UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 20, 2021

SYNLOGIC, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-37566**	**26-1824804**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

301 Binney St., Suite 402 **Cambridge, MA**	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 401-9975

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	**SYBX**	**The Nasdaq Capital Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging Growth Company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On September 20, 2021, Synlogic, Inc. (the "Company") provided slides to accompany its press release announcing positive data from clinical studies evaluating both SYNB1618 and SYNB1934, investigational Synthetic Biotic™ medicines for the treatment of Phenylketonuria (PKU) (the "Press Release"). A copy of the slides is furnished as Exhibit 99.1 to this Current Report on Form 8-K. The Company has also updated its investor presentation (the "Investor Presentation"), which the Company expects to use in connection with general corporate presentations and will be made available on the Company's website or distributed by the Company in hardcopy or electronic form. A copy of the updated Investor Presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K. The Investor Presentation is current as of September 20, 2021, and the Company disclaims any obligation to update the Investor Presentation after such date.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

On September 20, 2021, Synlogic issued the Press Release which is filed as Exhibit 99.3 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	Slide Presentation of Synlogic, Inc. dated September 20, 2021
99.2	Investor Presentation of Synlogic, Inc. dated September 20, 2021
99.3	Press release dated September 20, 2021
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Synlogic, Inc.

Date: September 20, 2021

By: /s/ Gregg Beloff
Name: Gregg Beloff
Title: Interim Chief Financial Officer

Exhibit 99.1

synlogic

Designed for Life

Phenylketonuria Clinical Program Update

20 September 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 August 12, 2021, 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 could 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.

Our Program Today

01 **Interim Analysis of SYNB1618 Phase 2 SynPheny-1 Study**
Dr. Aoife Brennan, CEO

02 **SYNB1934 Phase I Data, Dose Cohorts 1-3**
Dr. David Hava, CSO

03 **Platform Implications and Next Steps in PKU**
Dr. Aoife Brennan, CEO

04 **Q&A**
Management Team

Progress in Phenylketonuria

Dr. Aoife Brennan, MB CHB
President & CEO

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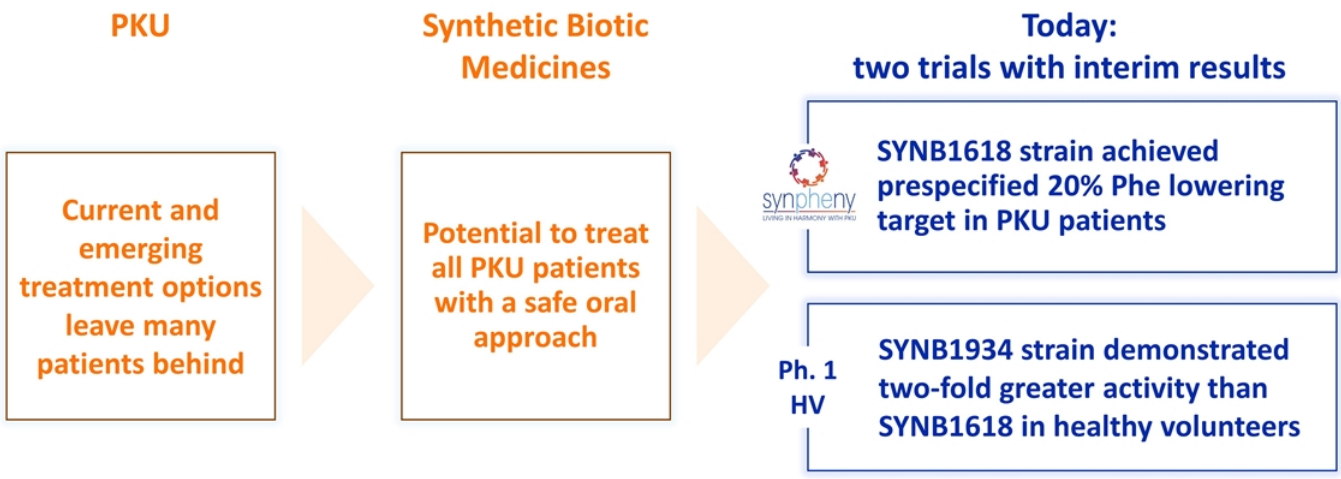
Synthetic Biotic Medicines: a novel approach in Phenylketonuria (PKU)



PKU remains an area of high unmet need

Patients

Julia,
living with PKU

Pediatrics
~5,000 U.S.

25% out of Phe control

Adults
~12,300 U.S.

65% out of Phe control

90% of patients and caregivers express need for greater natural protein intake [1]

Challenges

- Extremely challenging low protein diet with **low compliance**
- Substantial need for increased intake of **natural protein** enabled by Phe reductions
- Significant risk of **neurocognitive impairment** in patients with elevated Phe levels

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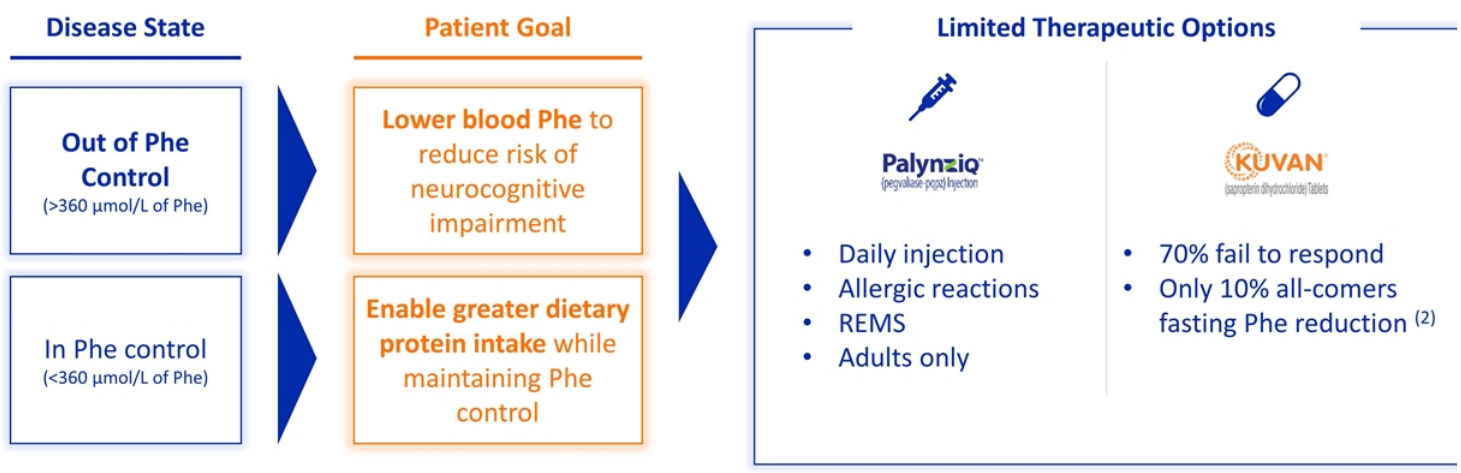
[1] Puurunen et al, Global PKU Patient Meeting, September 2021

PKU patients are poorly served today



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

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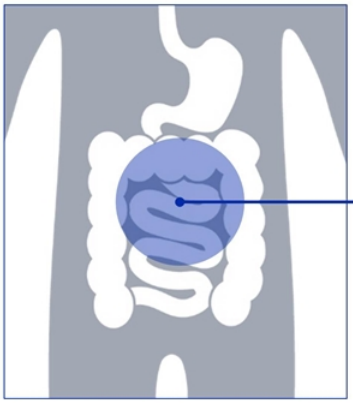
(2) Kuvan FDA statistical review, 25 Nov 2007

Synthetic Biotic Medicines: Differentiated product candidates for the treatment of PKU

Synthetic Biotic medicines for the treatment of PKU present a compelling opportunity to change patients' lives

Intuitive and direct approach to treating PKU

Oral therapy,
3 x day with meals



Dietary Phe

Converted by Synthetic Biotic to harmless metabolites (TCA)

Reduce plasma Phe *or* enhance protein tolerance

Unique mechanism of action generates quantitative, measurable biomarker of Phe metabolism: TCA (trans-cinnamic acid)

Interim Analysis of SYNB1618 SynPheny-1 Phase 2 Study in PKU

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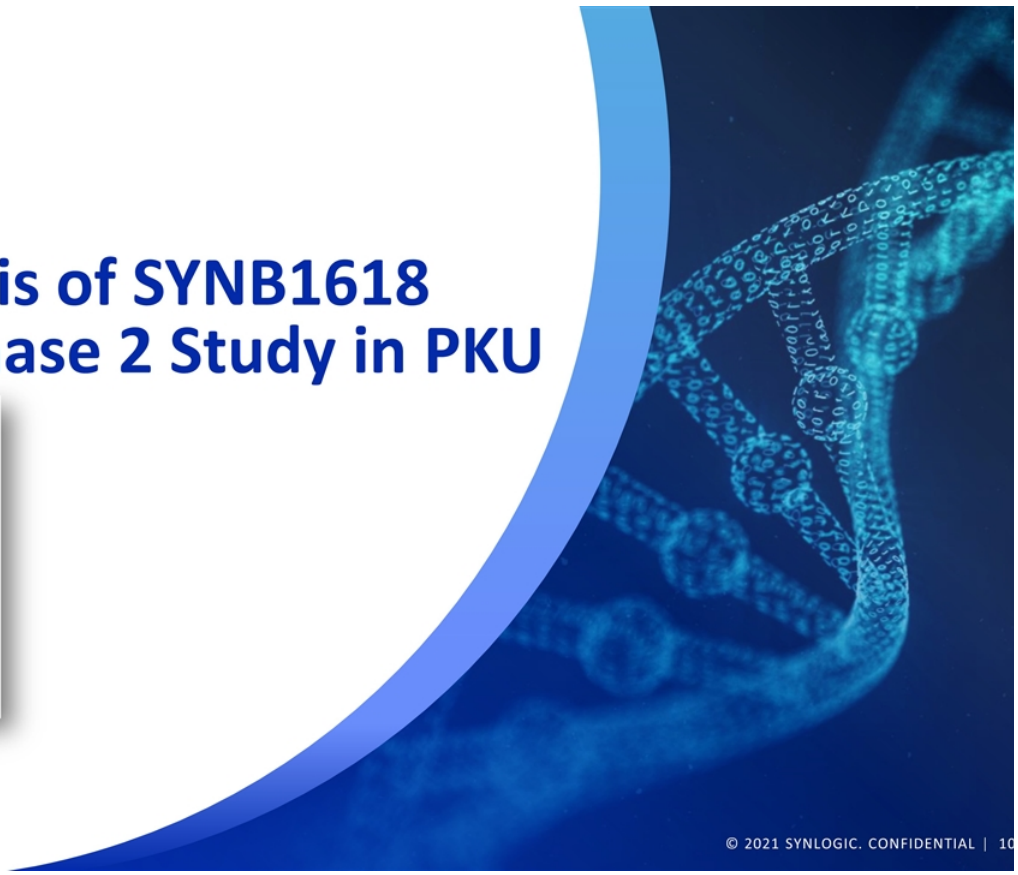
LIVING IN HARMONY WITH PKU



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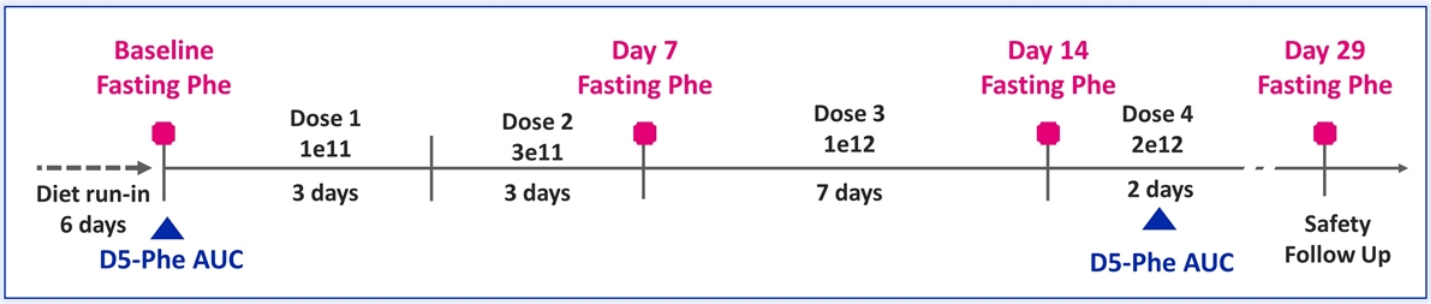
SYNB1618 Phase 2 SynPheny-1 study in PKU: Design



Population

- IA of 8 subjects receiving SYNB1618
- Adult PKU patients, plasma Phe levels ≥ 600 µmol/L
- Stable diet
- No use of Kuvan or Palynziq

