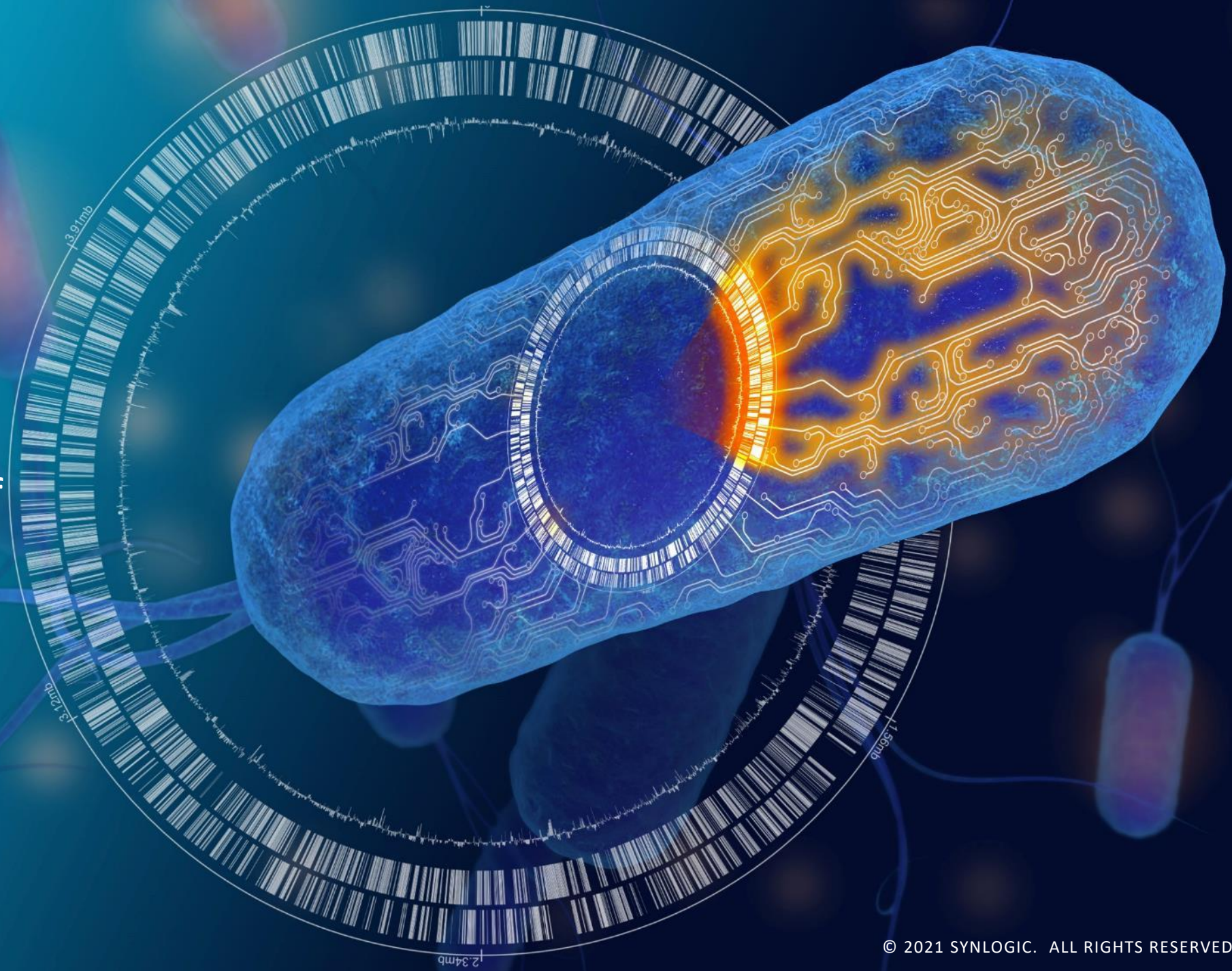
synlogic

Bringing the Transformative Power of Synthetic Biology to Medicine

Corporate Presentation
April 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 proof of concept data expected across multiple programs in 2021

Metabolic programs: Two PoC opportunities

SYNB1618 in Phenylketonuria (PKU)

Proof of mechanism demonstrated in Phase 1 with healthy volunteers

Phase 2 SynPheny patient data expected second half of 2021

SYNB8802 in Enteric Hyperoxaluria

Proof of mechanism demonstrated in Phase 1A with dietary hyperoxaluria induced in healthy volunteers

Phase 1B patient data expected second half of 2021

Immunomodulation

SYNB1891 in Solid Tumors

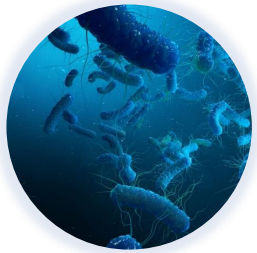
Monotherapy target engagement, meaningful pharmaco-dynamic effects, good safety

Combination with anti-PD1 and dose escalation ongoing

2021 data with potential to demonstrate clinical benefit of the Synthetic Biotic platform

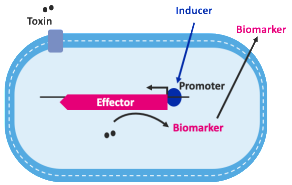
A new class of medicines

Synthetic Biotic platform



Non-pathogenic **bacterial chassis**

+



Programable, engineering

Targeted & controllable, **patient friendly** treatment

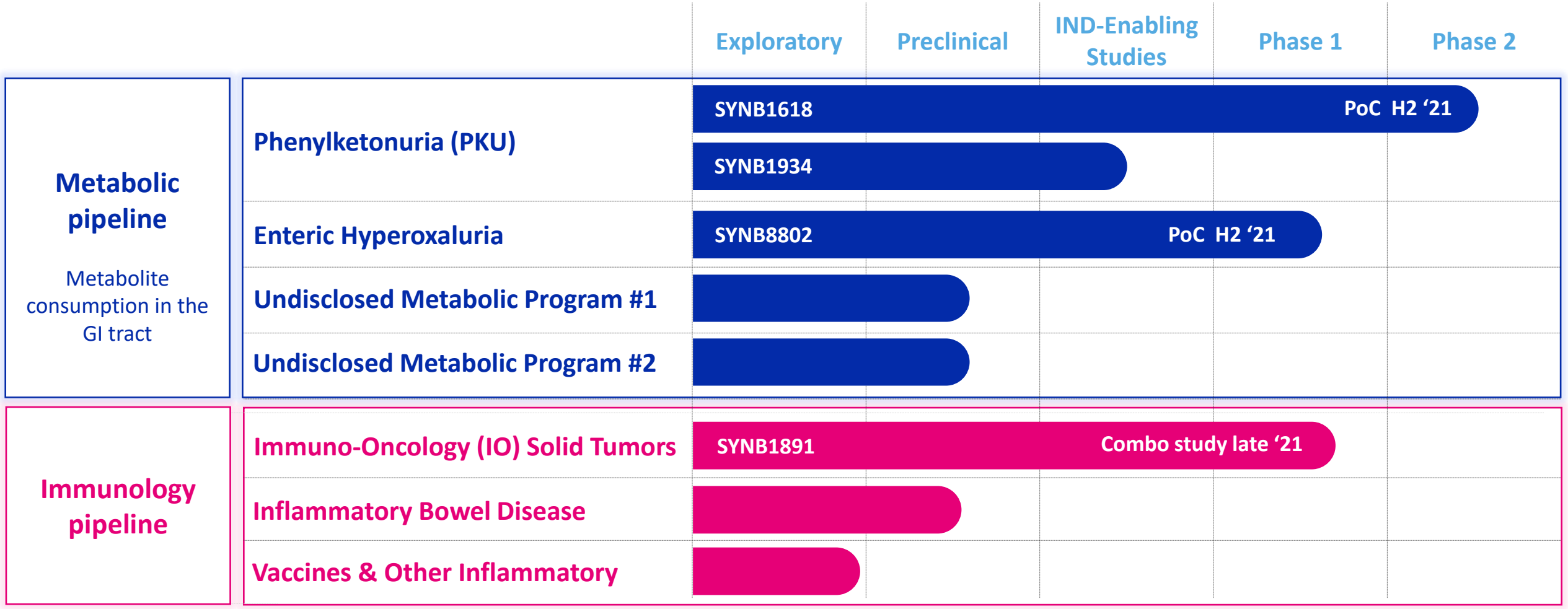
Robust pipelines

Rare metabolic therapies that **consume toxic metabolites** from the GI tract

Therapies that leverage the ability of **bacteria to interact with the immune system**

Enabling engine of synthetic biology, manufacturing and translational capabilities
Creates multiple product opportunities

Robust pipelines with meaningful catalysts



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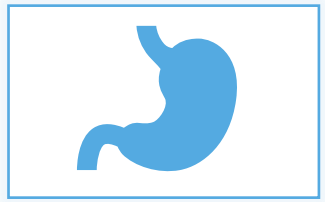
Synthetic Biotic medicines: a novel approach to metabolic disease

Why metabolic disease?

Unmet Medical Need



Validated Biology

Rationale

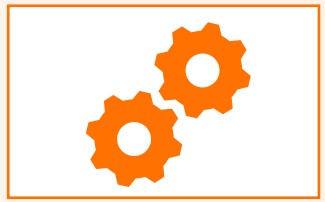
High **unmet need** across inherited and acquired metabolic diseases

Multiple **large and underserved markets**

Diseases with **known pathophysiology**

Dietary intervention **validates GI approach**

Why Synthetic Biotic medicine?



Unique Advantages

Proof of Mechanism

Bacteria **evolved to survive in the GI tract**

Ability to deploy multiple enzyme pathways

Drug-like approach without genetic drift or colonization

Multiple programs **demonstrate** SYNB compounds can **consume toxic metabolites** in the human GI tract

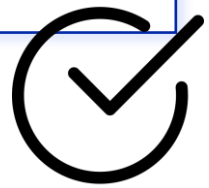
Applying Synthetic Biotic medicines to PKU and Enteric Hyperoxaluria

	Phenylketonuria (PKU)	Enteric Hyperoxaluria (HOX)
Unmet Medical Need	Many patients unable to control Phe ~30% BH4 oral therapy response rates	High kidney disease risk No effective interventions or treatments
Validated Biology	Lower dietary Phe intake = lower plasma Phe levels = improved cognitive outcomes	Lower dietary oxalate intake = lower urinary oxalate = improved kidney outcomes
Unique Advantages	Modality able to consume Phe in the GI tract before it can cause damage	Modality able to consume oxalate throughout GI tract, including colon
Platform Proof of Mechanism	SYNB1618 consumes Phe and produces the TCA biomarker in both HVs and patients	SYNB8802 consumes oxalate in healthy volunteers at clinically meaningful levels

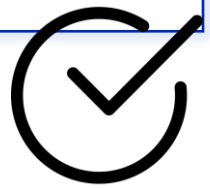
Phenylketonuria (PKU)

Current and emerging treatment options leave many patients behind

SYNB1618 demonstrates potential to lower Phe in PKU patients



Phase 2 Phe-lowering trial initiated



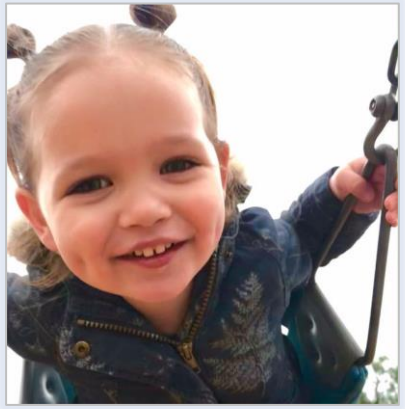
Patient need: parents expect their children to reach full potential

Historically

Prospect of severe mental disability and institutionalization.

