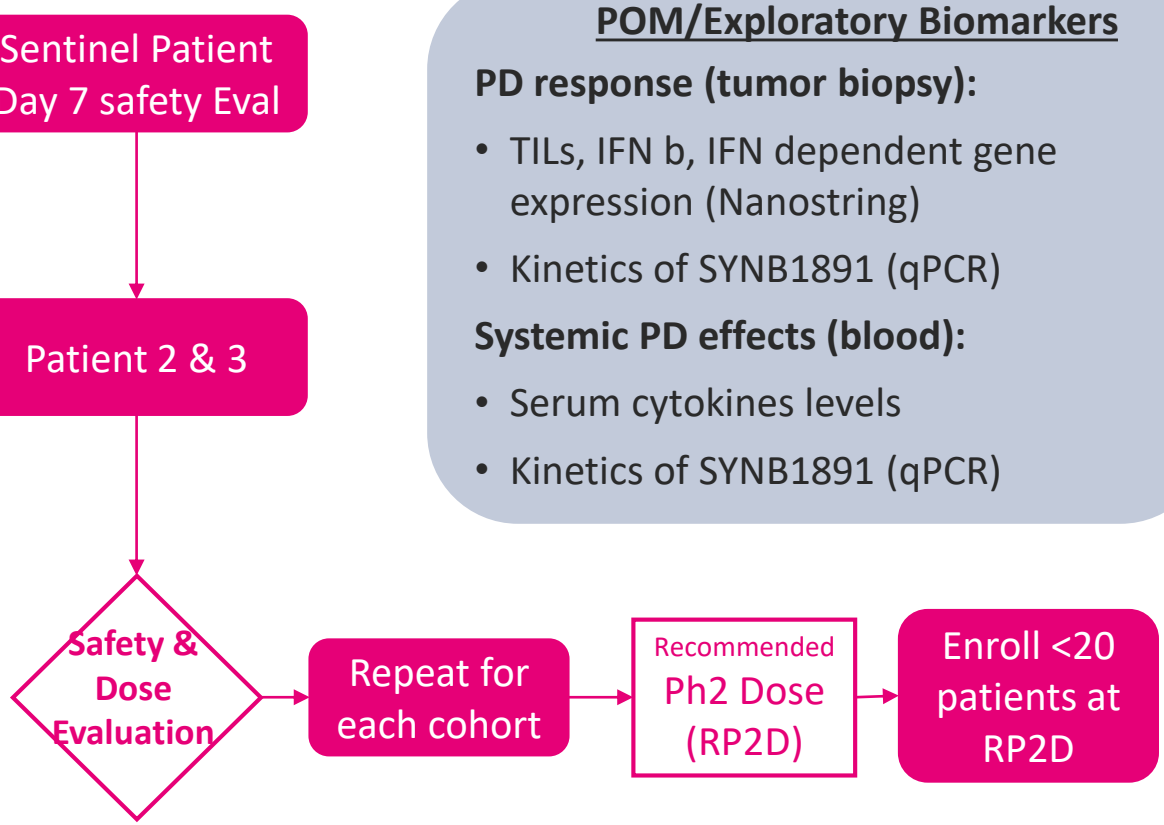
Proof of Mechanism: Exploratory Biomarkers in Advanced Solid Tumors or Lymphomas

Arm 1: Monotherapy Cohorts



Starting dose 1 log below monotherapy MTD

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)

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Financial Summary as of 2nd Quarter 2020

Balance Sheet (unaudited)	30 June 2020	31 Mar 2020
Cash, Cash Equivalents, and Short & Long Term Marketable Securities	$109.1M	$114.3 M

Statement of Operations (unaudited)	Three Months Ended	
	30 June 2020	30 June 2019
R&D Expenses	$12.9 M	$9.7 M
G&A Expenses	$3.5 M	$3.7 M
Net Loss	$(15.5) M	$(12.3) M
*Net Loss Per Share **	*$(0.44)*	*$(0.45)*