Endpoints

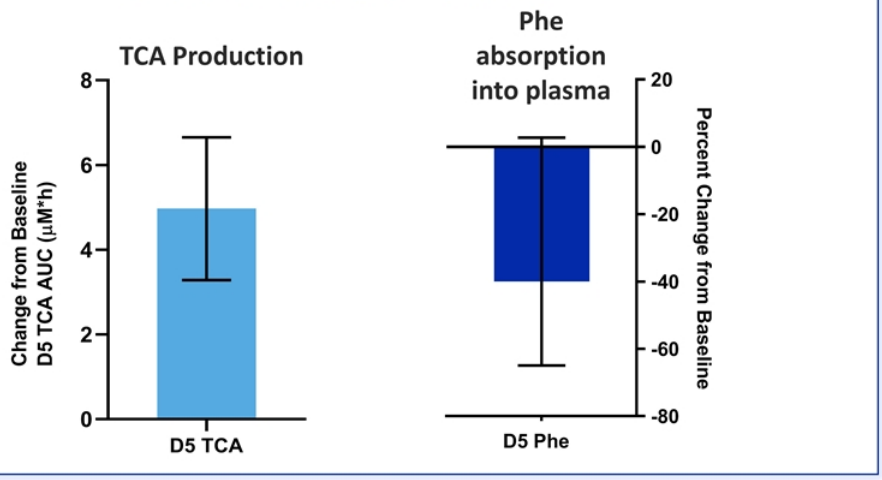
- Fasting Plasma Phe levels (day -1, 7, 14, 29)
- Labelled D5-Phe 24hr AUC, change from baseline after meal challenge (day -1, 15)

Diet Control

- 6-day diet run in
- Individualized diet plan to match baseline Phe intake
- Stable study diet: diet run-in through 2 weeks post treatment

SYNB1618 metabolized Phe into TCA and prevented Phe absorption after meal challenge

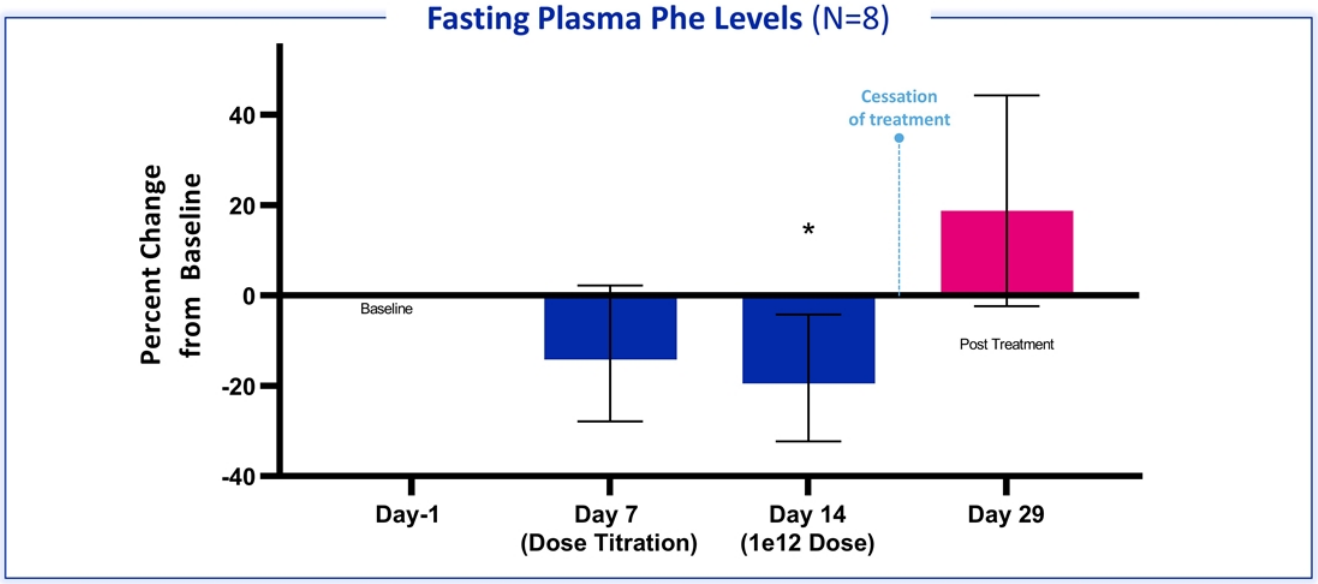
D5 Phe Meal Challenge
(2e12 dose, N=8, Days -1 and 15)



4 of 8 patients experienced >40% D5-Phe lowering after meal challenge

Percent change from baseline +/- 95% confidence interval. TCA = trans-cinnamic acid. AUC = Area under curve.

SYNB1618 reduced fasting plasma Phe levels



4 of 8 patients experienced **>30% reduction** in fasting Plasma Phe at Day 7 or Day 14

Percent change from baseline +/- 95% confidence interval. * = Statistically significant

Summary of interim safety analysis

Gut restricted	Generally well tolerated	No treatment-related discontinuations
Clearance upon cessation of dosing as expected	Tolerability profile **consistent with experience** in healthy volunteers **Mild to Moderate GI AEs**	**No SAEs** or new safety issues identified

Safety analysis cut-off: 30 July 2021. Includes all patients (N = 9) through Day 15. Does not include Day 29 assessments for all patients. One discontinuation for anxiety, not drug related.

SYNB1934 Phase 1 Study Results

Dr. David Hava, PhD
Chief Scientific Officer

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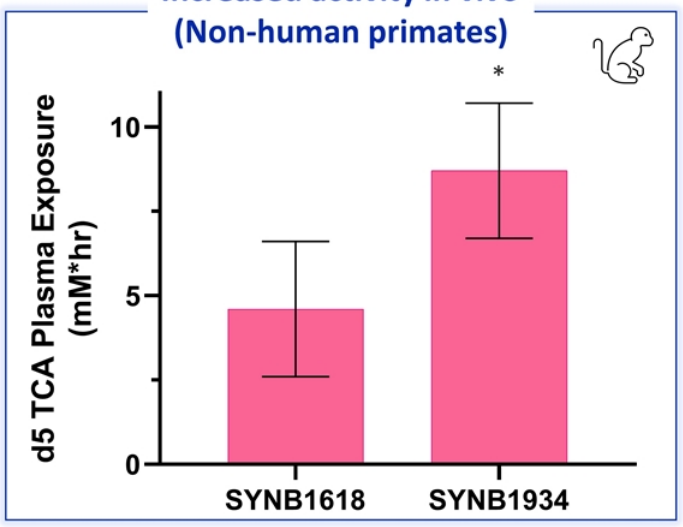
Synthetic biology platform optimized activity of therapeutic strain

SYNB1934

- Developed from SYNB1618 using directed evolution of PAL3 enzyme in whole cell assay
- Potential to provide increased Phe lowering activity and flexibility to optimize clinical profile

Increased activity *in vivo*
(Non-human primates)



Increased activity two-fold in non-human primates using directed evolution approach

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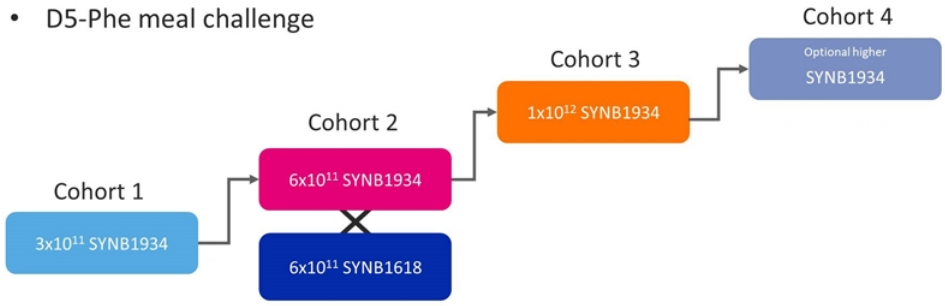
Monahan et al, SEED 2021. * = Statistically significant. Error bar is mean +/- standard deviation.

SYNB1934 Ph. 1 study allows head-to-head comparison of strains

Study Design

- Four-day dose ramp, two days dosing
- D5-Phe meal challenge

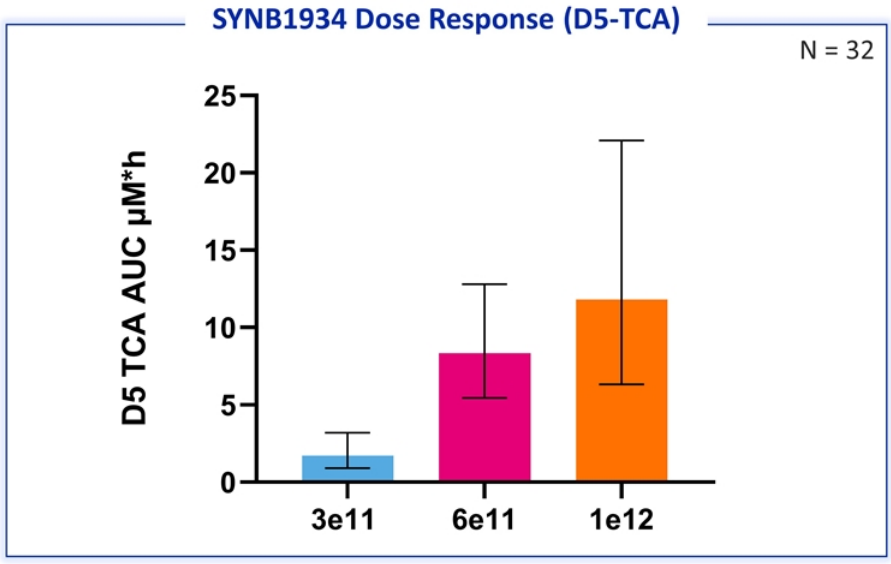


Endpoints

- Safety and tolerability
- Biomarkers of Phe consumption
- SYNB1934 clearance after cessation of dosing

Study will determine if SYNB1934 has improved activity over SYNB1618

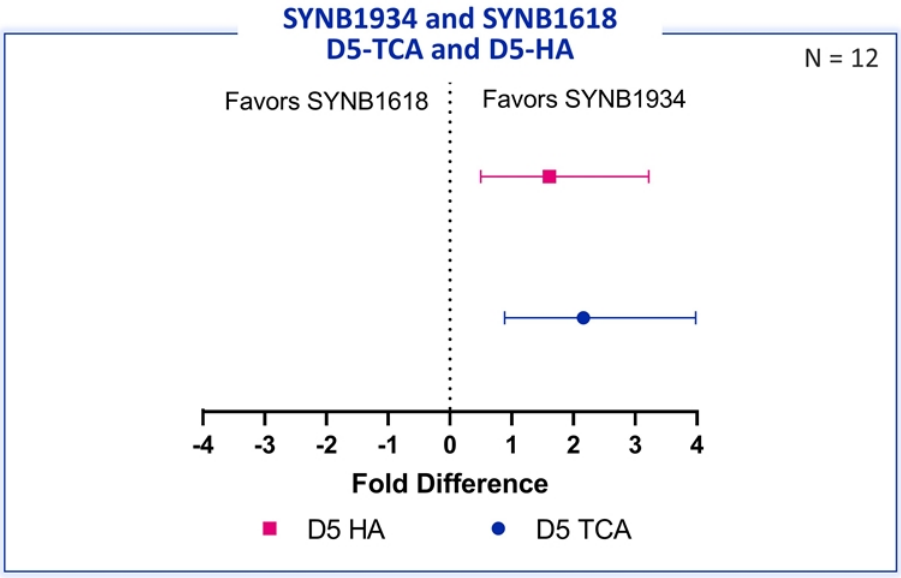
SYNB1934 metabolized labeled D5-Phe in a dose dependent manner



SYNB1934 exhibited clear and consistent dose responsive activity in humans

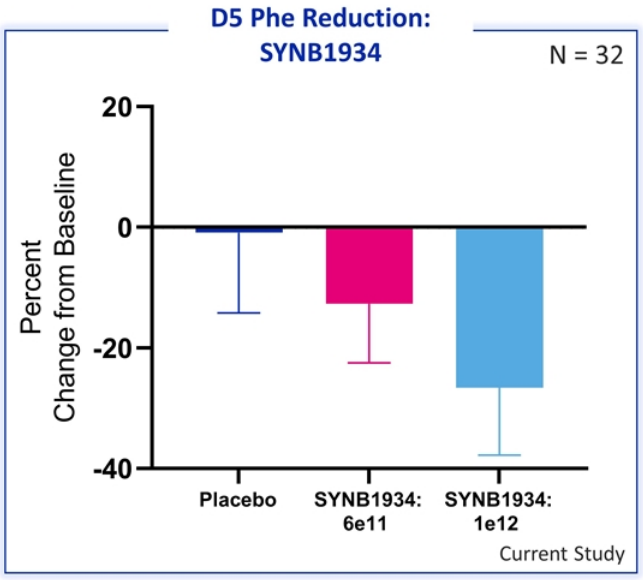
Mean +/- 90% confidence interval. TCA = *trans*-cinnamic acid

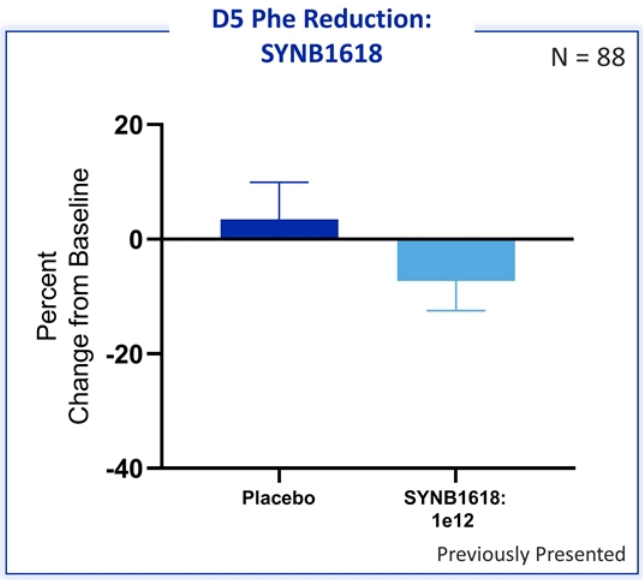
SYNB1934 demonstrated two-fold improvement over SYNB1618 in biomarkers of Phe metabolism