Parents wanted PKU child to avoid institutionalized care before adulthood.

Today



Julia,
living with PKU

Early diagnosis and strict diet control enables better Phe management.

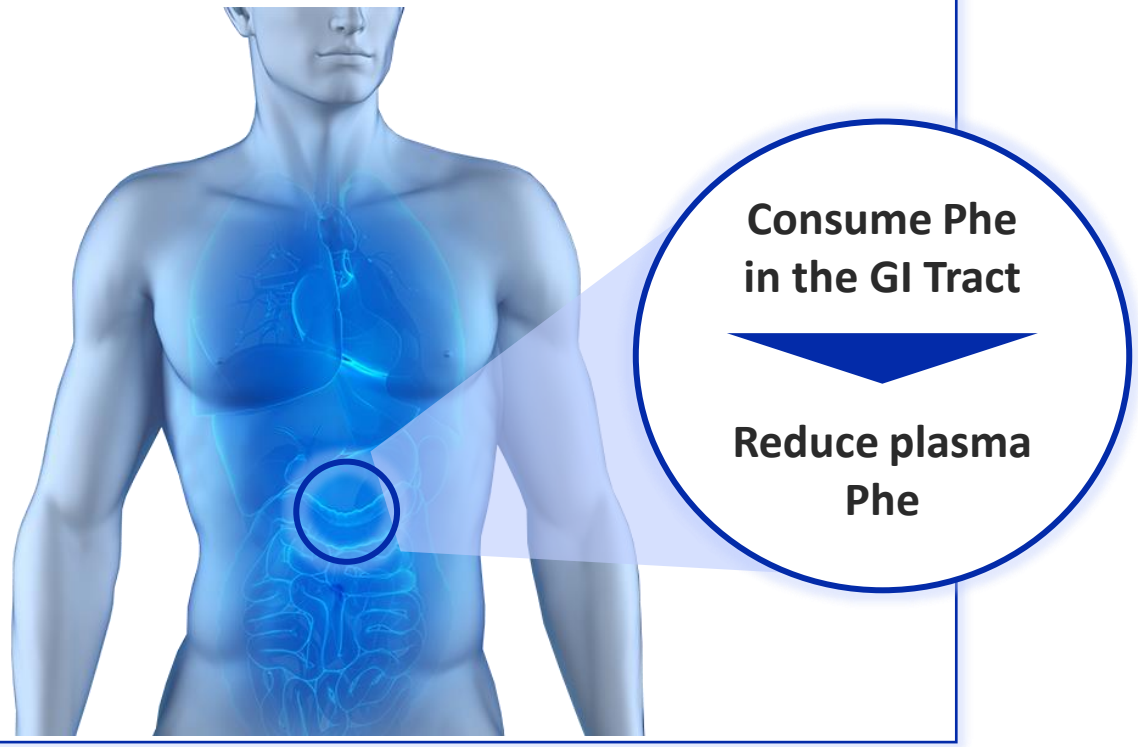
Parents expect PKU child to achieve full potential.

Reality: 25% – 65% of patients still struggle to maintain blood Phe within target range

An innovative approach in area of high unmet medical need

Our approach

Oral therapy,
3 x day with meals



Meaningful biomarker-driven patient outcomes

Lower blood Phe

Addition of more natural protein into the diet

Synlogic has initiated a Ph2 Study in PKU patients (SynPheny)

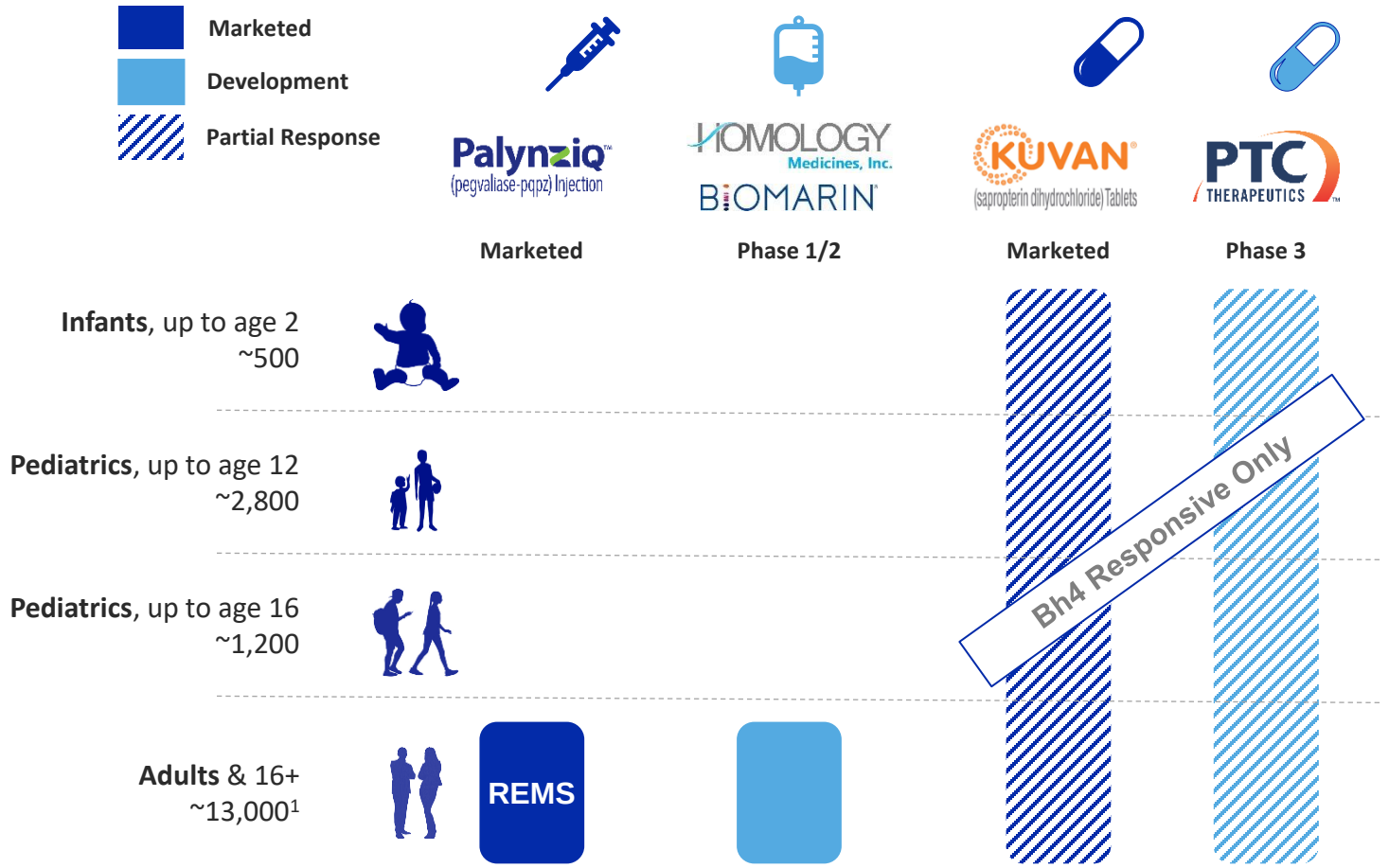
Multiple areas of unmet need continue across PKU patient types

Patients	Disease	Goal	Product Use
Adults ~12,300 U.S. 65% out of Phe control	Out of Phe Control	**Lower blood Phe**	**Monotherapy**
Pediatrics ~5,000 U.S. 25% of out of Phe control	In Phe control	**Addition of more natural protein/day**	**Combination** Prescribed with Kuvan

~70% fail to respond to Kuvan

Significant market opportunity, large unmet need, with potential for new products to capture share

SYNB1618 is uniquely positioned to address those needs



SYNB1618

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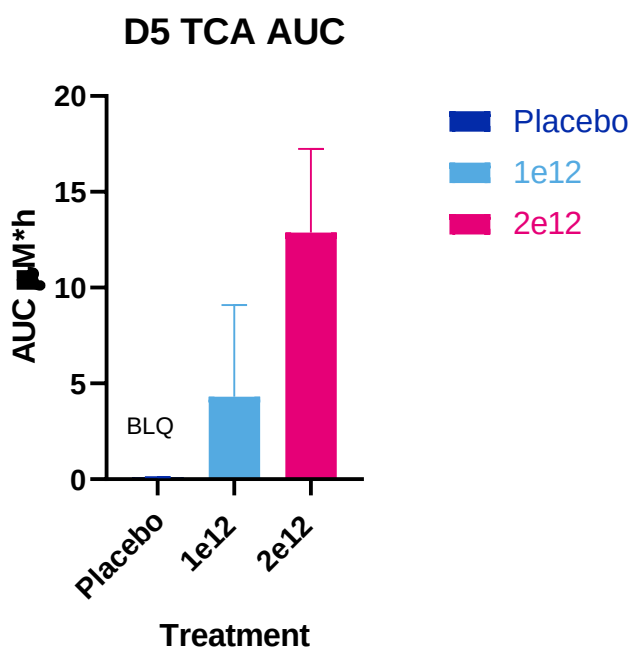
Phase 2

- 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"*

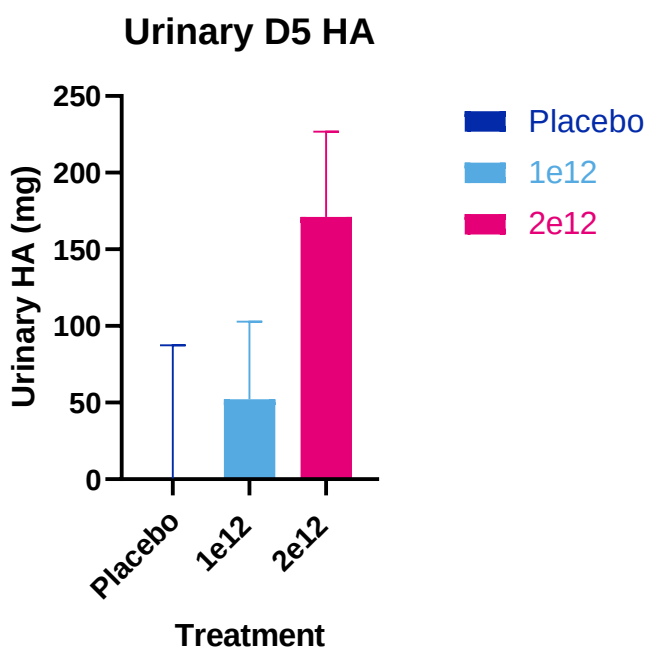
Solid oral SYNB1618 reduced Phe and elevated biomarkers in Ph1