Strong Cash Position With Runway Into 2022

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

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SYNB1891 I/O	Ph.1 Monotherapy read-out						
	Initiate Ph.1 combination study arm						
	Ph.1 Combination therapy read-out						

Significant Clinical Readouts Within Our Current Cash Window

Synlogic Leadership

Aoife Brennan, MB ChB
President & CEO

Richard Riese, MD PhD
CMO

Gregg Beloff, JD
Interim CFO

Antoine Awad
Chief Operating Officer

Dave Hava, PhD
Chief Scientific Officer

Amanda Kay, PhD
Head of BD & Strategy

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 Pharmaceuticals

Patricia Hurter
Lyndra Therapeutics

Collaborators

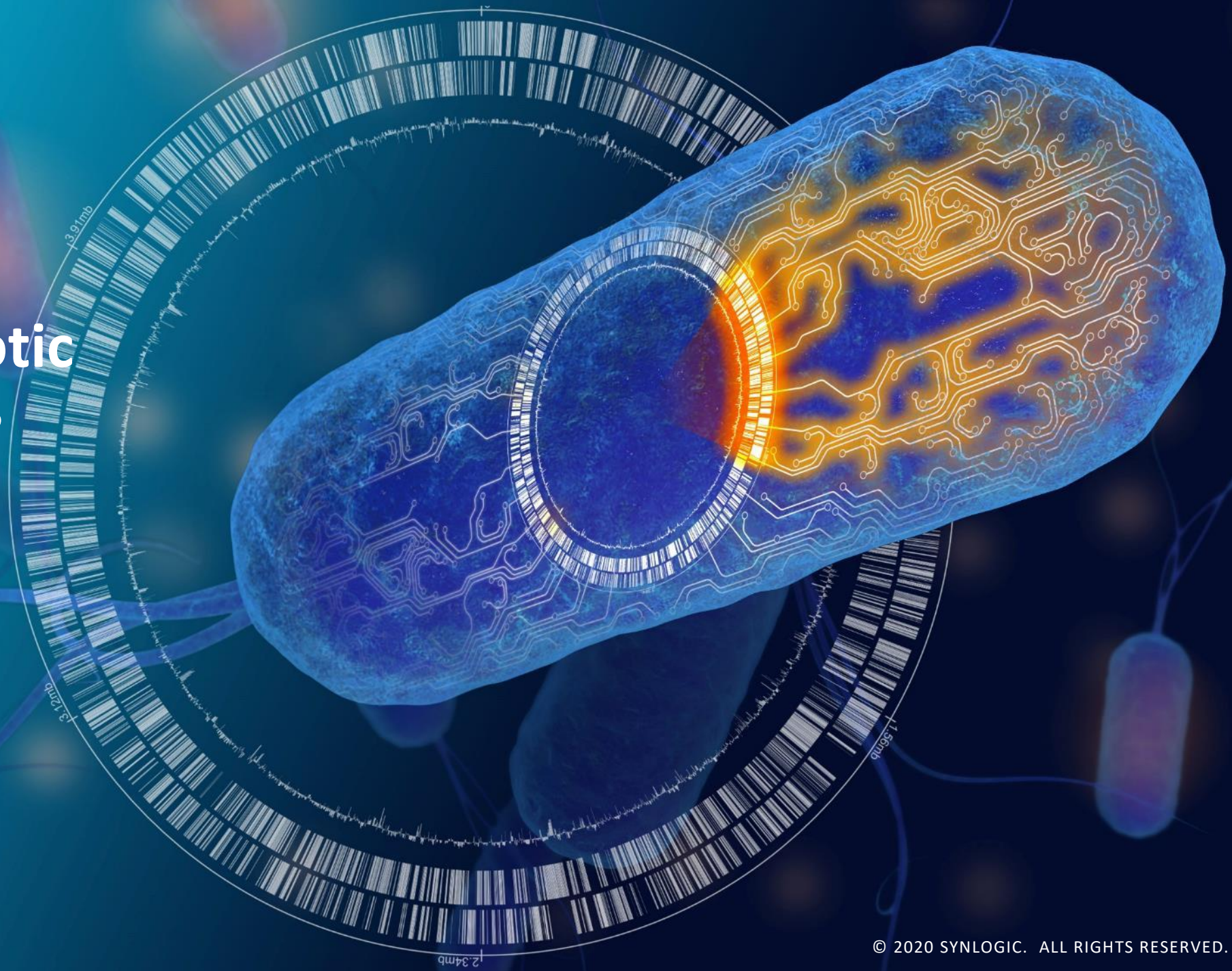
GINKGO BIOWORKS
THE ORGANISM COMPANY

Corporate Overview