Mean +/- 90% confidence interval. TCA = *trans*-cinnamic acid HA = hippuric acid

Robust labeled D5-Phe reduction in healthy volunteers at multiple dose levels





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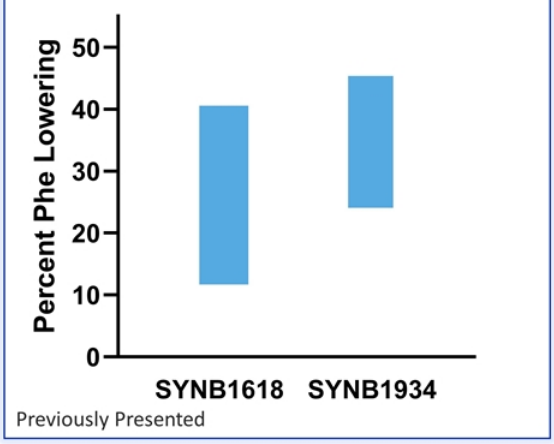
Percent change from baseline +/- 90% confidence interval. Cross study comparison. N = total study (all cohorts)

Prospective modeling for SYNB1618 predicted clinical activity

Prospective Model Results
(1e12 Live Cells)



Previously Presented

SYNB1618 Modeling	Clinical Observation
Model predicted **15-40%** Phe lowering with SYNB1618 1e12 dose	Mean **20%** Phe lowering with SYNB1618 at 1e12 dose
Model predicted **20-45%** Phe lowering with SYNB1618 at 2e12 dose	Mean **40%** Phe lowering with SYNB1618 at 2e12 dose after meal challenge

Prospective biomarker driven modeling suggests SYNB1934 provides opportunity for increased Phe lowering

synlogic Model range represents relative activity of enzymes: PAL and LAAD

SYNB1934 to be evaluated in new arm of SynPheny-1 study

	Healthy volunteers	PKU Patients
SYNB1618 1e12 dose	**7%** D5-Phe reduction post-meal	**20%** Fasting plasma Phe
SYNB1934 1e12 dose	**27%** D5-Phe reduction post-meal	***Expectation of improved clinical profile***

Portfolio Implications and Next Steps in PKU

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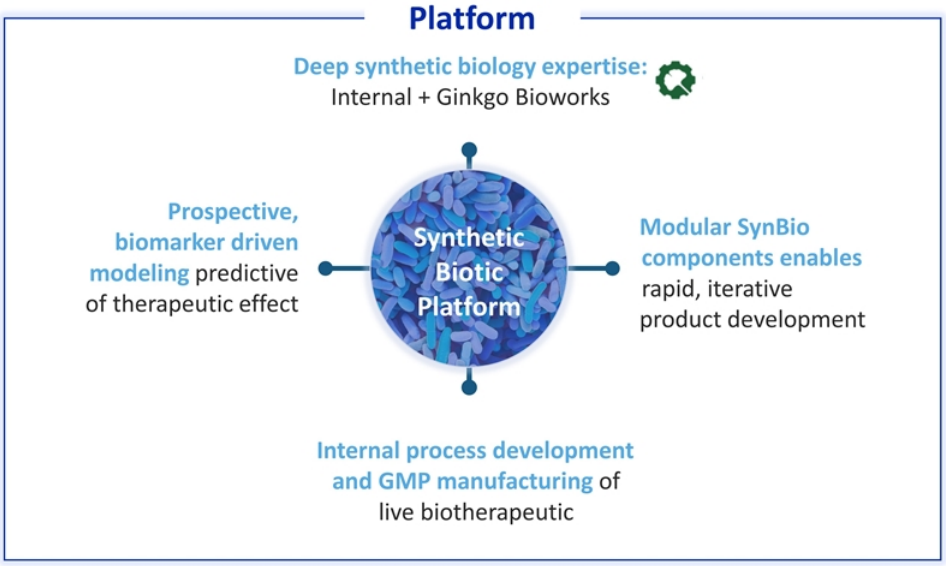
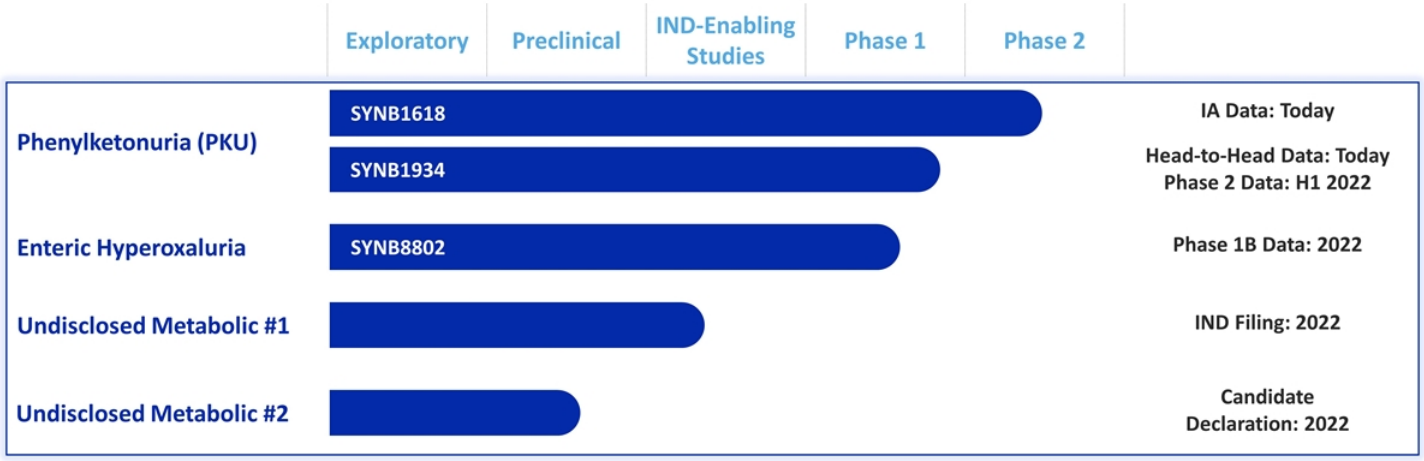
Synthetic Biotic Platform is enabling engine for drug development



- Prospective modeling defines target product profiles
- Optimization of strains creates compelling clinical profiles
- Integrated translational and manufacturing capabilities enables rapid path to and through clinic

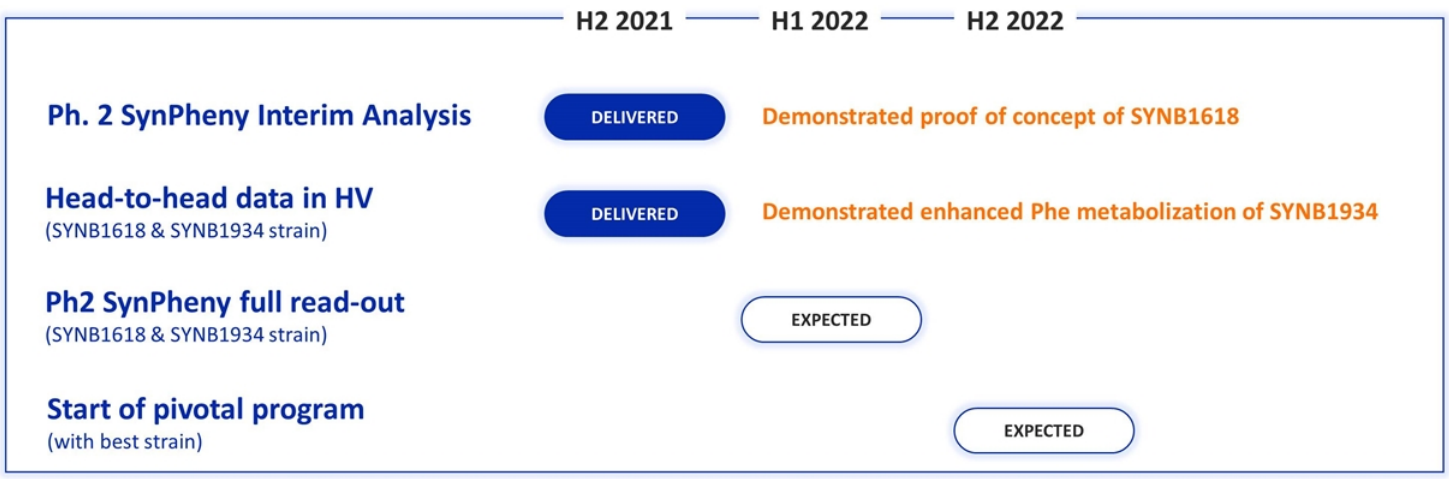
Integrated platform can repeatedly and rapidly generate optimized clinical candidates

Synthetic Biotic platform enables portfolio of high value metabolic indications



We are applying biomarker driven predictive modelling and strain optimization across the portfolio of metabolic indications

PKU program to rapidly advance towards pivotal program



Significant additional value inflection points in PKU program in 2022

Synthetic Biotic Medicines: a novel approach in Phenylketonuria (PKU)

synpheny
LIVING IN HARMONY WITH PKU

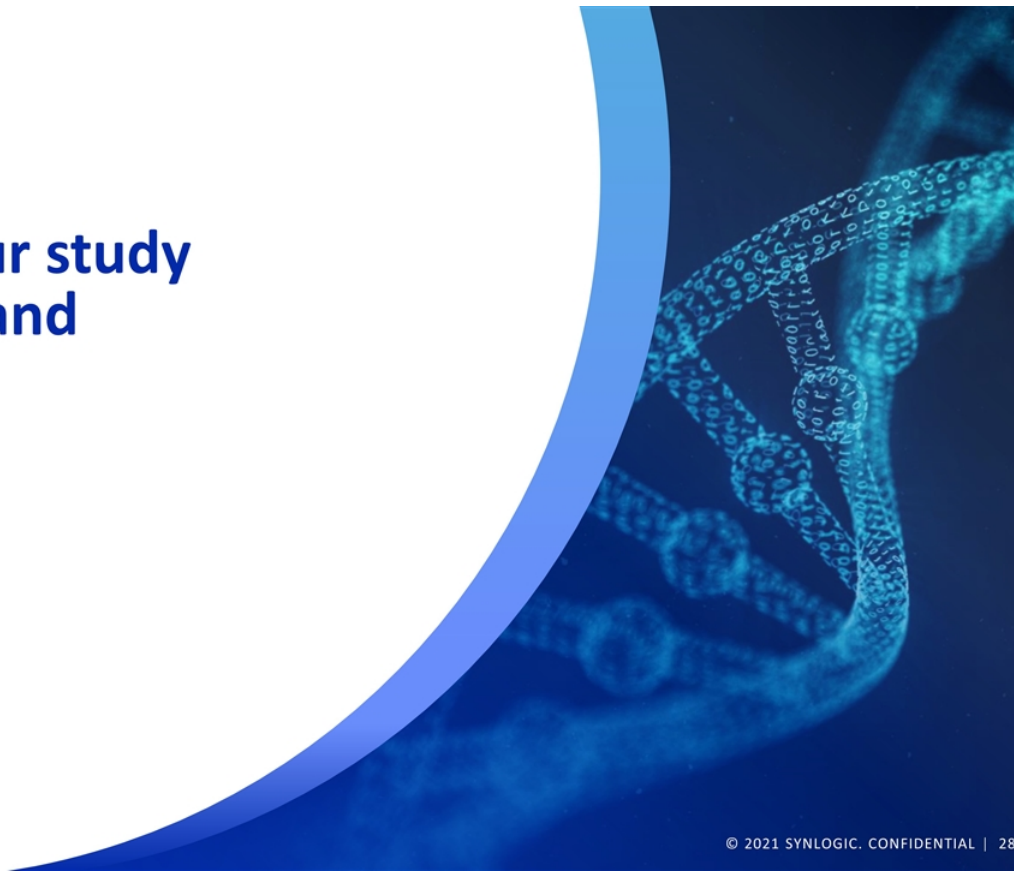
SYNB1618 strain achieved prespecified 20% Phe lowering target in PKU patients

SYNB1934 Ph. 1 HV

SYNB1934 strain demonstrated two-fold greater activity than SYNB1618 in healthy volunteers

Synlogic intends to begin pivotal study planning and advance the best asset into Phase 3 in 2022

Thank you to our study sites, patients, and investigators



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Available For Questions

Aoife Brennan, MB ChB
President & CEO

Daniel Rosan
Head of Finance & Investor Relations

Dave Hava, PhD
Chief Scientific Officer

Antoine Awad
Chief Operating Officer

Exhibit 99.2

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Bringing the Transformative Power of Synthetic Biology to Medicine