D5 Phe Converted to D5 TCA

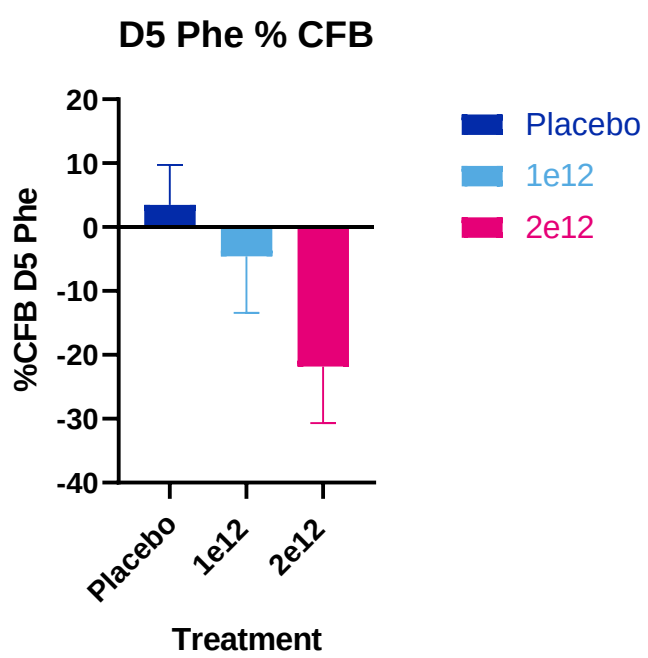


Data are means and 90% CI

D5 TCA Converted to D5 HA



Plasma D5 Phe Blunted

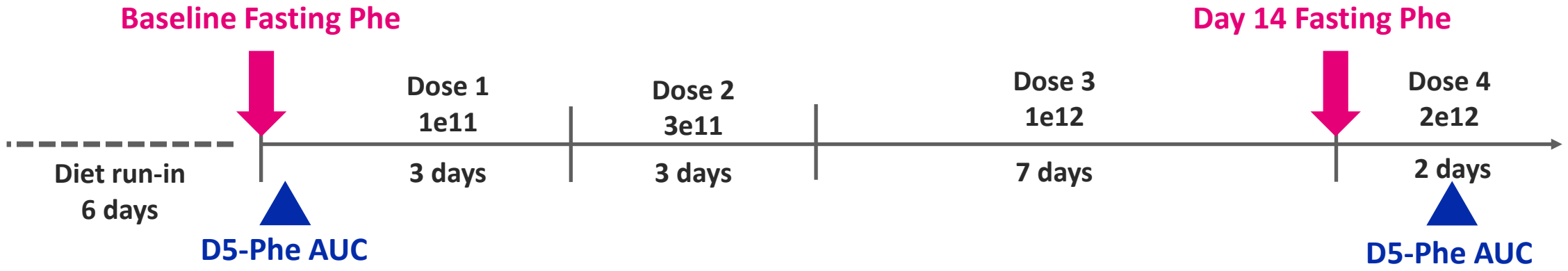


Achieved Proof of Mechanism: SYNB1618 consumed D5 Phe in GI tract & lowered plasma D5 Phe

SynPheny-1 design enables Proof of Concept

synpheny
LIVING IN HARMONY WITH PKU

TRIAL DESIGN



TRIAL OUTPUTS

Phe lowering in patients

Plasma Phe lowering in fasted state at 1e12 live cells over 7 days

Post meal D5-Phe AUC lowering at 2e12 live cells

Strict dietary management to maintain constant Phe intake

Safety & tolerability

Continuously assessed throughout dosing period

N = 12

Validation of PD models

Understand relationship of **strain specific biomarkers** with plasma Phe lowering

Opportunity for multiple clinically relevant outcomes

synpheny
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 study

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

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Enteric Hyperoxaluria (HOX)

Enteric Hyperoxaluria results in significant, irreversible, and progressive kidney damage

SYNB8802 offers potential for best-in-class urinary oxalate lowering

SYNB8802 proof of mechanism established: proof of concept on track for 2021 data read out

Hyperoxaluria: Primary vs. Enteric

	Primary Hyperoxaluria	Enteric Hyperoxaluria
Pathology	Rare genetic condition	Dietary oxalate hyperabsorption
Onset	Pediatric	Adult
Trigger	Genetic liver enzyme deficiency	Underlying insult to bowel: including IBD, bariatric surgery, other chronic GI conditions
UOx. Levels	90 – 500 mg / 24 hrs (~10x normal)	45 – 130 mg / 24 hrs (~3x normal)
U.S. Patients	~5,000 – 8,000	~200,000 – 250,000
Key Players	Dicerna pharmaceuticals; Alnylam PHARMACEUTICALS	Allena PHARMACEUTICALS; synlogic
Clinical consequences	**Limited ability to manage with diet | Nephrocalcinosis | Recurrent, chronic kidney stones | Impaired renal function | Systemic Oxalosis**	

Enteric Hyperoxaluria: An important cause of renal failure

33-Year-Old Female with Crohn's

- 33 yo woman with 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 two 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 remain markedly elevated in all patients, despite aggressive medical regimen

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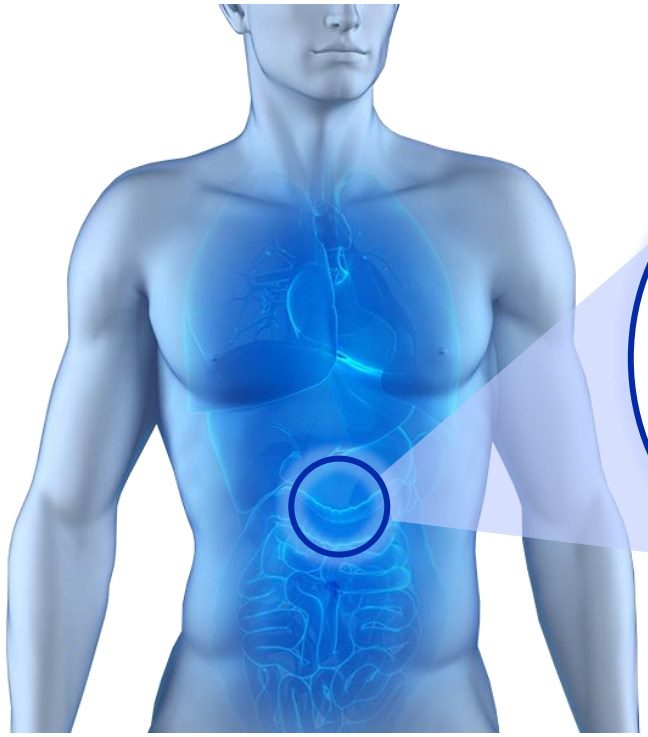
Nazzal et al. Nephrol Dial Transplant 2016

An innovative approach in area of high unmet medical need

Our approach

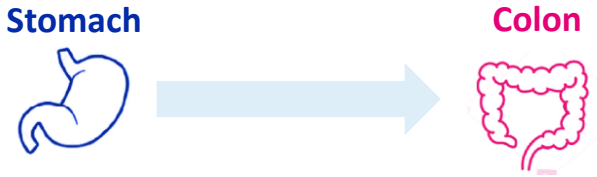
Oral therapy



Consume Oxalate the GI Tract

Reduce Oxalate in the urine

Differentiation from other approaches



Consumes oxalate throughout GI tract

Ph 1B Proof of Concept in Enteric Hyperoxaluria patients (Roux-en-Y population) initiated

SYNB8802 consumes Oxalate throughout the GI tract

Oxalate absorption

Pathway	Absorption		
Dietary Oxalate	Healthy state	Disease state	
Stomach	✓	✓	Healthy people absorb ~10% of dietary oxalate, mostly via stomach and small intestine
Small intestine	✓	✓	
Colon		✓	Patients absorb ~20-30% of dietary oxalate, through entire GI tract including colon

Optimal treatment

synlogic	Oral enzyme	Oxalobacter formigenes
✓	✓	✗
✓	?	✗
✓	✗	✓

Absorbs oxalate throughout GI tract, esp. in colon

Ph1 design provides POC opportunity in 2021

Phase 1A

Dietary Hyperoxaluria (Healthy Volunteers)

Multiple Ascending Dose

High oxalate & low calcium diet run-in

Induce dietary hyperoxaluria

N = 45 subjects

Endpoints

Primary: Safety & tolerability

Secondary: Microbial kinetics of strain

Exploratory: (1) Plasma and urine biomarkers

(2) Dose frequency assessment

Phase 1B

Enteric Hyperoxaluria Patients

Cross-over

Enteric Hyperoxaluria patients (Roux-en-Y population)

Three times/day (TID) dosing

N = 20 patients, baseline UOx >70 mg/day

Endpoints:

Primary: Change in Urinary Oxalate

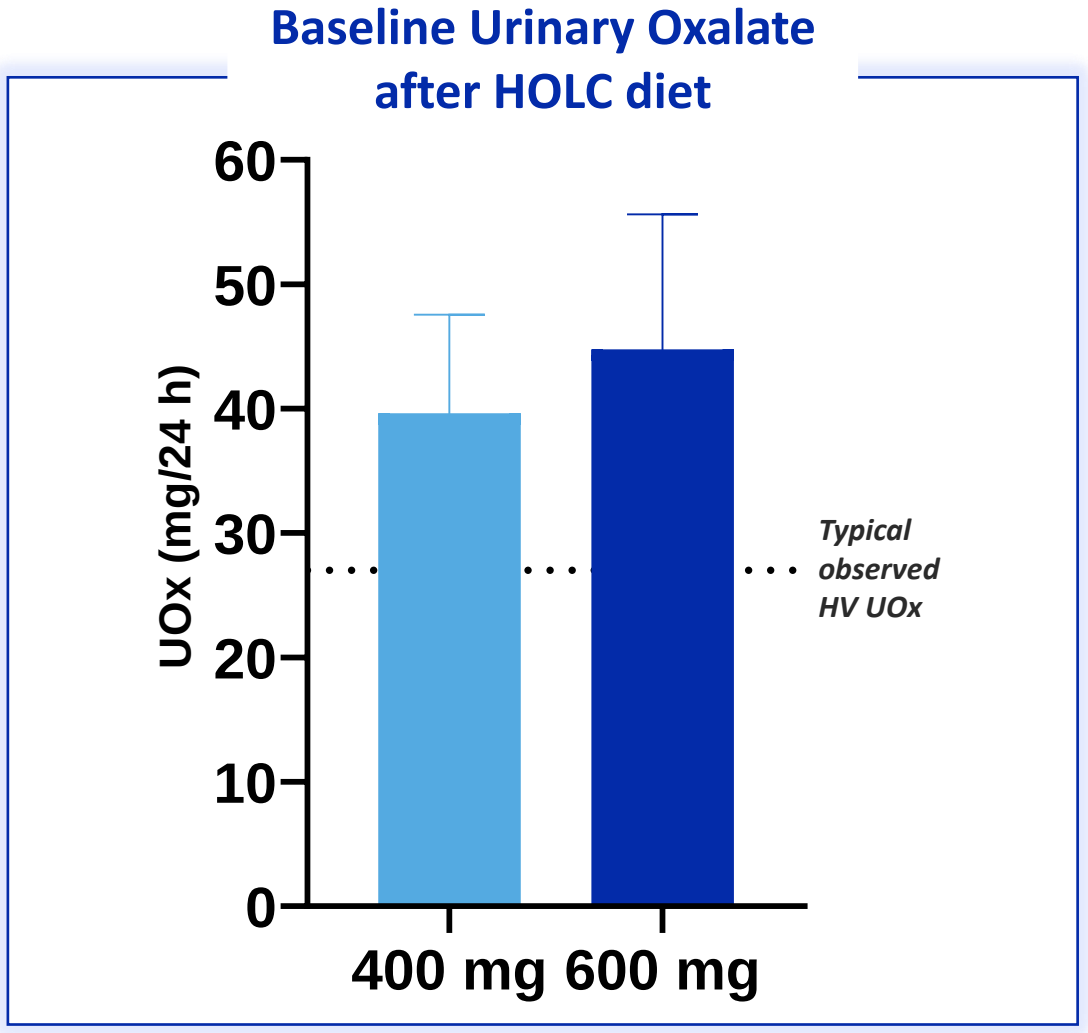
Secondary: (1) Microbial kinetics of strain