- **The premier Synthetic Biology** platform to **engineer bacterial Synthetic Biotic medicines** that benefit patients in new ways
- **Team**, **technology** and **portfolio** to succeed
- **Core focus:** Rapidly progressing **metabolic programs**
  - **SYNB1618 PKU** Phase 2 *synPheny* FPI expected late 2020
  - Advanced IND for **SYNB8802 in Enteric Hyperoxaluria**: FIH expected early 2021
- **Partnership Opportunities:** I**mmunomodulation** in immunology and oncology
  - **SYNB1891** monotherapy continues to enroll: data expected late 2020
- Strong cash position

Appendix:

Engineering Synthetic Biotic Therapeutics



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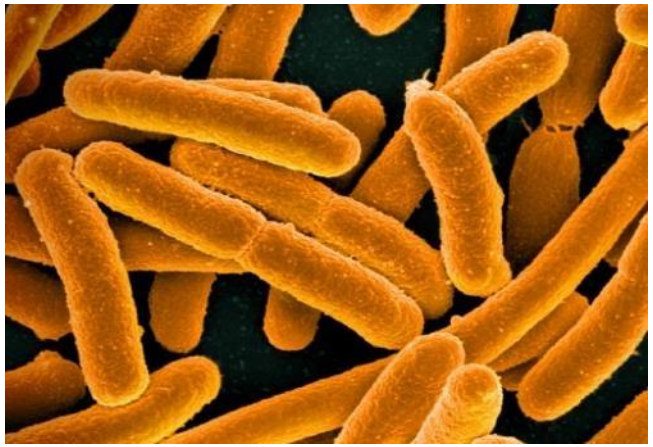
Synthetic Biotic Medicines: A New Class of Cellular Medicines