Corporate Presentation

September 2021

Forward Looking Statements

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Multiple high value indications accessible with Synthetic Biotic Medicines

Metabolic programs

Phenylketonuria (PKU)

SYNB1618 strain achieved prespecified 20% Phe lowering target in PKU patients in interim analysis

SYNB1934 strain demonstrated two-fold greater activity than SYNB1618 in healthy volunteers

Enteric Hyperoxaluria

Proof of mechanism demonstrated by SYNB8802 in Phase 1A with dietary hyperoxaluria induced in healthy volunteers

Phase 1B patient data expected 2022 in patients with enteric hyperoxaluria

Immunology

Solid Tumors

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

Combination with anti-PDL1: ongoing

Inflammatory Bowel Disease

Advancing research collaboration with Roche on novel IBD target

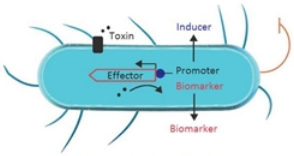
Clinical benefit of the Synthetic Biotic platform demonstrated

A new class of medicines

Synthetic Biotic platform

Non-pathogenic
bacterial chassis

+



Programable, engineering

Targeted & controllable, **patient friendly** treatment

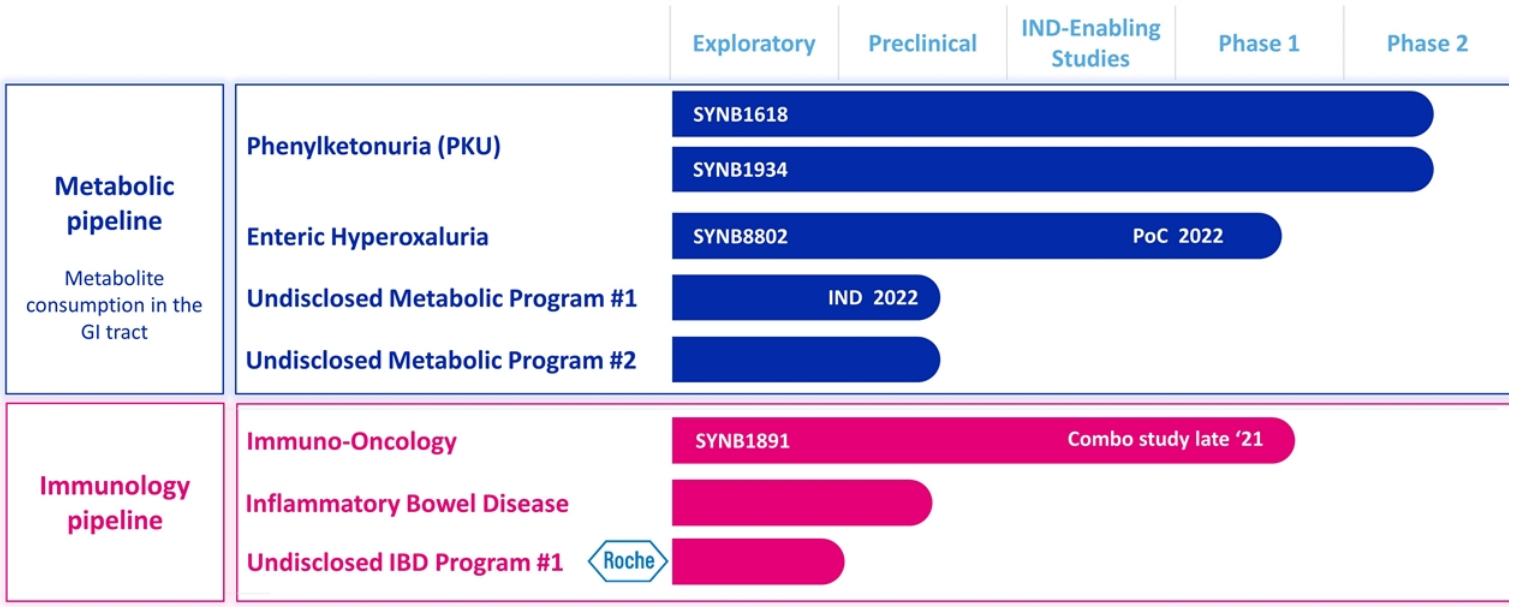
Robust pipeline

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



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 Concept

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

Ability to deploy multiple enzyme pathways

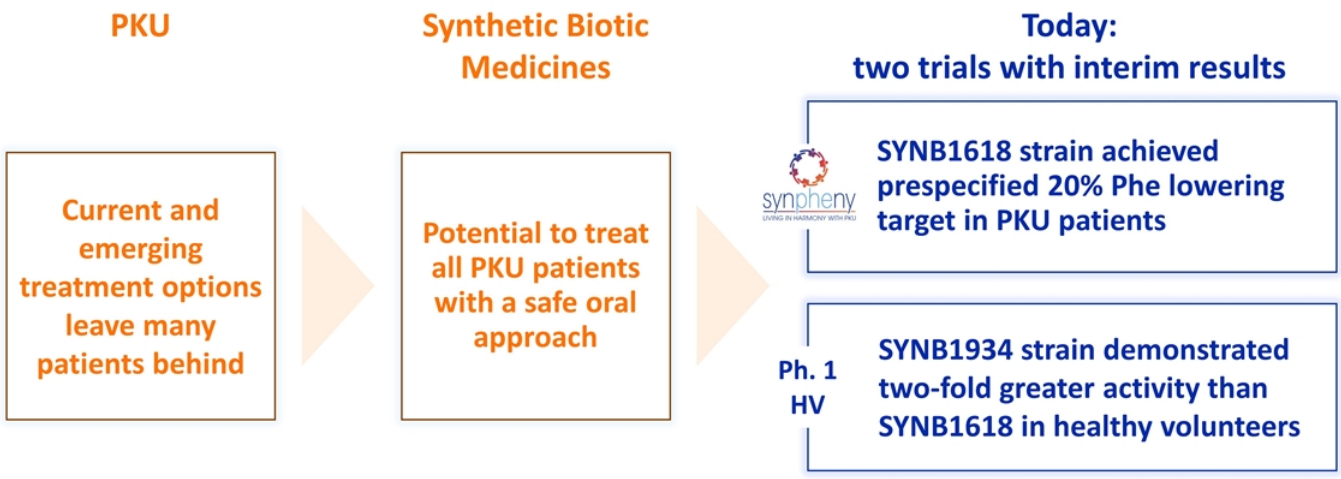
Drug-like approach without genetic drift or colonization

PKU data **demonstrates** SYNB compounds can **consume toxic metabolites** in the human GI tract and impact systemic levels of that metabolic

Applying Synthetic Biotic medicines to PKU and Enteric Hyperoxaluria

	Phenylketonuria (PKU)	Enteric Hyperoxaluria (HOX)
 **Unmet Medical Need**	Many patients unable to control Phe ~70% pts do not respond to BH4 oral therapy	Recurrent and chronic kidney stones; Increased risk of chronic kidney disease progression 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 Concept**	SYNB1618 consumes Phe and lowers fasting Plasma Phe levels in patients with PKU	SYNB8802 consumes oxalate in healthy volunteers at clinically meaningful levels

Phenylketonuria (PKU)



PKU remains an area of high unmet need

Patients

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Pediatrics
~5,000 U.S.

25% out of Phe control

Adults
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65% out of Phe control

90% of patients and caregivers express need for greater natural protein intake [1]

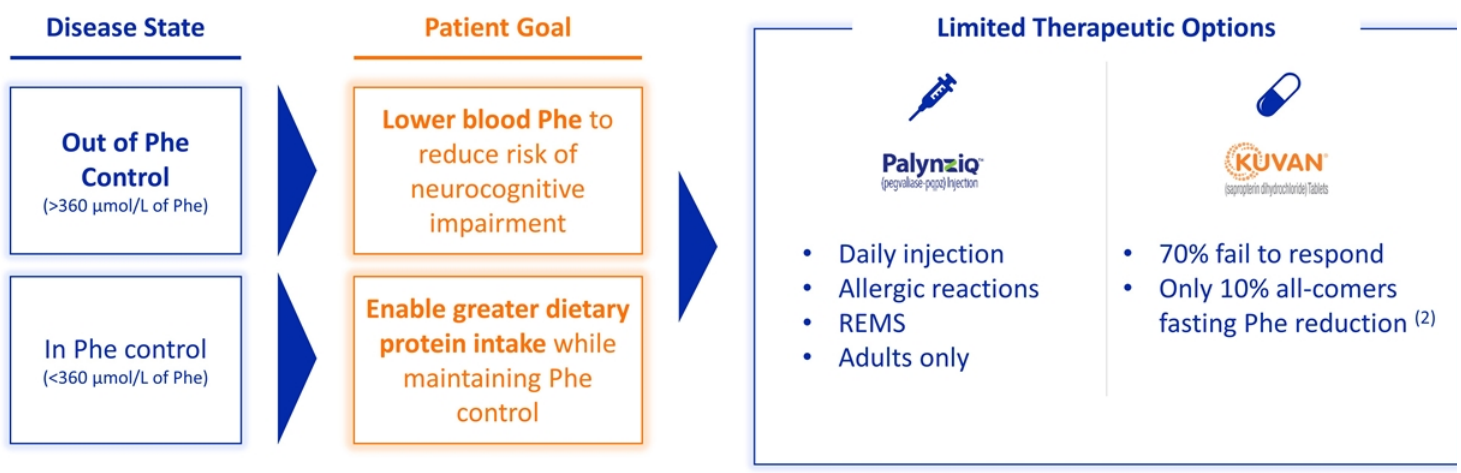
Challenges

- Extremely challenging low protein diet with **low compliance**
- Substantial need for increased intake of **natural protein** enabled by Phe reductions
- Significant risk of **neurocognitive impairment** in patients with elevated Phe levels

synlogic

[1] Puurunen et al, Global PKU Patient Meeting, September 2021

PKU patients are poorly served today



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

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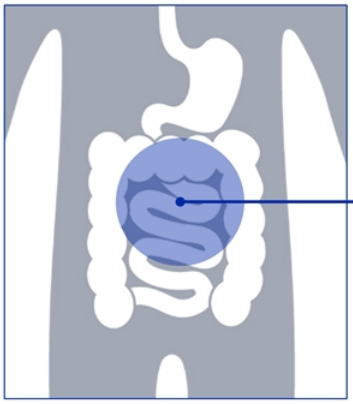
Oral therapy,
3 x day with meals



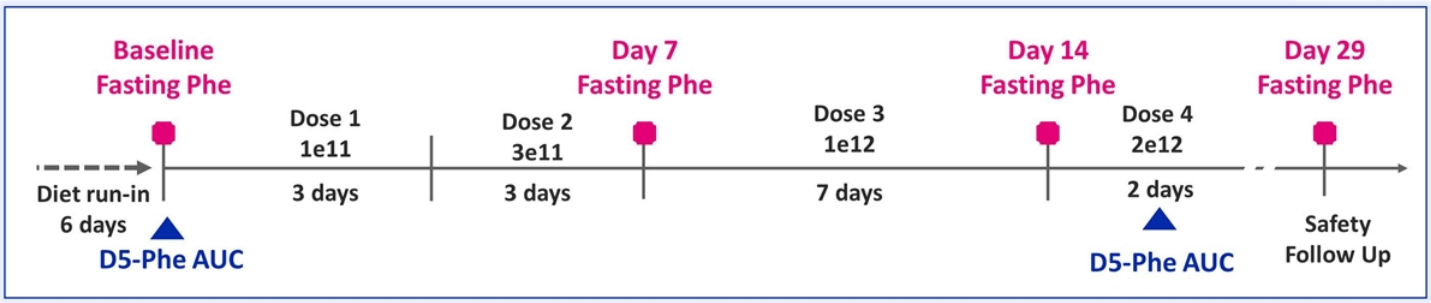
Dietary Phe

Converted by Synthetic Biotic to harmless metabolites (TCA)

Reduce plasma Phe *or* enhance protein tolerance

Unique mechanism of action generates quantitative, measurable biomarker of Phe metabolism: TCA (trans-cinnamic acid)

SYNB1618 Phase 2 SynPheny-1 study in PKU: Design



Population

- IA of 8 subjects receiving SYNB1618
- Adult PKU patients, plasma Phe levels ≥ 600 µmol/L
- Stable diet
- No use of Kuvan or Palynziq

Endpoints

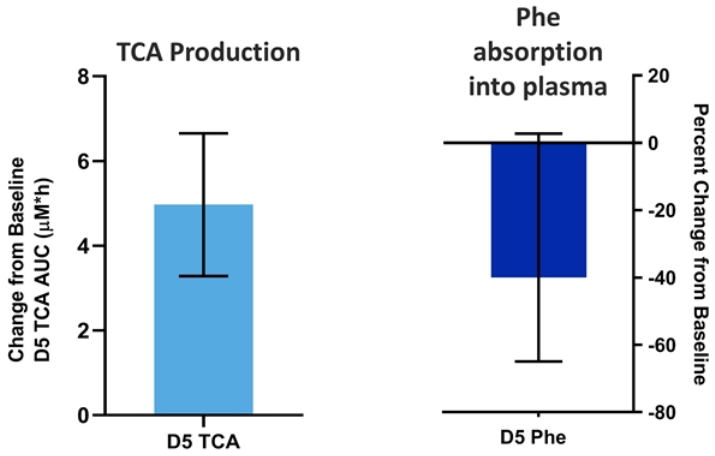
- Fasting Plasma Phe levels (day -1, 7, 14, 29)
- Labelled D5-Phe 24hr AUC, change from baseline after meal challenge (day -1, 15)