(2) Safety and tolerability

Dietary hyperoxaluria model is translationally relevant to patient population

High oxalate diet successfully elevated UOx levels in HV

- American diet contains approx. 200-250 mg oxalate/day
- HV subjects were given a high oxalate, low calcium diet (HOLC) during the diet run-in and treatment phases of the study
- Urinary oxalate levels elevated to >1.5X typically observed in healthy volunteers
- Dietary intake carefully measured on in-patient unit, including weighing of meals consumed

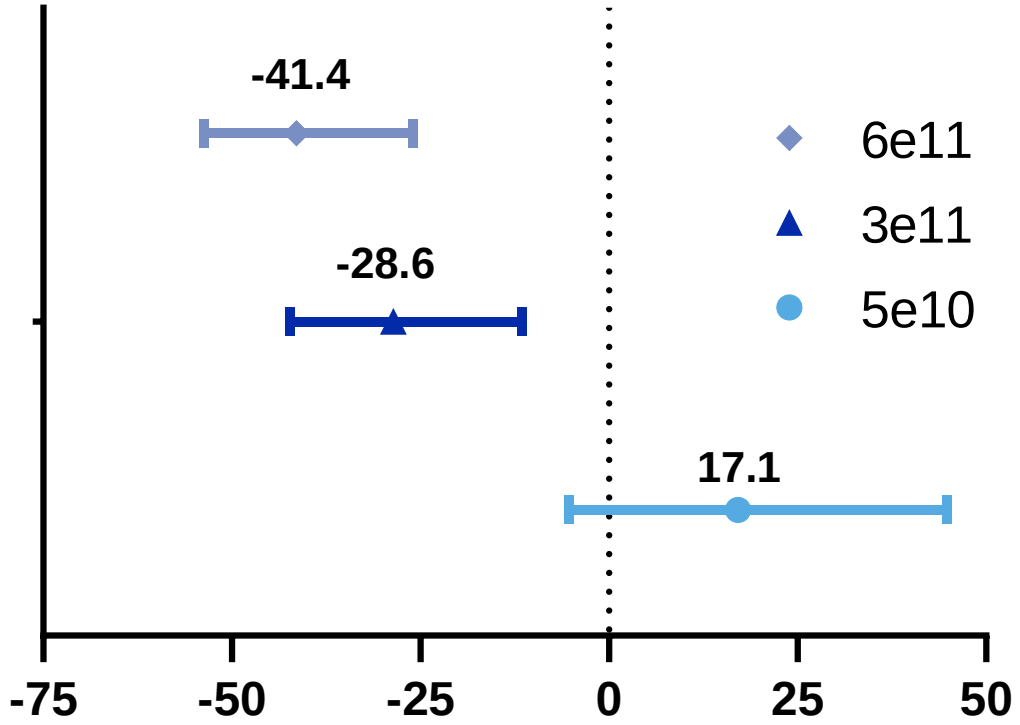


Historically Uox in HV is <40 mg/24h. Examples: Langman 2018, (27 mg), Quintero 2020, (19.8mg), Captozyme 2018 (28 mg). Mean +/- SD shown.

Dose-responsive and reproducible Uox lowering demonstrated

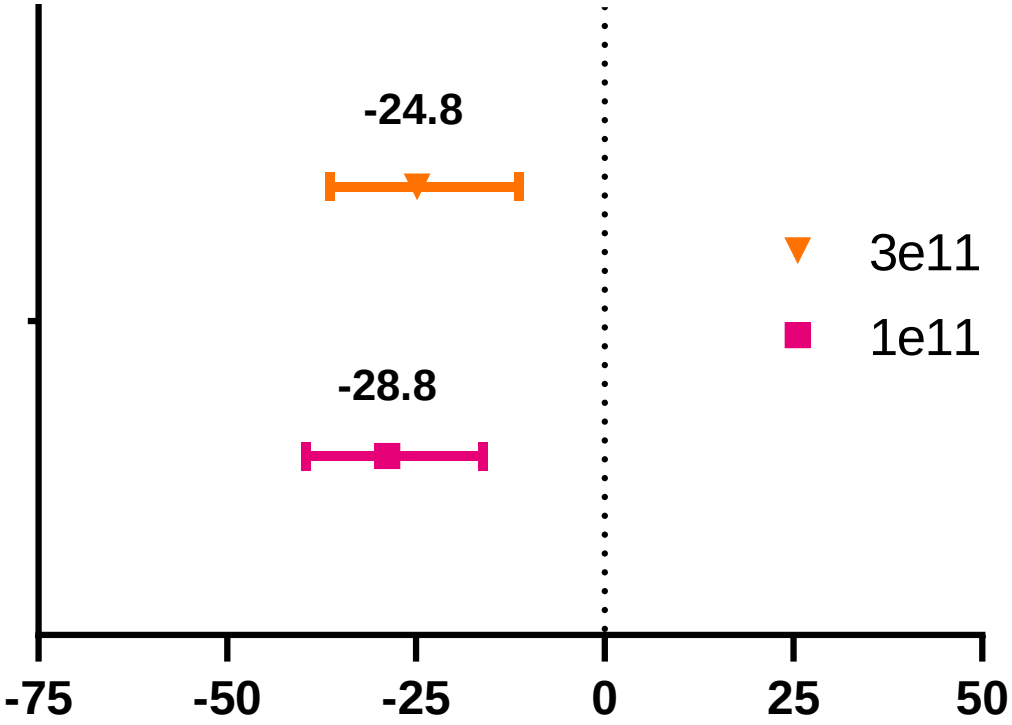
Efficacy Analysis (% Change from Baseline in 24h UOx over Pbo)