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

Bacterial Chassis
Non-pathogenic



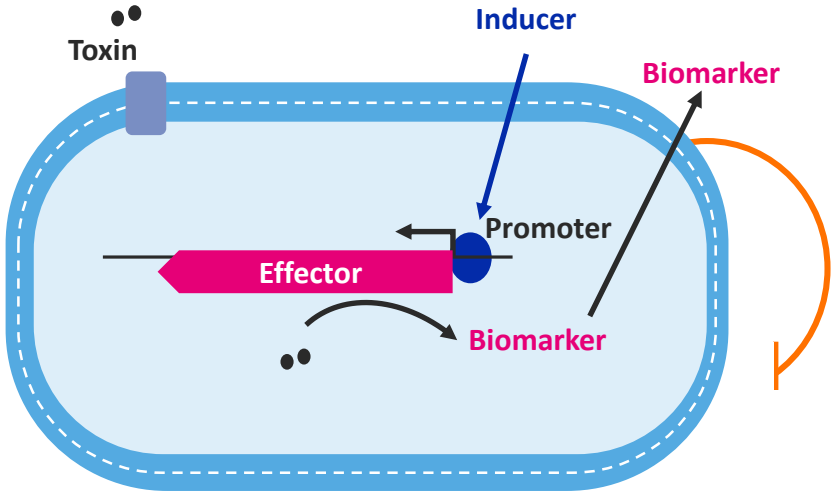
Synthetic Biology
Reusable Parts

Bacterial Chassis

Inducer-Promoter Switch

Effector Design

Safety Features



Reusable Parts Enable Rapid Iteration Of Rationally Designed Prototypes

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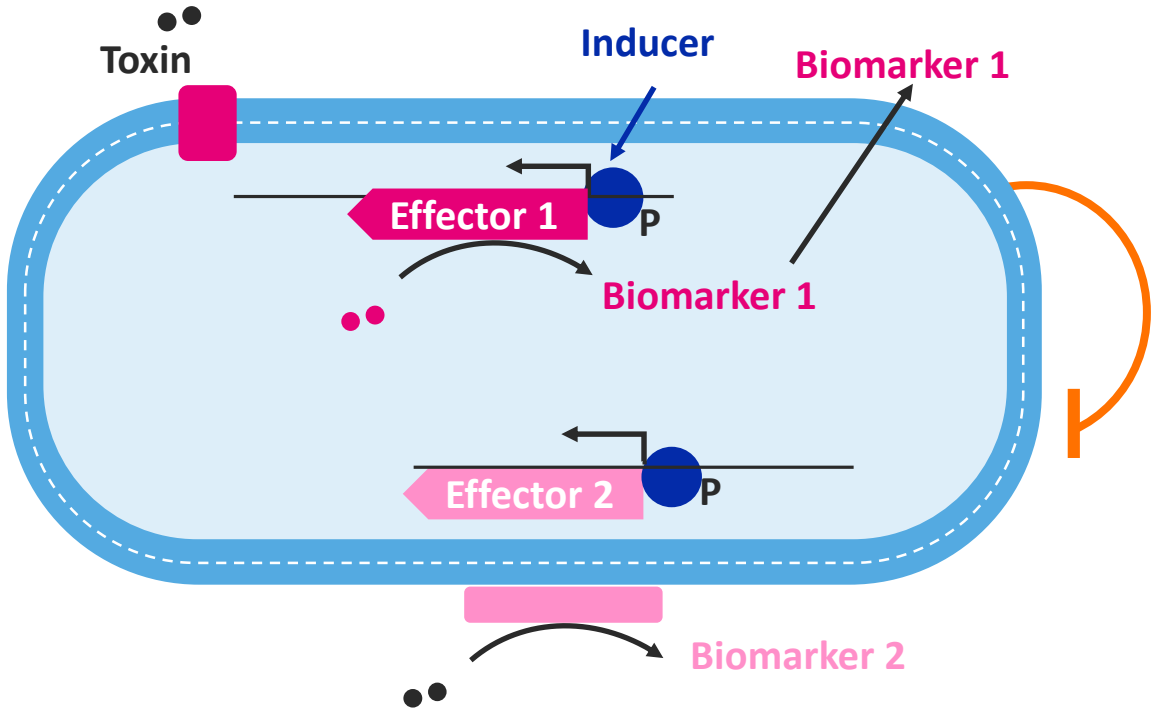
Photo credit: NIH Image Gallery