Diet Control

- 6-day diet run in
- Individualized diet plan to match baseline Phe intake
- Stable study diet: diet run-in through 2 weeks post treatment

SYNB1618 metabolized Phe into TCA and prevented Phe absorption after meal challenge

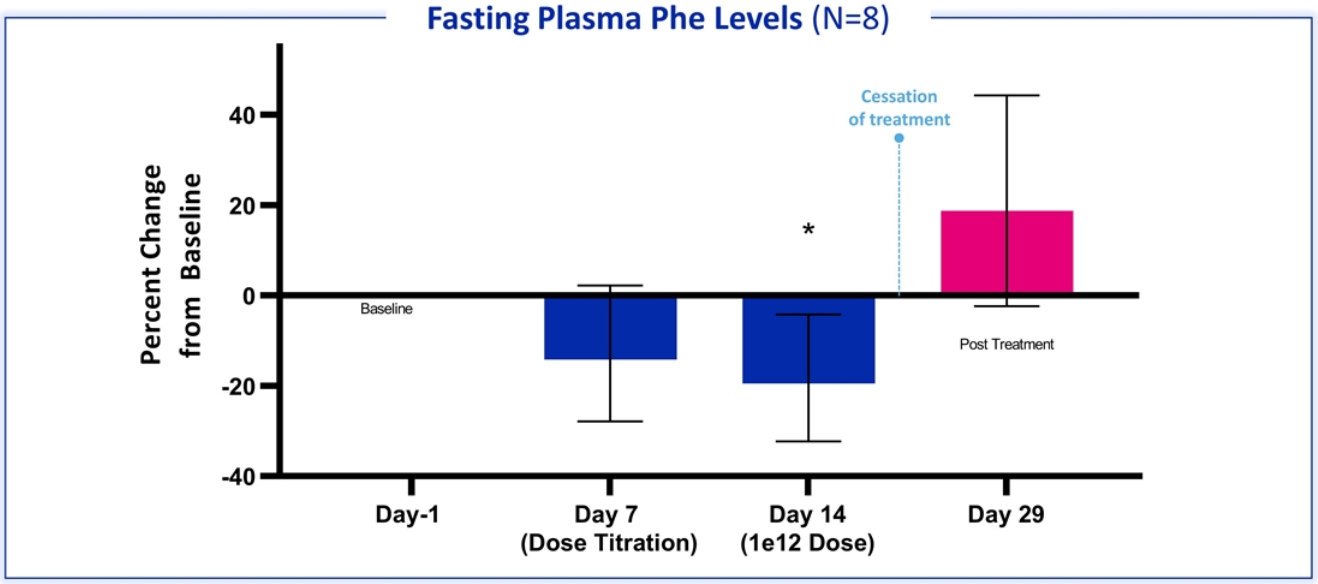
D5 Phe Meal Challenge
(2e12 dose, N=8, Days -1 and 15)



4 of 8 patients experienced >40% D5-Phe lowering after meal challenge

Percent change from baseline +/- 95% confidence interval. TCA = trans-cinnamic acid. AUC = Area under curve.

SYNB1618 reduced fasting plasma Phe levels



4 of 8 patients experienced **>30% reduction** in fasting Plasma Phe at Day 7 or Day 14

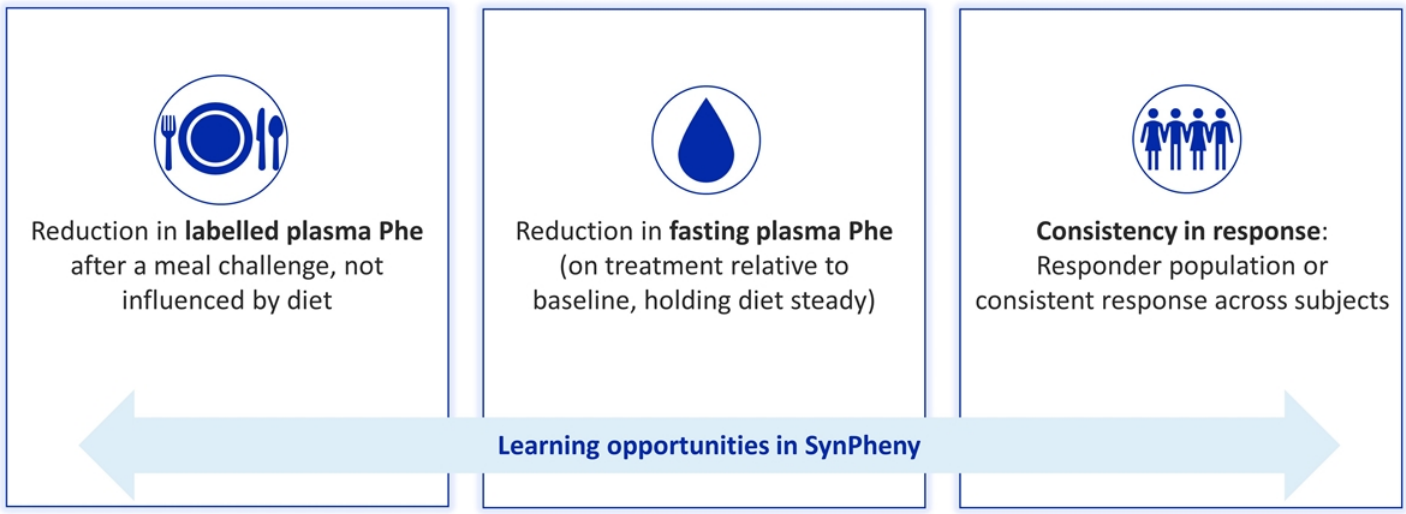
Percent change from baseline +/- 95% confidence interval. * = Statistically significant
Kuvan FDA statistical review, 25 Nov 2007

Summary of interim safety analysis

Gut restricted	Generally well tolerated	No treatment-related discontinuations
Clearance upon cessation of dosing as expected	Tolerability profile **consistent with experience** in healthy volunteers **Mild to Moderate GI AEs**	**No SAEs** or new safety issues identified

Safety analysis cut-off: 30 July 2021. Includes all patients (N = 9) through Day 15. Does not include Day 29 assessments for all patients. One discontinuation for anxiety, not drug related.

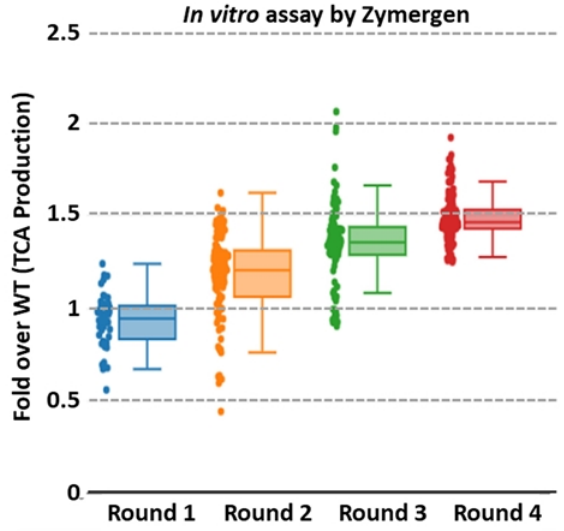
SynPheny POC Study in PKU



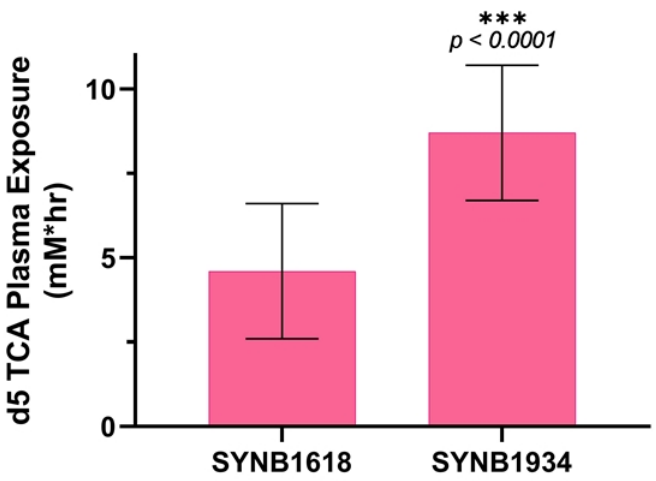
Interim analysis demonstrated 20% reduction in labelled plasma Phe, providing clinically meaningful endpoint for patients without other treatment options

SYNB1934: An evolved strain with potential for improved Phe-lowering

Directed Evolution



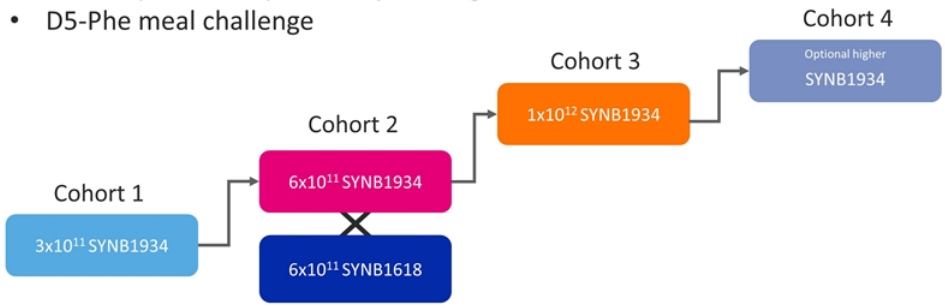
Non-Human Primates: Biomarker of Phe-Consumption



SYNB1934 Ph. 1 study allows head-to-head comparison of strains

Study Design

- Four-day dose ramp, two days dosing
- D5-Phe meal challenge

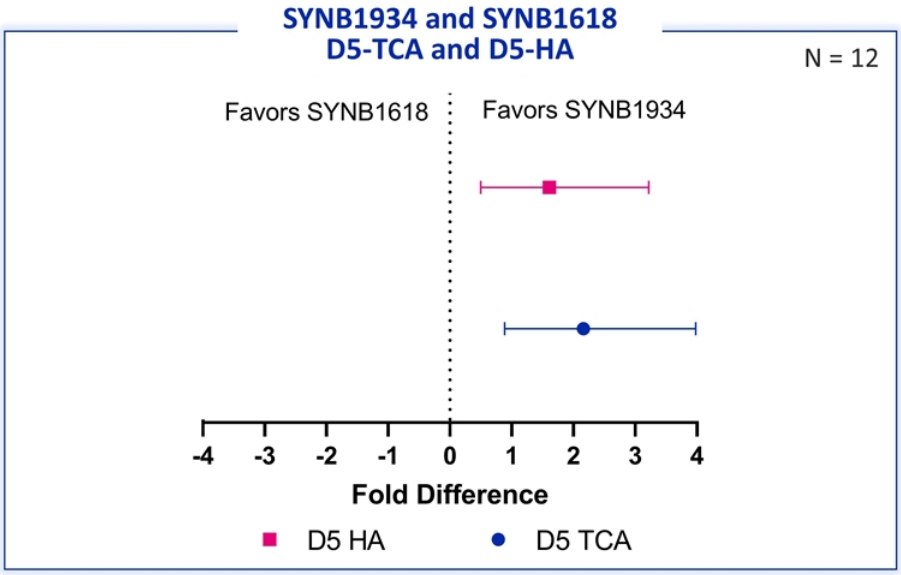


Endpoints

- Safety and tolerability
- Biomarkers of Phe consumption
- SYNB1934 clearance after cessation of dosing

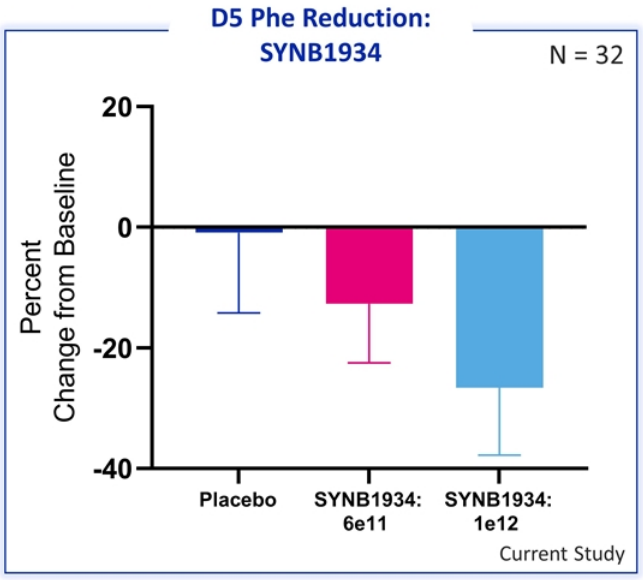
Study will determine if SYNB1934 has improved activity over SYNB1618