600mg Daily Oxalate



Lower is better

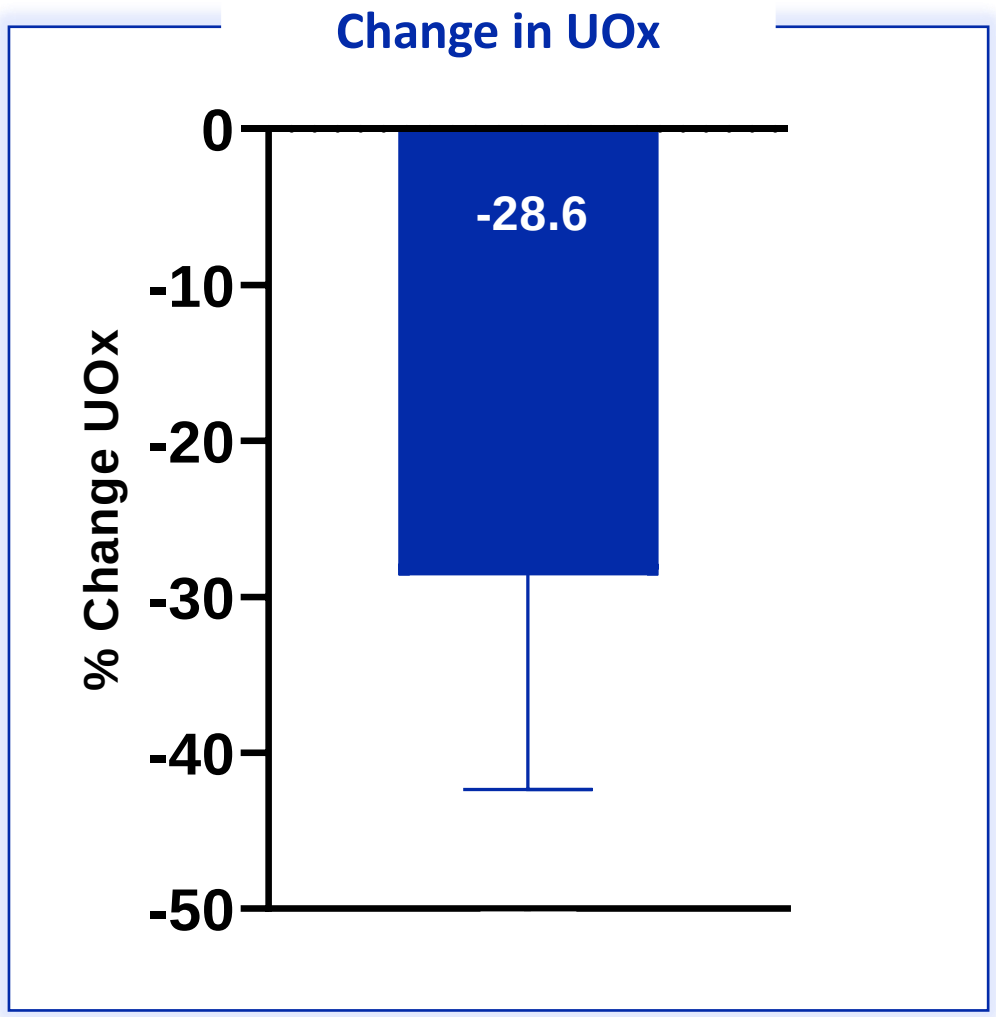
400mg Daily Oxalate

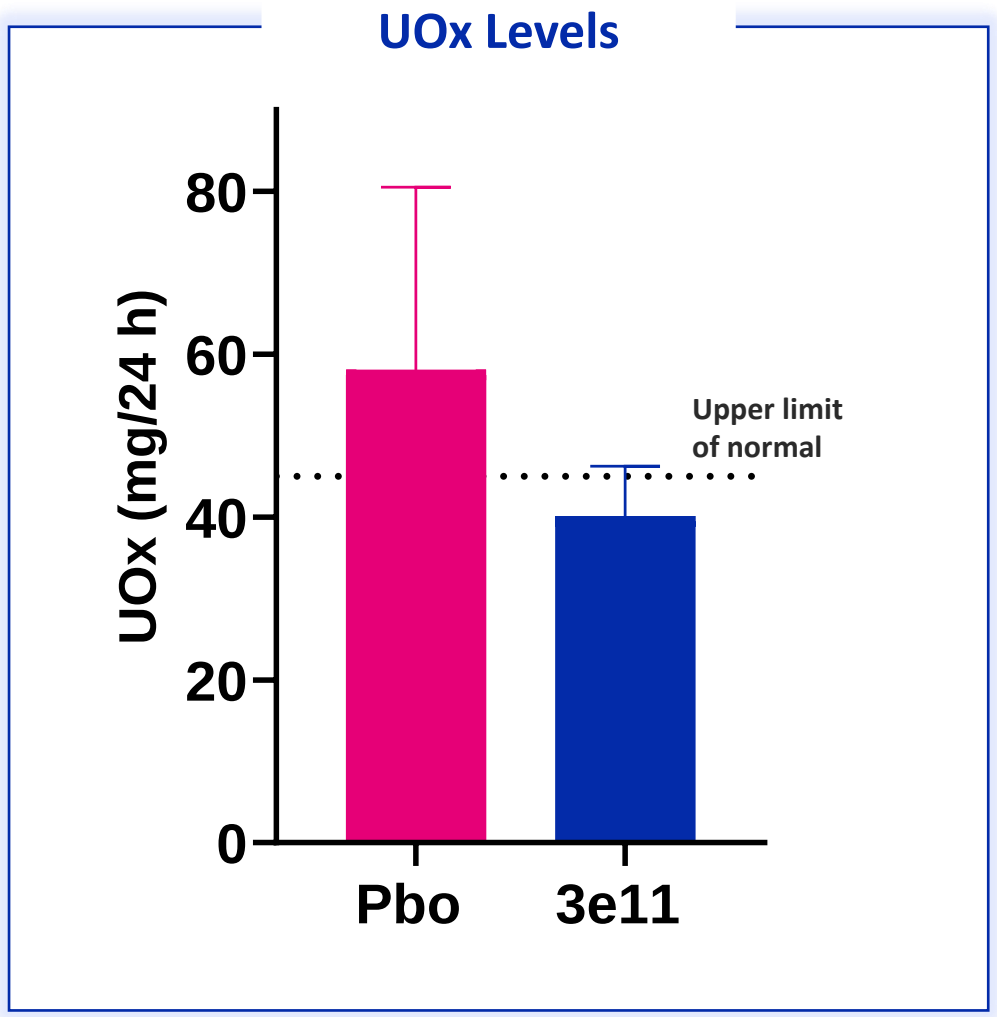


Lower is better

LS mean change over Placebo, +/- 90% CI, all days baseline and treated

SYNB8802 3e11 live cells dose advancing to Ph1B in patients





Clinically meaningful lowering of urinary oxalate demonstrated at a well tolerated dose

LS mean change over Placebo, +/- 90% std error of mean, all days; and 24hr UOx after 5 days of dosing, +/- 90% std error of mean. 600mg daily oxalate.

Opportunity for multiple clinically relevant outcomes in Phase1B

SYNB8802 has established **urinary oxalate lowering** in Dietary Hyperoxaluria (HV) model

Potential for **urinary oxalate lowering** in Enteric Hyperoxaluria population (Roux-en-Y)

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

Learning opportunities in Phase 1

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

SYNB8802 Summary: 3e11 live cells moving into patients

- SYNB8802 was generally well tolerated in healthy volunteers. No serious or systemic adverse events. Most frequent AEs mild or moderate, transient, and GI-related
- Dose responsive changes in urinary oxalate levels were observed with a significant reduction in urinary oxalate relative to placebo across three dose levels
- Baseline urinary oxalate reduction of 28.6% compared to placebo
- Mean 24-hour urinary oxalate level of 40.1 mg for subjects, compared to 58.1 mg for placebo, at the end of dosing
- 3e11 live cells dose will advance to patient studies

Synlogic is entering a data rich period in the clinic

		H1 2021	H2 2021
PKU	Ph2 SynPheny proof of concept read-out		SYNB1618
Enteric Hyperoxaluria	Ph1A study in HV read-out	SYNB8802	
	Initiate Ph1B study in patients	SYNB8802	
	Ph1B proof of concept read-out		SYNB8802
Immuno-Oncology	Ph1 Arm 2 combination read-out		SYNB1891

Robust portfolio with significant clinical readouts in 2021

Strong balance sheet. Funding through near-term milestones

Summary Results

Balance Sheet (unaudited)	31 Dec 2020	31 Dec 2019
Cash, Cash Equivalents, and Marketable Securities	$100.4 M	$127.1M

	Three Months Ended		For the Year Ended	
Statement of Operations (unaudited)	**31 Dec 2020**	**31 Dec 2019**	**31 Dec 2020**	**31 Dec 2019**
R&D Expenses	$11.4 M	$11.3 M	$47.5 M	$41.9 M
G&A Expenses	$3.3 M	$3.5 M	$13.5 M	$14.7 M
Net Loss	$(14.6 M)	$(12.8 M)	$(59.2 M)	$(51.4 M)
Net loss per share – basic and diluted*	$(0.39)	$(0.37)	$(1.65)	$(1.70)
*Weighted Average Shares Outstanding**	*37.8 M*	*34.2 M*	*35.8 M*	*30.3 M*

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

Experienced leadership team and Board

Leadership Team

Aoife Brennan, MB ChB
President & CEO

Richard Riese, MD PhD
Chief Medical Officer

Dave Hava, PhD
Chief Scientific Officer

Antoine Awad
Chief Operating Officer

Caroline Kurtz, PhD
Chief Development Officer

Daniel Rosan
Head of Finance & Investor Relations

Board of Directors

Peter Barrett, *Chair*
Atlas Venture

Mike Burgess
Turnstone Biologics

Michael Heffernan
Collegium

Patricia Hurter
Lyndra Therapeutics

Lisa Kelly-Croswell
Boston Medical Center Health System

Chau Khuong
Orbimed Advisors

Nick Leschly
Bluebird Bio

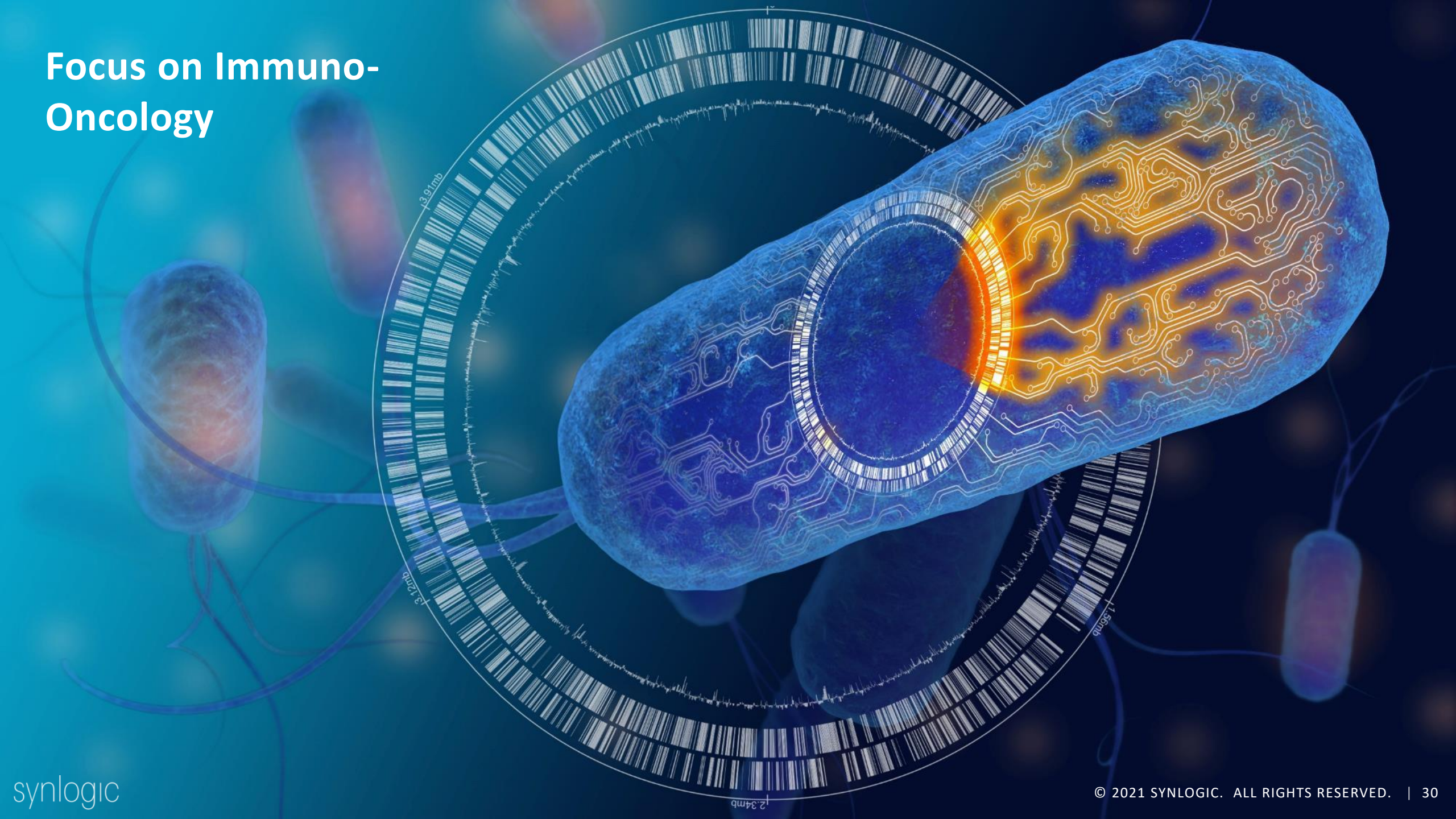
Ed Mathers
NEA

Richard Shea
Syndax

Collaborators

GINKGO BIOWORKS
THE ORGANISM COMPANY

Focus on Immuno-Oncology



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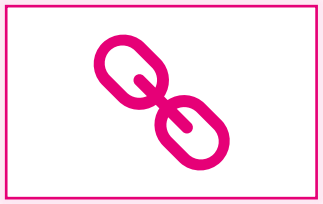
Synthetic Biotic medicines are well-suited to regulating the immune system

Why immunology?