Library of Parts To Generate Prototypes

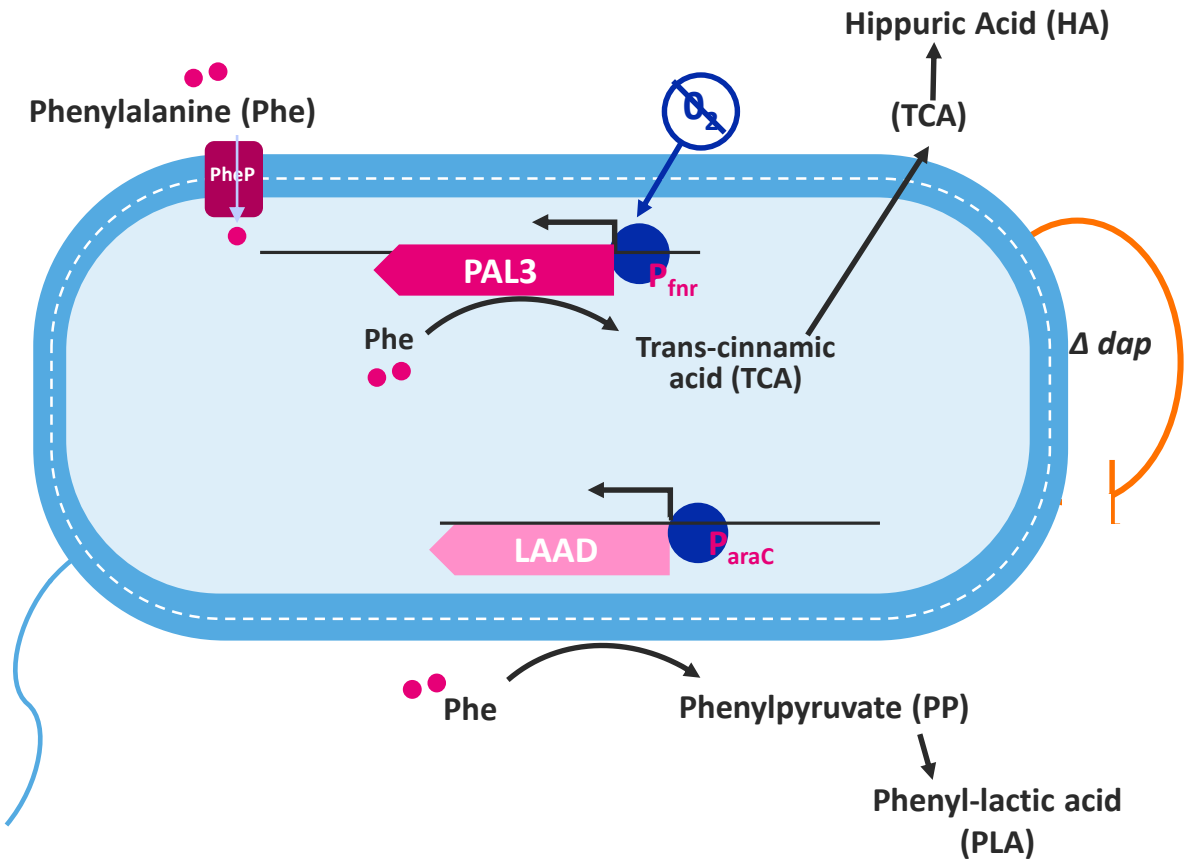
Synthetic Biology Library Rapidly Generates Drug Candidates

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 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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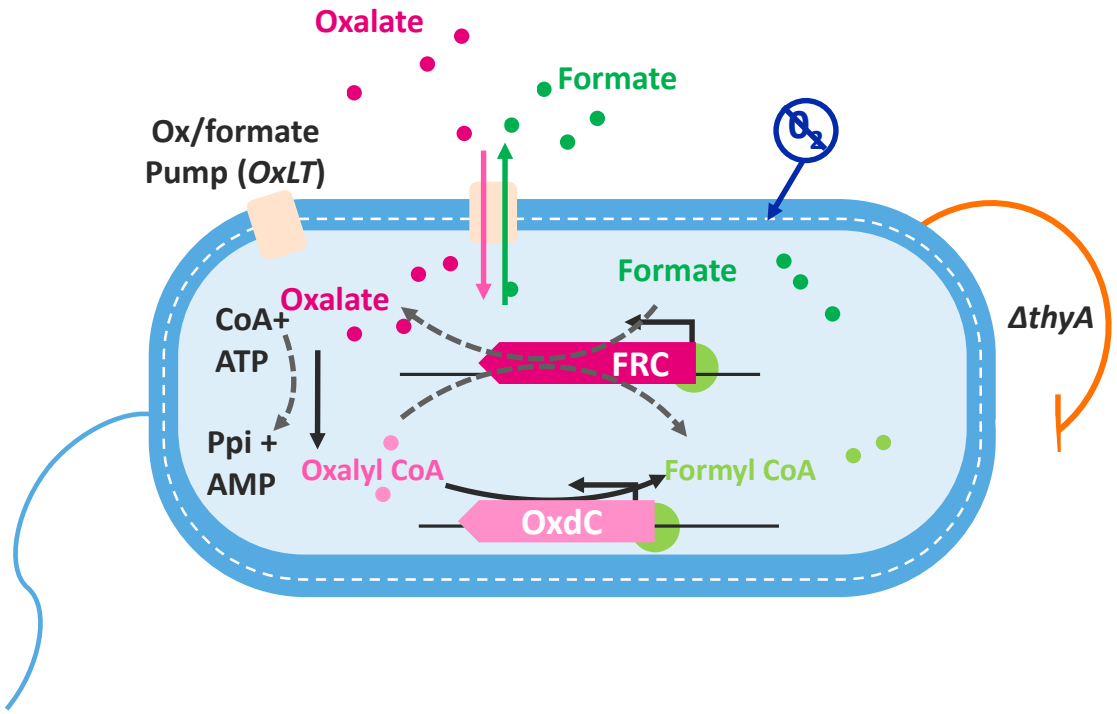
Hyperoxaluria strain SYNB8802