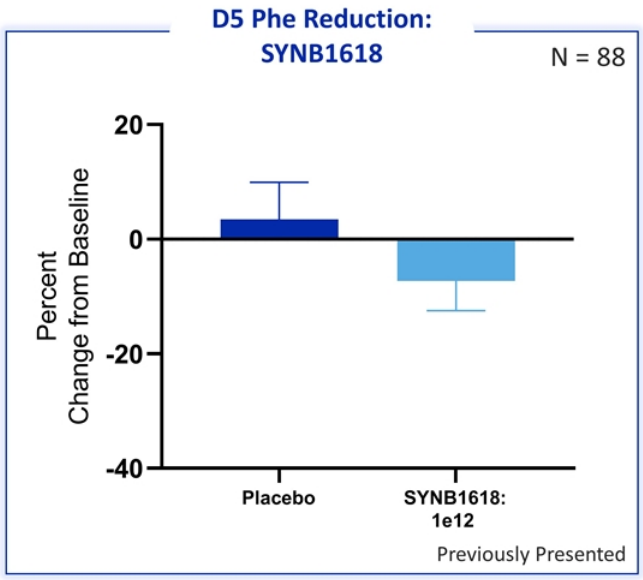
SYNB1934 demonstrated two-fold improvement over SYNB1618 in biomarkers of Phe metabolism



Mean +/- 90% confidence interval. TCA = *trans*-cinnamic acid HA = hippuric acid

Robust labeled D5-Phe reduction in healthy volunteers at multiple dose levels





Percent change from baseline +/- 90% confidence interval. Cross study comparison. N = total study (all cohorts)

Synthetic Biotic Medicines: a novel approach in Phenylketonuria (PKU)

synpheny
LIVING IN HARMONY WITH PKU

SYNB1618 strain achieved prespecified 20% Phe lowering target in PKU patients

SYNB1934 Ph. 1 HV

SYNB1934 strain demonstrated two-fold greater activity than SYNB1618 in healthy volunteers

Synlogic intends to begin pivotal study planning and advance the best asset into Phase 3 in 2022

Enteric Hyperoxaluria (HOX)

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

SYNB8802 proof of mechanism established: potential for best-in-class urinary oxalate lowering

Proof of concept data expected 2022

The Enteric Hyperoxaluria Patient Experience

Patients with underlying GI disorders faced with the burden of chronic and recurrent kidney stones

High levels of pain

No approved treatment options

Risk of impaired kidney function

"I would rather experience the pain of childbirth every year for the rest of my life than ever have one more stone."

- C., Female, 53 yrs. old, 7 stones

75,000 - 90,000 US patients with recurrent kidney stones have no available therapeutic options

synlogic

Source: Patel et al, 2017; Synlogic market research

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	Allena PHARMACEUTICALS; synlogic
Clinical consequences	**Limited ability to manage with diet | Nephrocalcinosis | Recurrent, chronic kidney stones | Impaired renal function | Systemic Oxalosis**	

An innovative approach in an area of high unmet medical need

Our approach

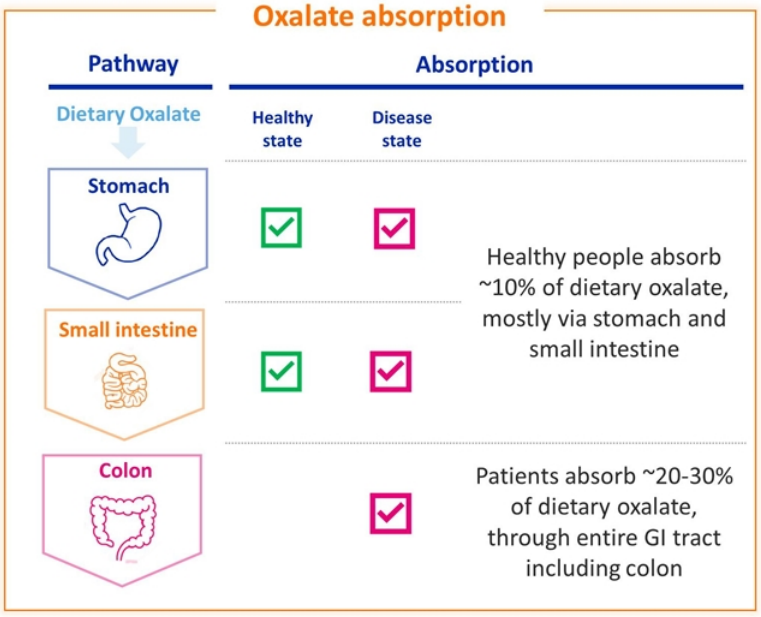
Oral therapy

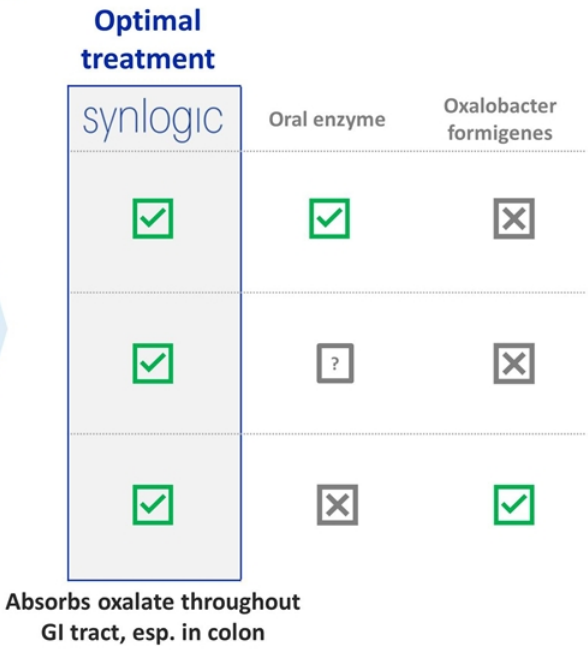
Differentiation from other approaches

Consumes oxalate in each GI compartment, throughout GI tract

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

SYNB8802 consumes Oxalate throughout the GI tract





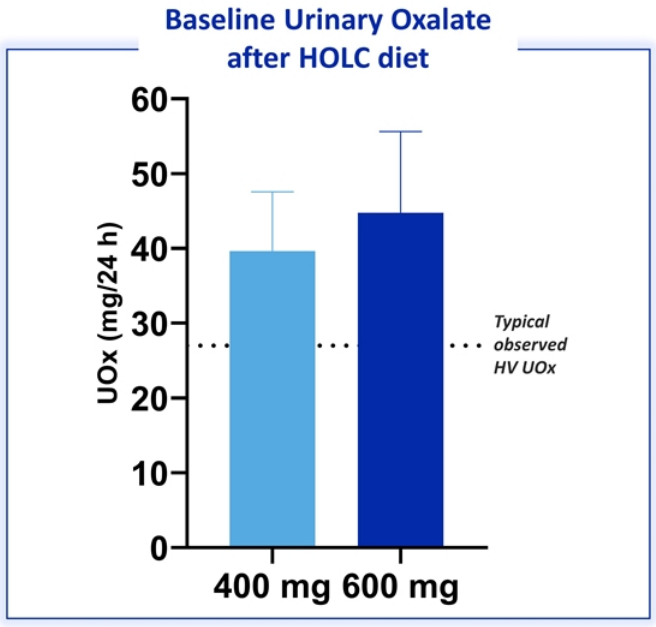
Ph1 design provides POC opportunity in 2021

Phase 1A Dietary Hyperoxaluria (Healthy Volunteers)	Phase 1B Enteric Hyperoxaluria Patients
Multiple Ascending Dose	**Cross-over**
High oxalate & low calcium diet run-in	Enteric Hyperoxaluria patients (Roux-en-Y population)
Induce dietary hyperoxaluria	Three times/day (TID) dosing
N = 45 subjects	N = 20 patients, baseline UOx >50 mg/day
Endpoints	**Endpoints:**
Primary: Safety & tolerability	***Primary:*** Change in Urinary Oxalate
Secondary: Microbial kinetics of strain	***Secondary:*** (1) Microbial kinetics of strain
Exploratory: (1) Plasma and urine biomarkers	(2) Safety and tolerability
(2) Dose frequency assessment	

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
- HV subjects absorb approx. 10% of dietary oxalate
- Urinary oxalate levels elevated to >1.5X typically observed in healthy volunteers
- Dietary intake carefully measured on in-patient unit, incl. weighing of meals consumed



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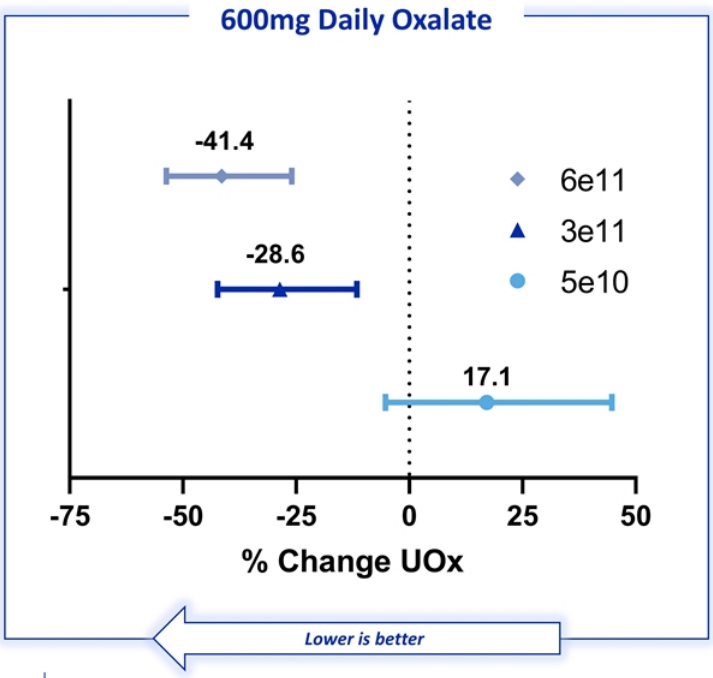
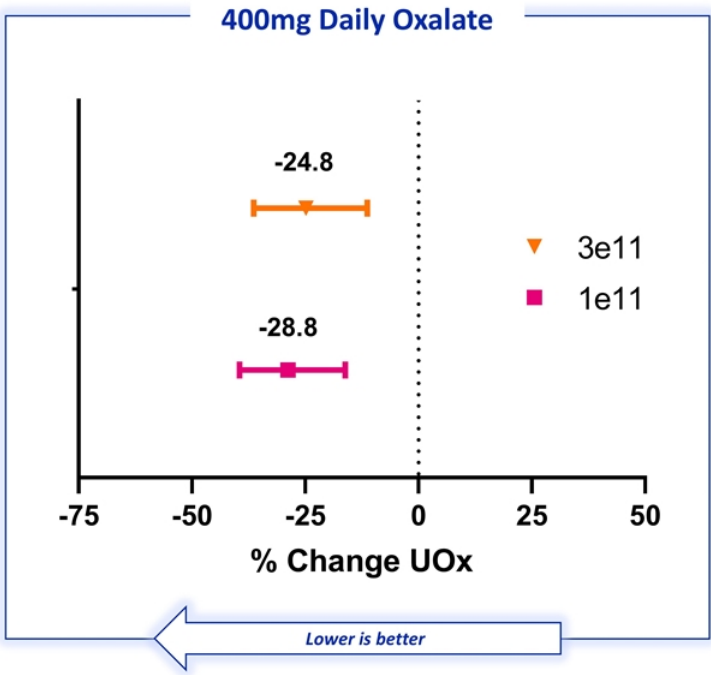
Historically Uox in HV is <40 mg/24h. Examples: Langman 2018, (27 mg), Quintero 2020, (19.8mg), Captozyme 2018 (28 mg). Mean +/- SD shown.