Unmet Medical Need

Rationale

Need for **novel treatments which upregulate (I/O) or downregulate (IBD)** immune responses

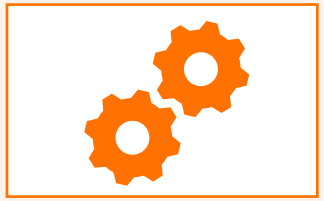


Cross-talk between bacteria and Immune System

Immune system has evolved to recognize bacteria

Bacteria have **evolved mechanisms** to control the immune response

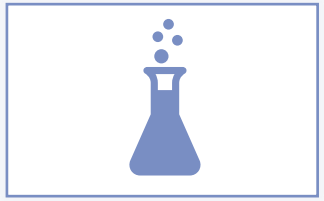
Why Synthetic Biotic medicine?



Unique Advantages

Multiple effectors can be **delivered to site of disease** from single strain

Targeted efficacy and improved safety



Platform attributes

Preclinical **POC for both immune stimulation and immunoregulation**

Multiple approaches (small molecules, peptides, human cytokines) available

Immuno-Oncology

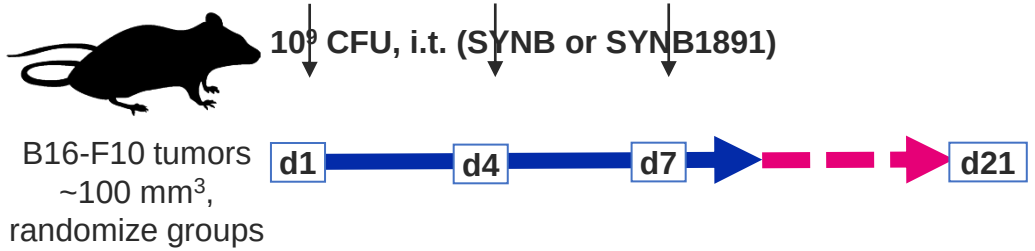
SYNB1891 potential for improved efficacy relative to other STING approaches

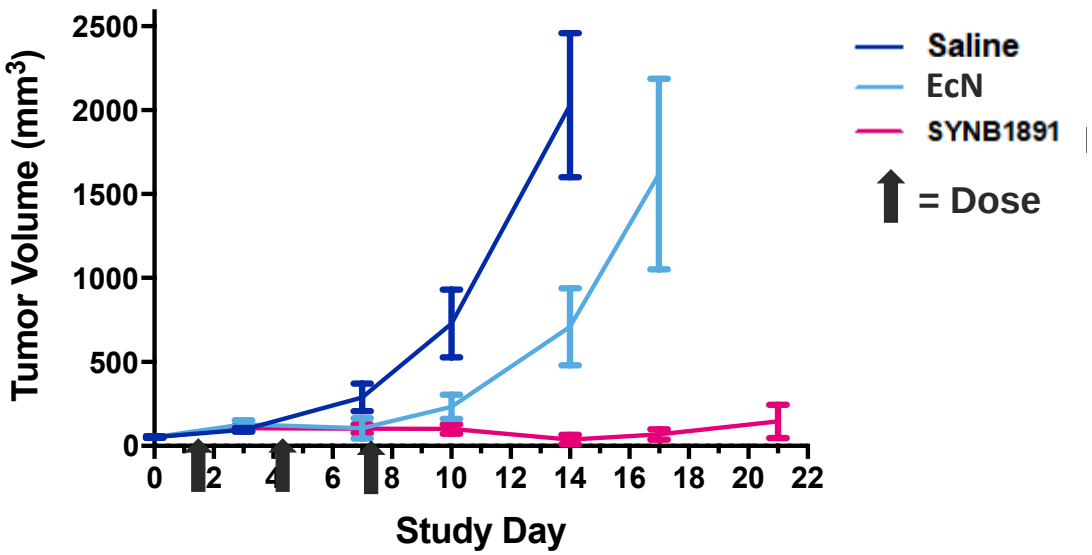
SYNB1891 monotherapy demonstrated meaningful pharmacodynamic effects

Phase 1 in combination with Tecentriq initiated: Data will be available in 2021

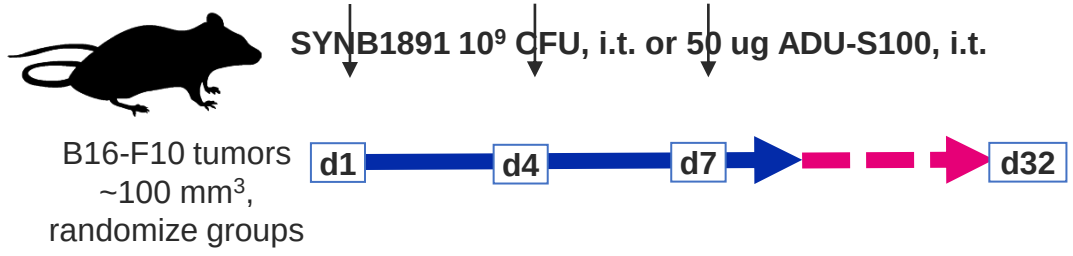
SYNB1891 induces potent anti-tumoral effects

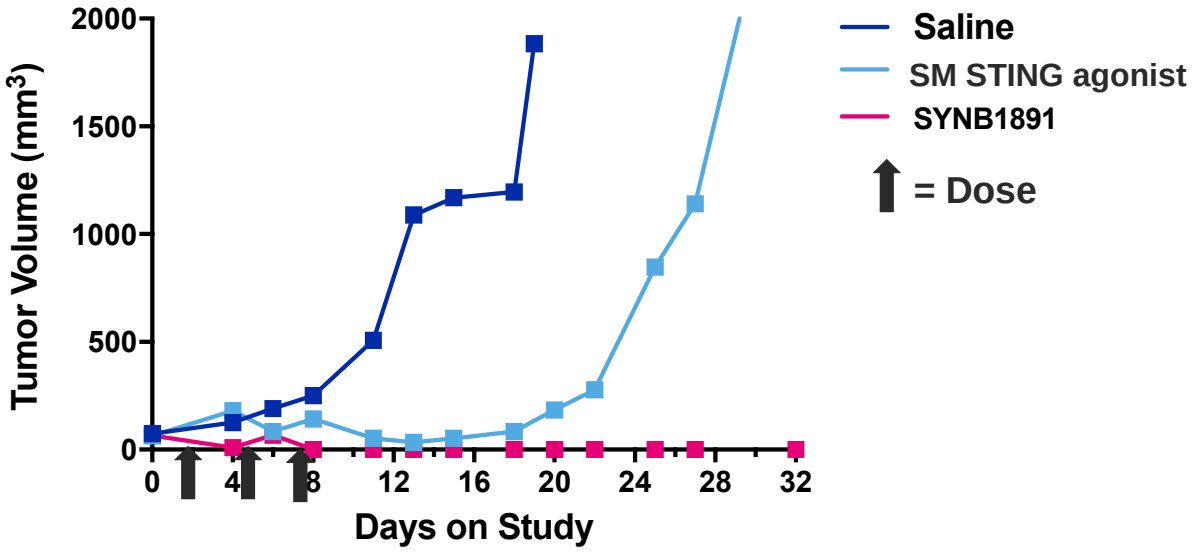
SYNB1891 superior to wild type EcN





SYNB1891 superior to small molecule STING



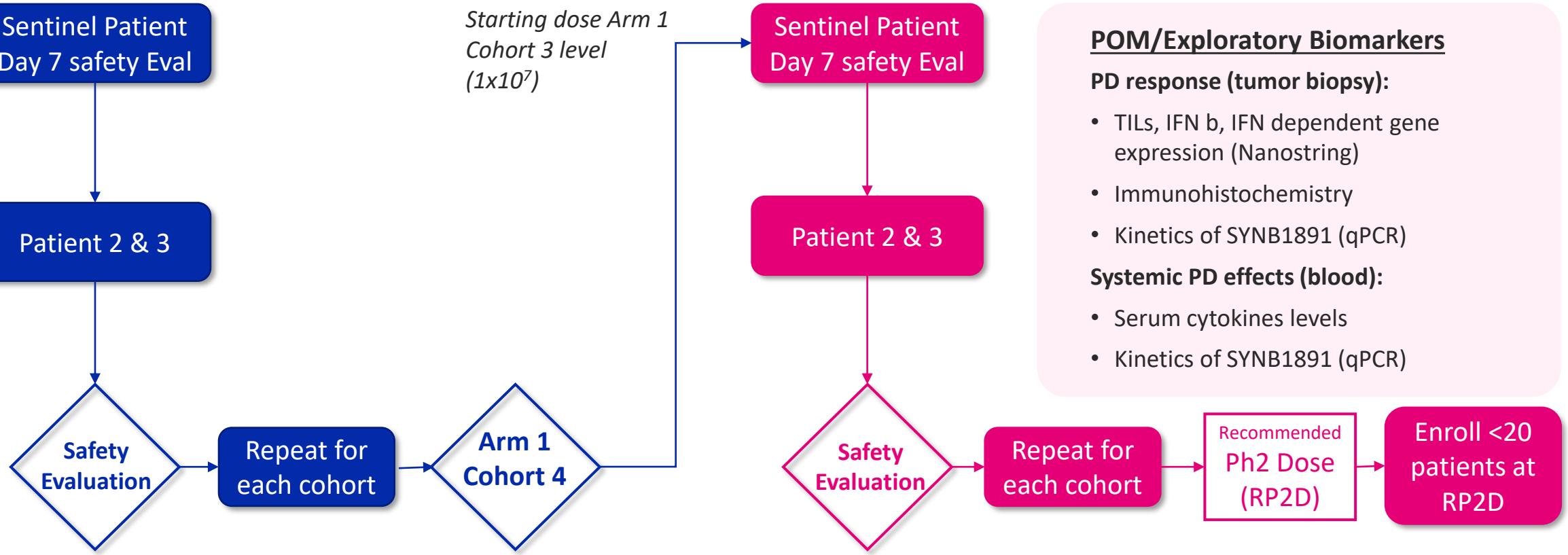


Phase 1 design: multidose tolerability, IT mono and combo

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)
- Immunohistochemistry
- Kinetics of SYNB1891 (qPCR)

Systemic PD effects (blood):

- Serum cytokines levels
- Kinetics of SYNB1891 (qPCR)

Combination with PD-1 will identify Phase 2 dose, provide evidence of target engagement, safety, and support for target tumor type