Engineered to convert oxalate to formate

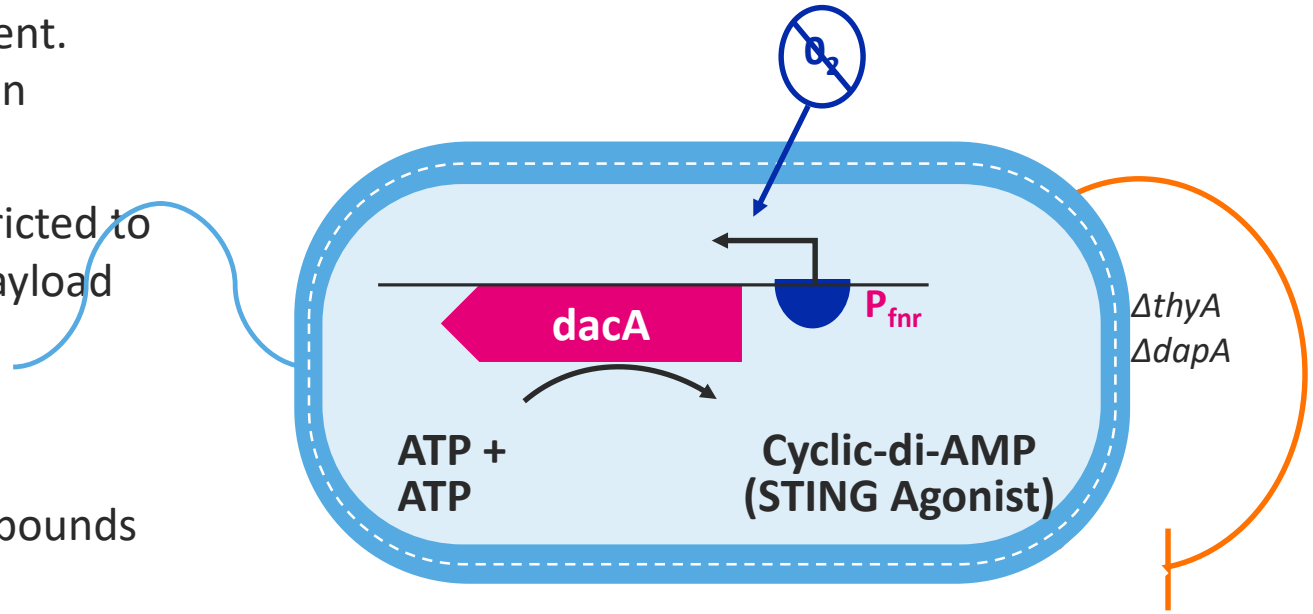
Component	Approach	Benefit
Bacterial Chassis	*E. coli* Nissle	Decades of human use
Switch	FNR promoter	Inducer-promoter pair
Pump	*OxLT*	Pumps oxalate in & formate out
Effector 1	*OxdC and associated components*	Catalyzes conversion of oxalate to formate
Safety Features	*Δ thyA*	Controls growth



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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