Dose-responsive and reproducible Uox lowering demonstrated

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





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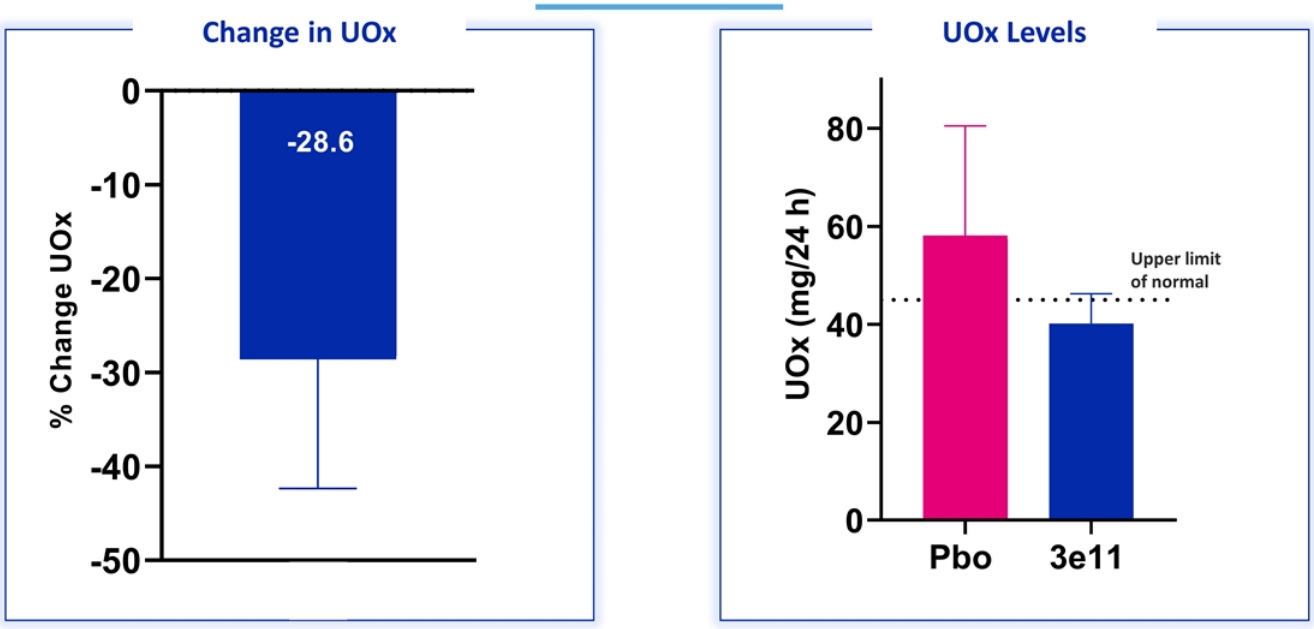
LS mean change over Placebo, +/- 90% CI, all days baseline and treated

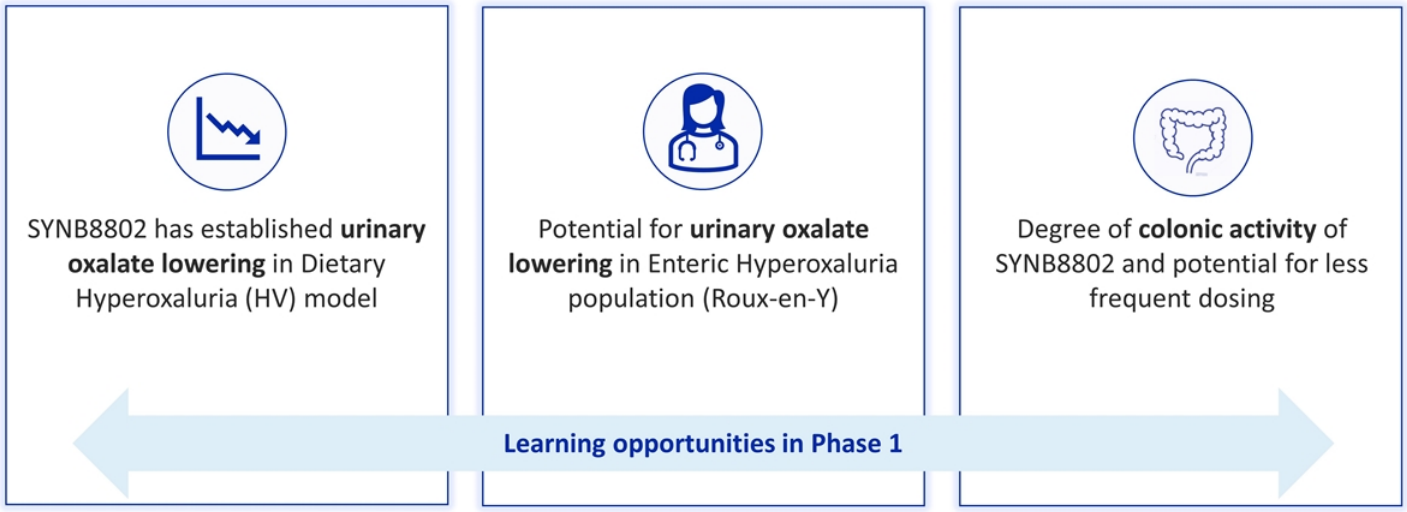
SYNB8802 3e11 live cells dose advancing to Ph1B in patients



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

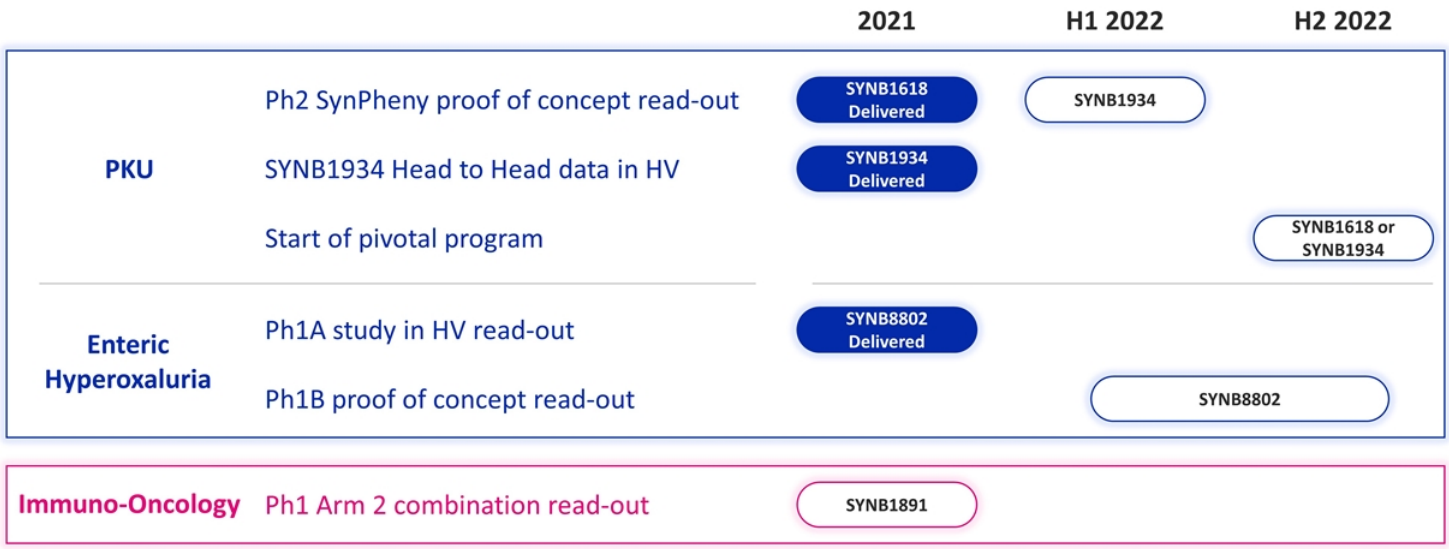


Potential to demonstrate meaningful urinary oxalate lowering in patients with active disease

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 continues to deliver meaningful data



Robust portfolio with significant milestones over the next 18 months

Second Quarter, 2021

Summary Results

Balance Sheet (unaudited)	30 June 2021	31 December 2020
Cash, Cash Equivalents, and Marketable Securities	$115.5 M	$100.4 M

	Three Months Ended	
Statement of Operations (unaudited)	**30 June 2021**	**30 June 2020**
R&D Expenses	$10.7 M	$12.9 M
G&A Expenses	$4.1 M	$3.5 M
Net Loss	$(14.5 M)	$(15.5 M)
Net loss per share – basic and diluted*	$(0.28)	$(0.44)
*Weighted Average Shares Outstanding**	*52.0 M*	*34.9 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

Dave Hava, PhD
Chief Scientific Officer

Caroline Kurtz, PhD
Chief Development Officer

Antoine Awad
Chief Operating 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