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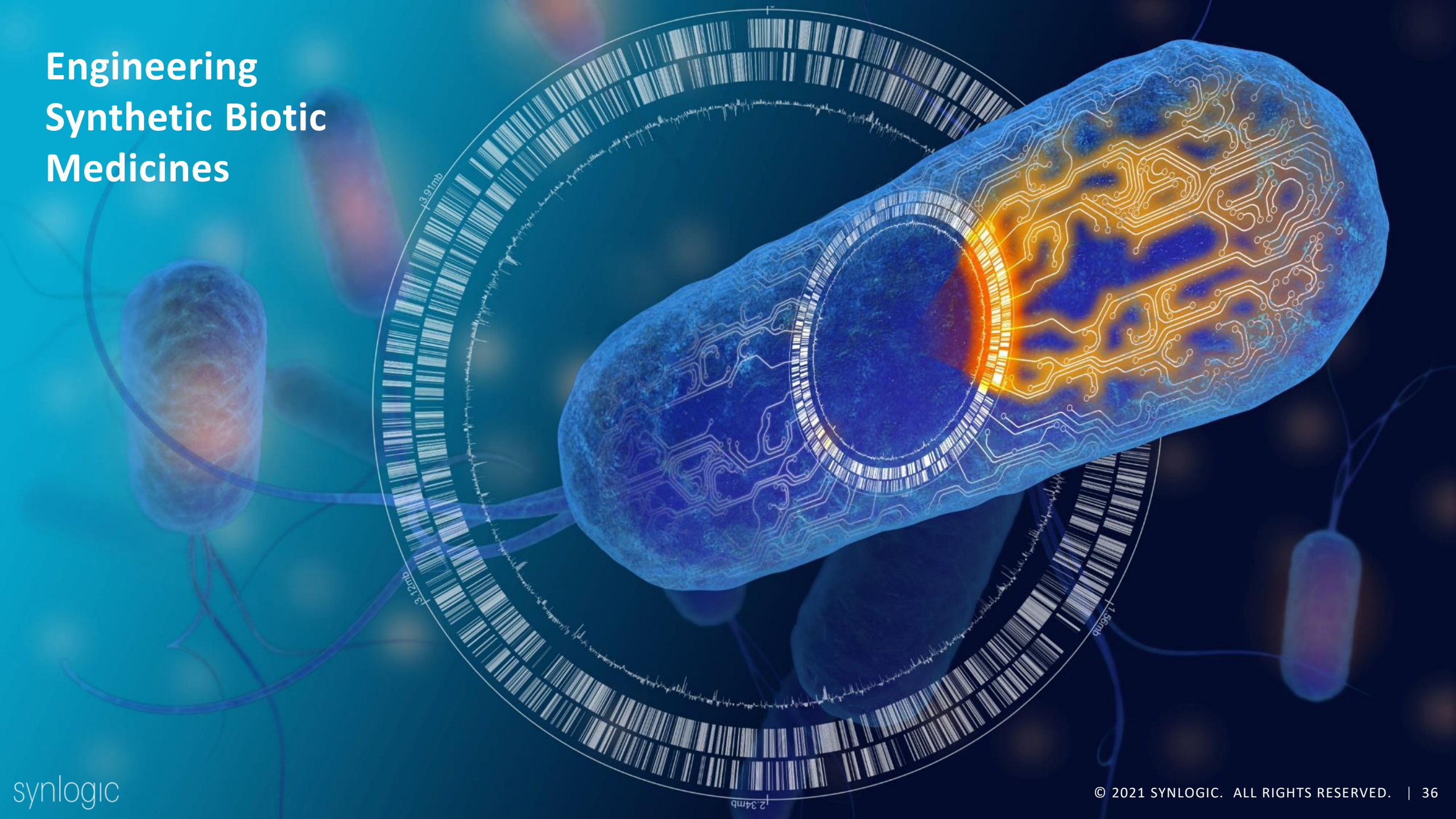
SYNB1891 advanced into combo. therapy arm of Ph. 1 with Tecentriq

- 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 late 2021**

Engineering Synthetic Biotic Medicines



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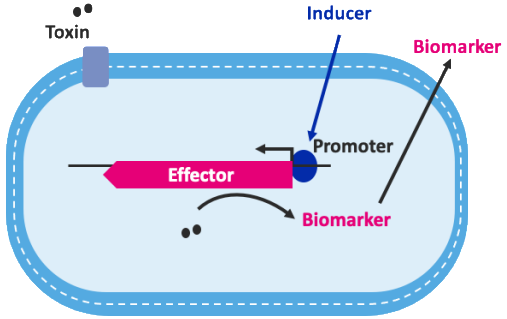
A new class of medicines

Non-pathogenic bacterial chassis

E. coli Nissle

+

Programable, controllable engineering



Inducer-Promoter Switch

Effector Design

Safety Features

=

Synthetic Biotic Medicine

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- Drug-like properties
- Does not colonize
- No *in vivo* reproduction or risk of genetic drift

Reusable parts enable rapid iteration of rationally designed prototypes

Synthetic Biotic Platform accelerates pathway into the clinic

Target selection

Unmet medical need

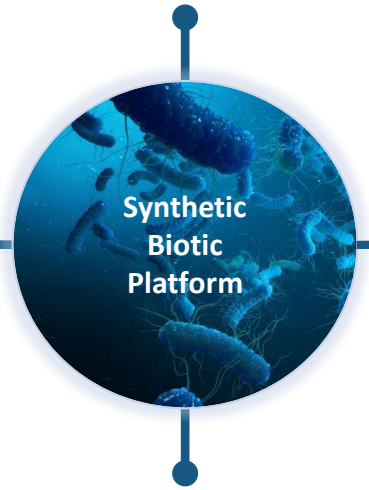
Validated biology

Unique SYBX advantages

Enabling Engine

Deep synthetic biology expertise

Modular SynBio components



Internal GMP manufacturing

Translational, clinical and regulatory

Resulting portfolio

Metabolic pipeline:
Metabolite consumption in the GI tract

Immunology pipeline:
Potential for partnership

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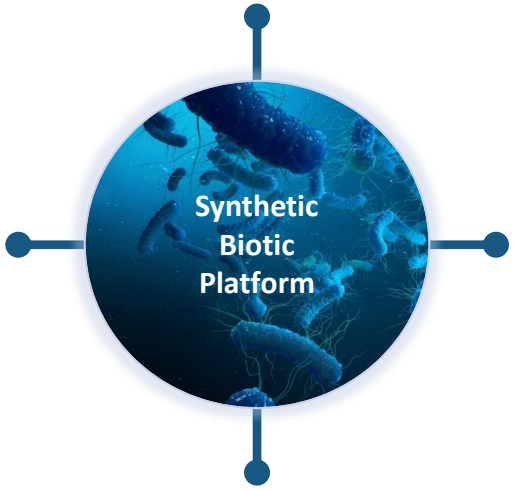
Synthetic Biotic Platform is enabling engine for drug development

Deep synthetic biology expertise:
Internal + Ginkgo Bioworks



Translational, clinical and regulatory experience for live biotherapeutic medicine

Modular SynBio components enables rapid, iterative product development

Internal process development and GMP manufacturing of live biotherapeutic

>200 humans dosed with Synthetic Biotic medicines

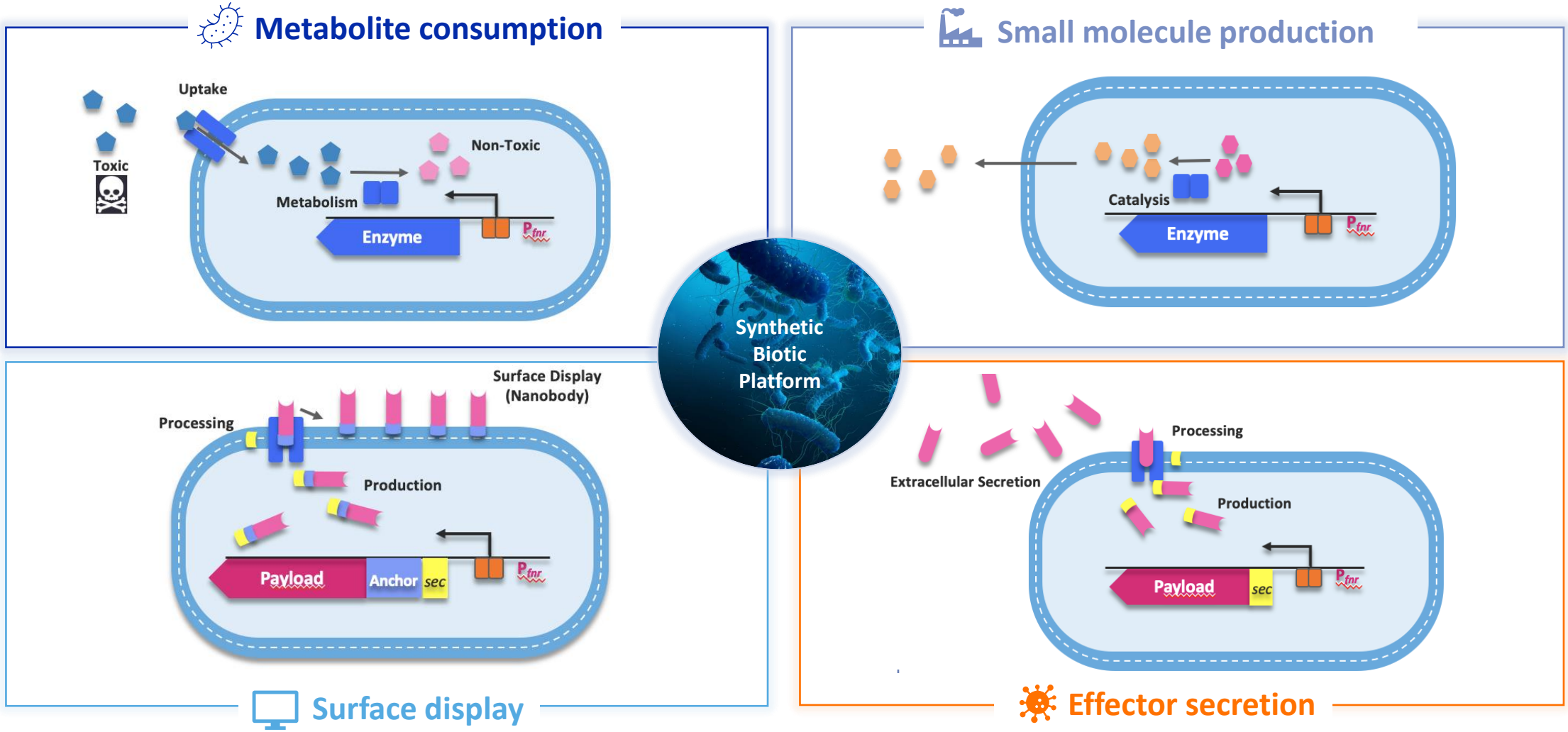
4 INDs opened with the U.S. FDA

Supportive regulatory feedback from global agencies

Safe chassis organism (>100 years of human experience)

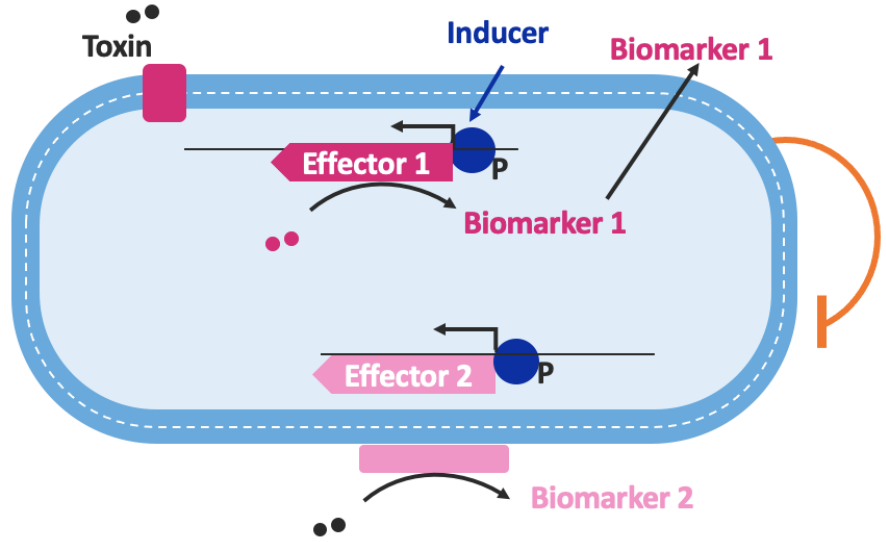
Rapid pipeline expansion possible with reusable engineering

Versatile platform enables diverse therapeutic strategies for range of diseases



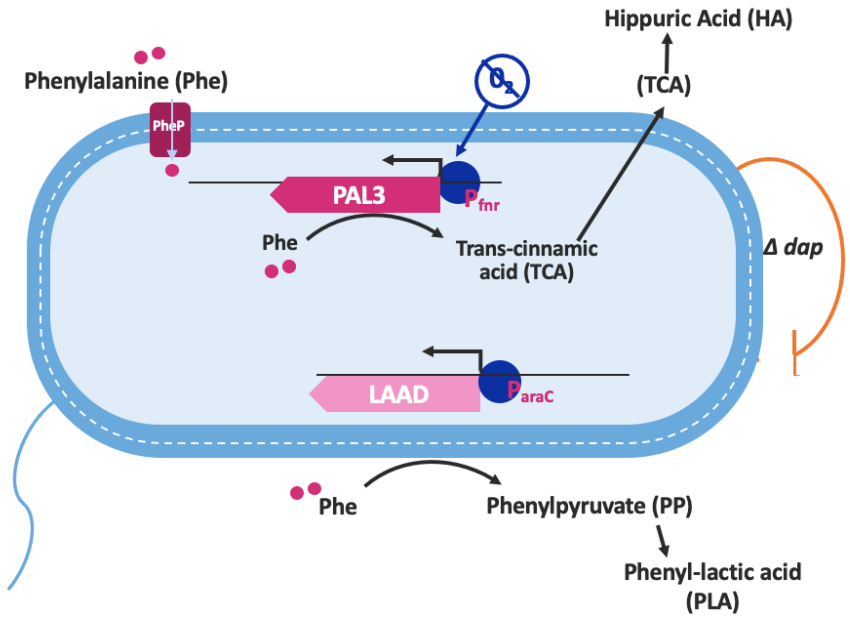
Reusable parts enable rapid iteration of rationally designed prototypes

Component	Library of parts
Therapeutic strategy	Metabolite consumption, small molecule production, effector secretion or surface display
Bacterial Chassis	Probiotic: Decades of human use & safety data
Effector(s)	Proteins for activity: Can generate biomarkers
Pump	Transports metabolites or proteins across cell membrane
Switch	Inducer-promoter pair: Controls gene expression
Safety Features	Auxotrophies: Prevents growth within or external to the body



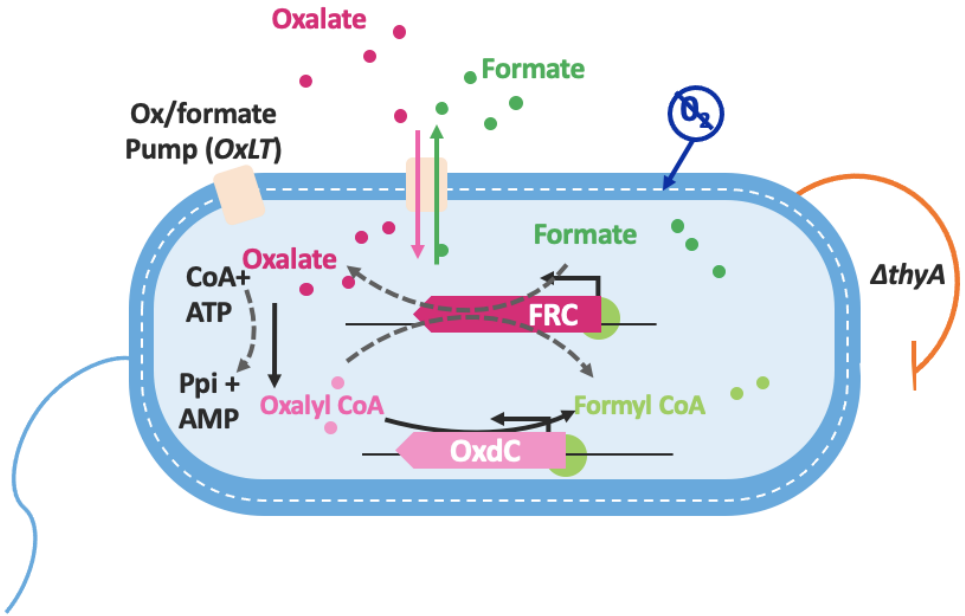
SYNB1618 Design

Component	SYNB1618 Design
Therapeutic strategy	**Metabolite consumption:** Built from Synthetic Library Specifically to Consume Phe
Bacterial Chassis	***E. coli* Nissle**
Effector(s)	***PAL3* Enzyme:** Degrades Phe to TCA (measurable biomarker of activity) ***LAAD* Enzyme:** Alt. Phe-consuming pathway
Pump	***PheP:*** Pumps Phe into cell
Switch	**FNR & AraC promoter:** Control expression during manufacturing and at site of action
Safety Features	***Δ dap:*** Auxotrophy – requires diaminopimelic acid (DAP) to grow



SYNB8802 Design

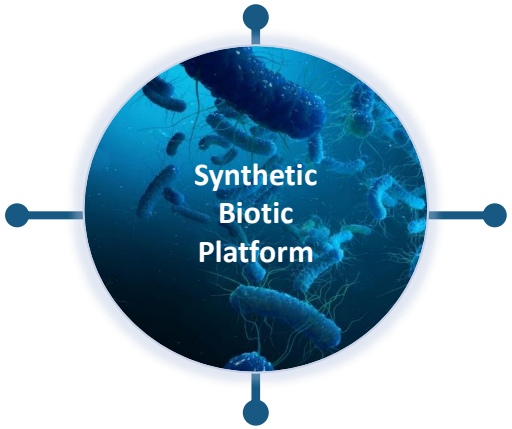
Component	SYNB8802 Design
Therapeutic strategy	**Metabolite consumption:** Engineered to Convert Oxalate to Formate for the Treatment of Enteric Hyperoxaluria
Bacterial Chassis	***E. coli* Nissle**
Effector(s)	***OxdC and associated components:*** Catalyzes conversion of oxalate to formate
Pump	***OxLT:*** Pumps oxalate in & formate out
Switch	**FNR promoter:** Inducer-promoter pair
Safety Features	***Δ thyA:*** Controls growth



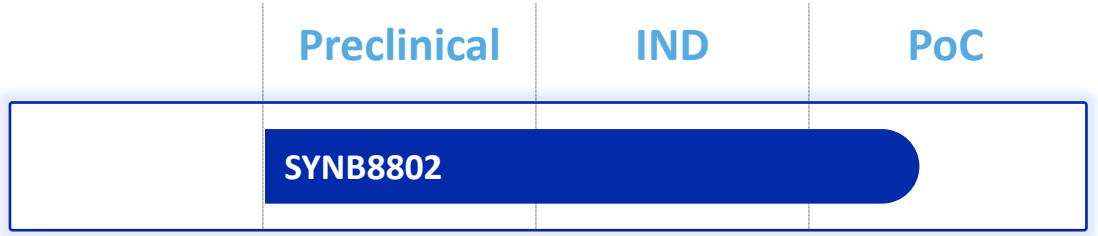
Reusable parts enables rapid progress to proof of concept: SYNB8802 case study

Target selection

Proprietary platform



Product Candidate



10 months from target selection to IND

PoC within 1 year

Planning

- ✓ Target with low toxic metabolite load, validated biology

Research & Synthetic Biology

- ✓ Re-use engineering parts
- ✓ Apply validated in vitro models

Product Development

- ✓ Leverage internal process development, quality, and manufacturing

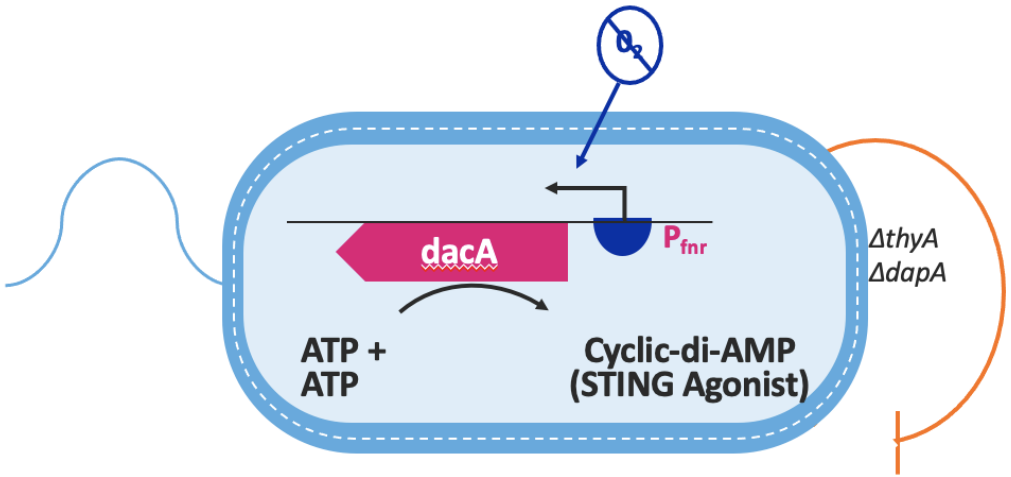
Clinical Development

- ✓ De-risk in healthy volunteers
- ✓ Rapid path to patient PoC: data expected H2 2021

Portfolio of metabolic opportunities available with similar engineering

SYNB1891 Design

Component	SYNB1981 Design
Therapeutic strategy	**Small molecule production:** Leveraging the ability of bacteria to interact with the immune system to turn a cold tumor hot
Bacterial Chassis	***E. coli* Nissle:** Targeting to antigen presenting cells in the tumor microenvironment. Innate immune activation
Effector(s)	**STING Agonist:** Innate immune activator compounds with chassis effect
Pump	Not necessary
Switch	STING-agonist production restricted to hypoxic TME for sustained payload delivery
Safety Features	Dual auxotrophies inhibit bacterial proliferation outside of tumor



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