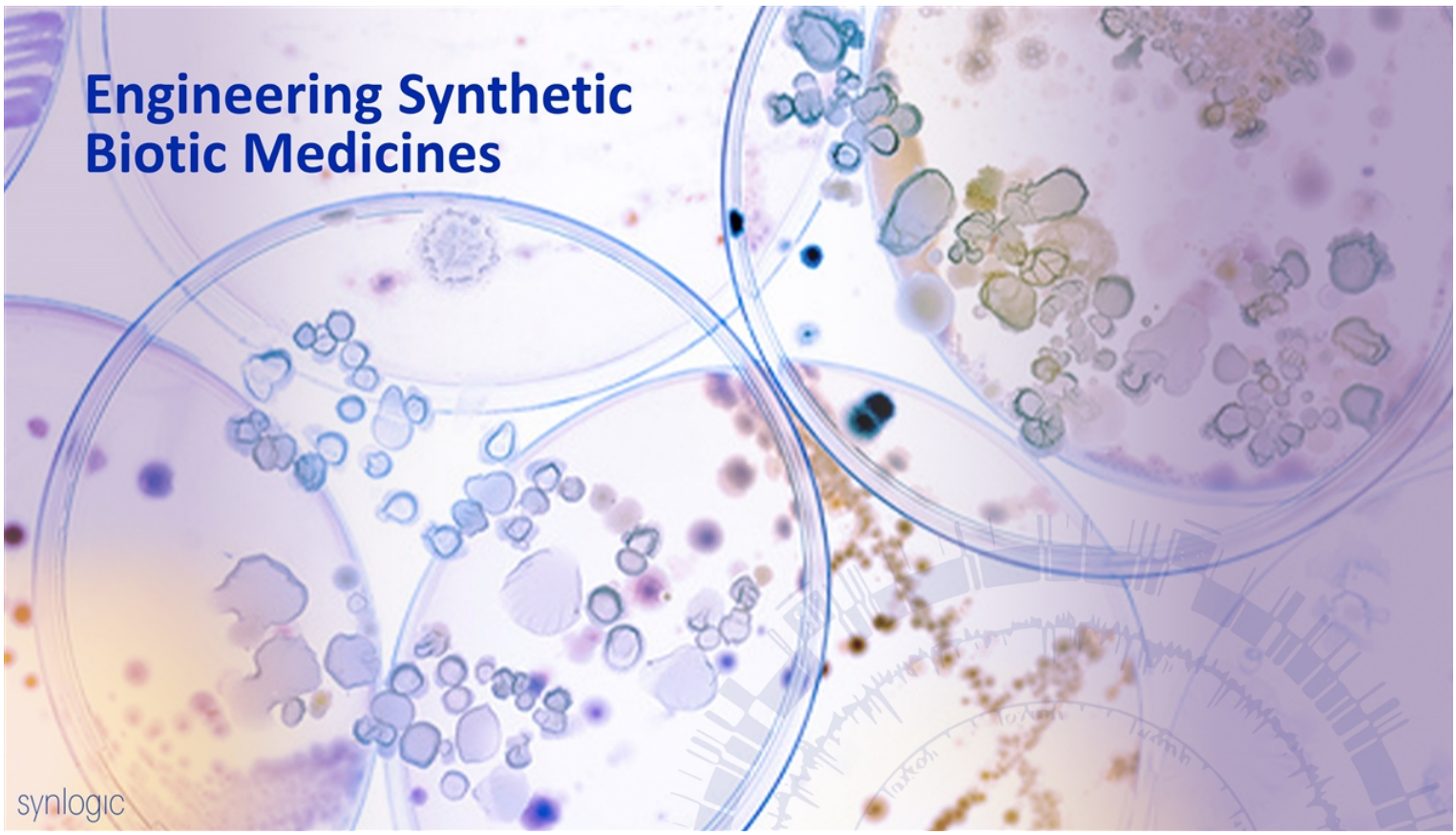
Nick Leschly
Bluebird Bio

Ed Mathers
NEA

Richard Shea
Syndax

Collaborators

GINKGO BIOWORKS
THE ORGANISM COMPANY


Engineering Synthetic
Biotic Medicines
synlogic

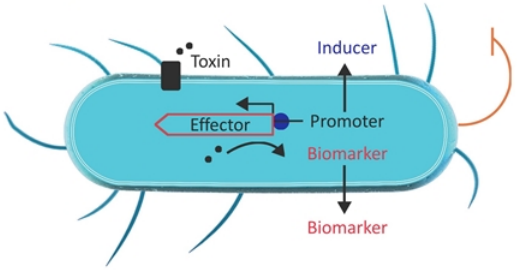
A new class of medicines

Non-pathogenic bacterial chassis

E. coli Nissle

+

Programable, controllable engineering



Inducer-Promoter Switch

Effector Design

Safety Features

=

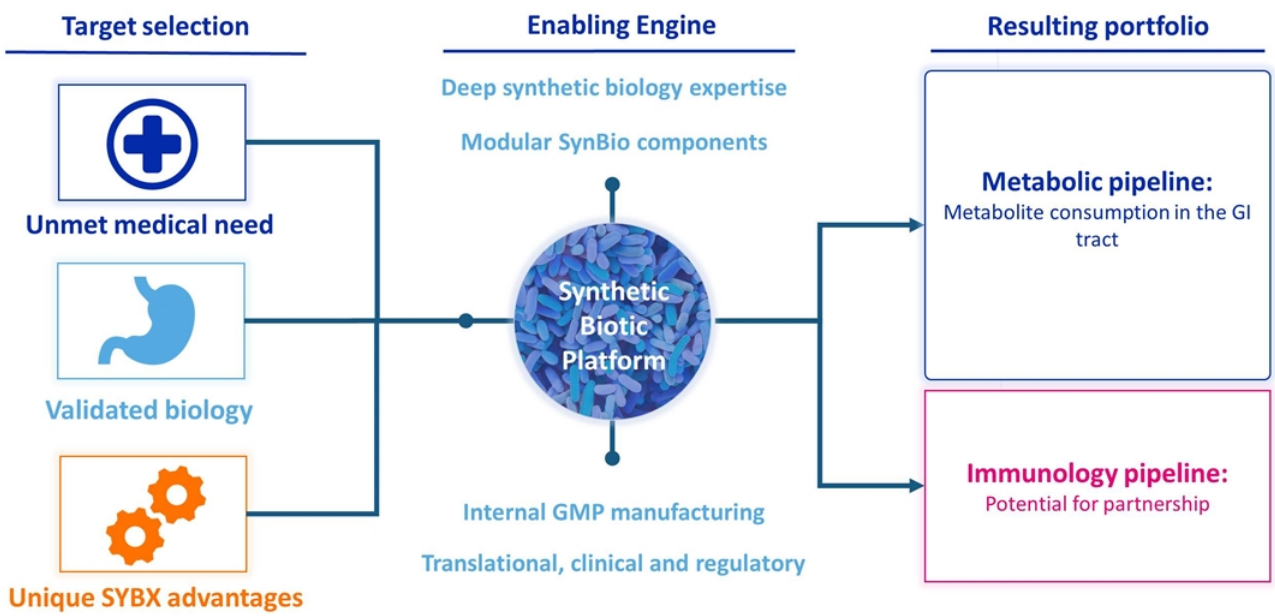
Synthetic Biotic Medicine

synlogic

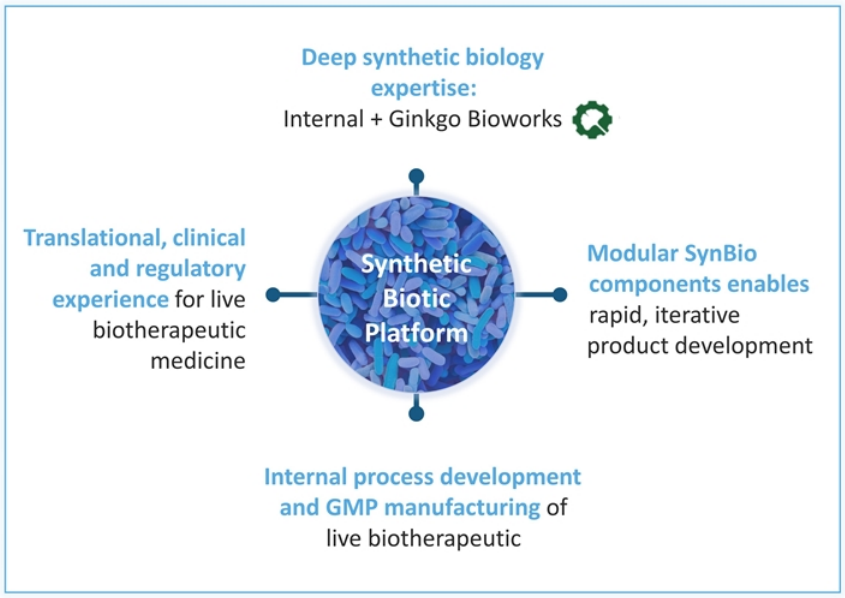
- Drug-like properties
- Does not colonize
- No *in vivo* reproduction or risk of genetic drift

Reusable parts enable rapid iteration of rationally designed prototypes

Synthetic Biotic Platform accelerates pathway into the clinic



Synthetic Biotic Platform is enabling engine for drug development



>200 humans dosed with Synthetic Biotic medicines

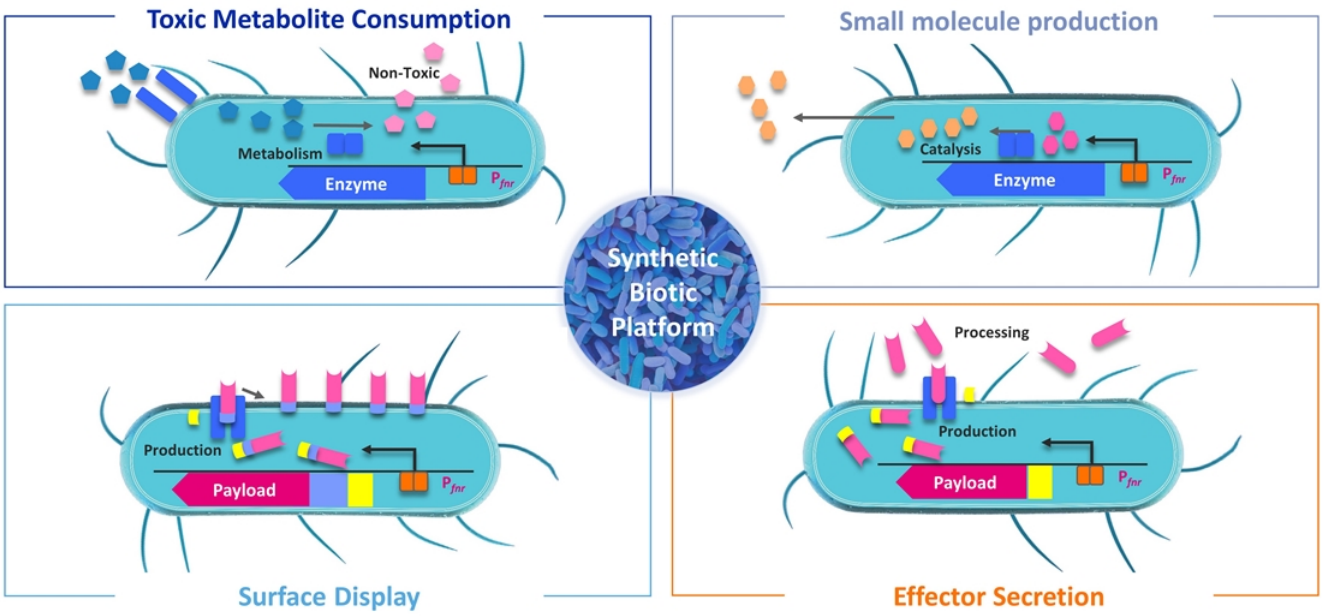
5 INDs opened with the U.S. FDA

Supportive regulatory feedback from global agencies

Safe chassis organism (>100 years of human experience)

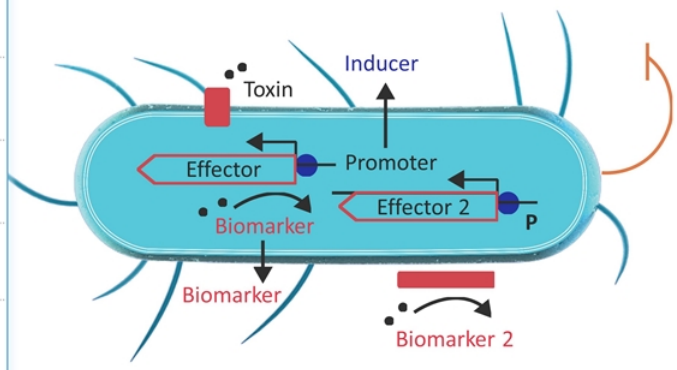
Rapid pipeline expansion possible with reusable engineering

Versatile platform enables diverse therapeutic strategies for range of diseases



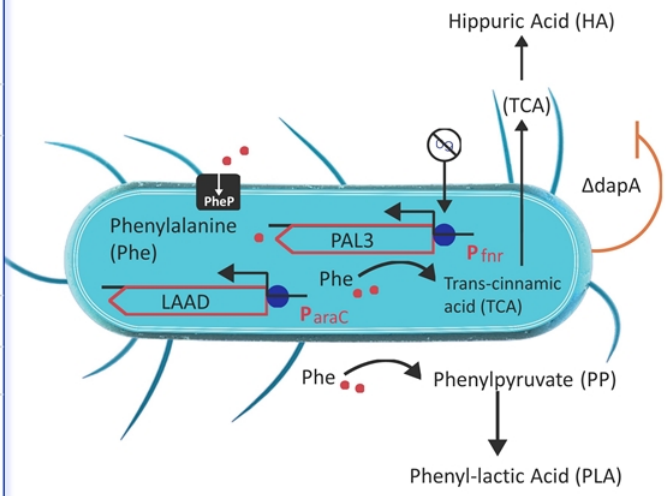
Reusable parts enable rapid iteration of rationally designed prototypes

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



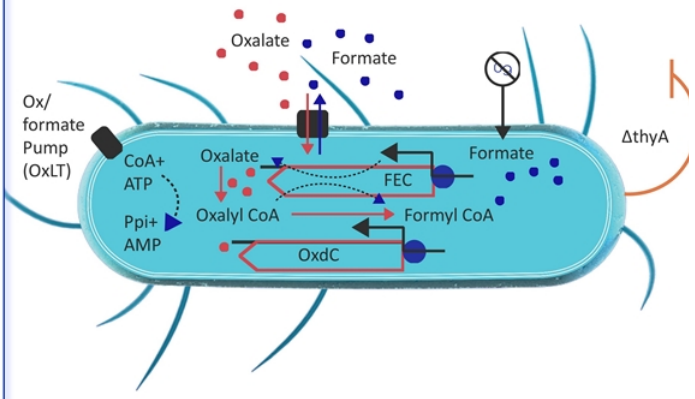
SYNB1618 & SYNB1934 Design

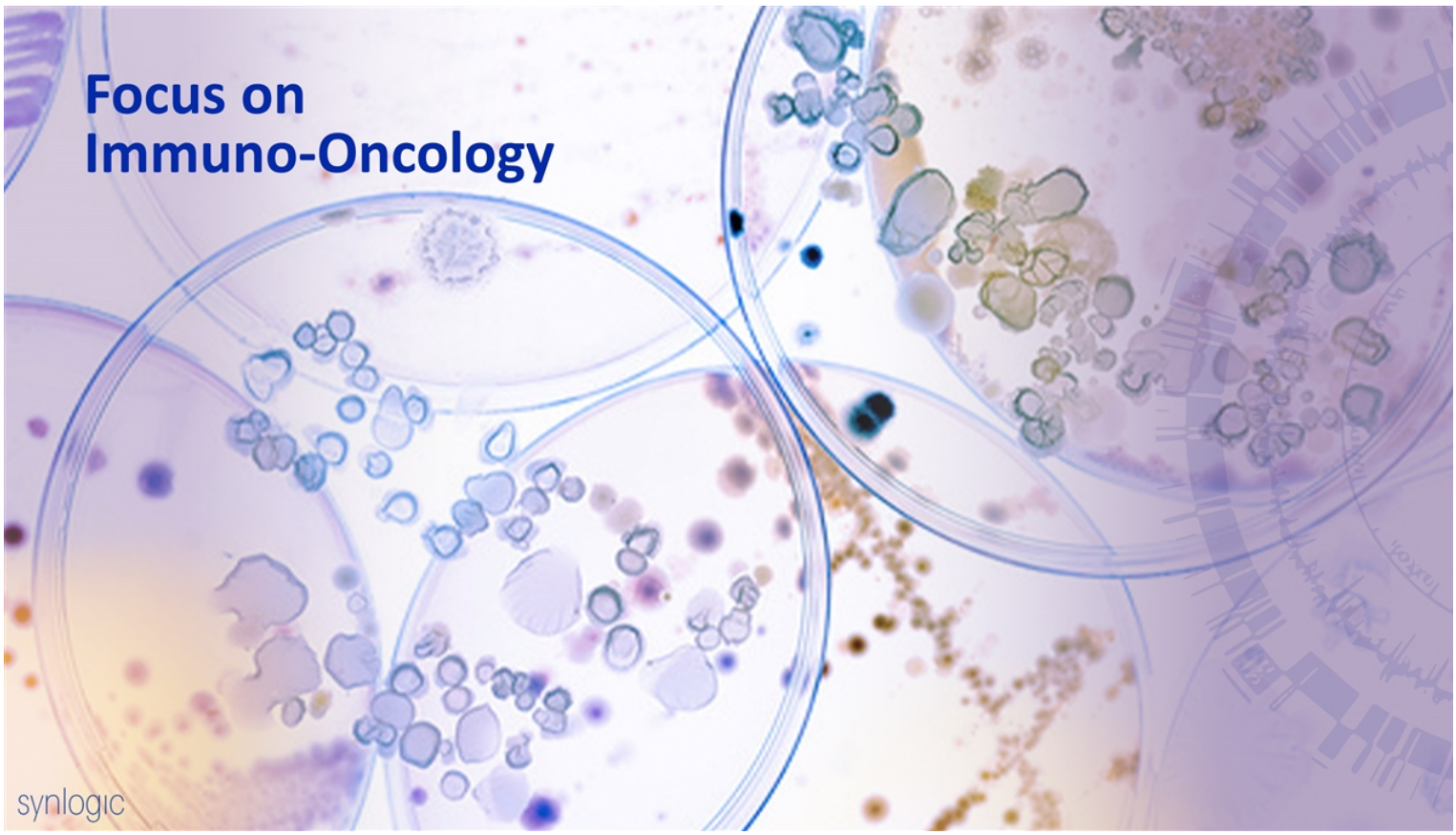
Component	Design
Therapeutic strategy	**Metabolite consumption:** Built from Synthetic Library Specifically to Consume Phe
Bacterial Chassis	***E. coli* Nissle**
Effector(s)	***SYNB1618: Wild Type* PAL3 Enzyme** ***SYNB1934*: Evolved PAL3 Enzyme** Degrades Phe to TCA (measurable biomarker of activity)
	***LAAD* Enzyme:** Alt. Phe-consuming pathway
Pump	***PheP:*** Pumps Phe into cell
Switch	**SYNB1618: FNR & AraC promoters** **SYNB1934: Ptac** Control gene expression
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




Focus on
Immuno-Oncology
synlogic

Immuno-Oncology

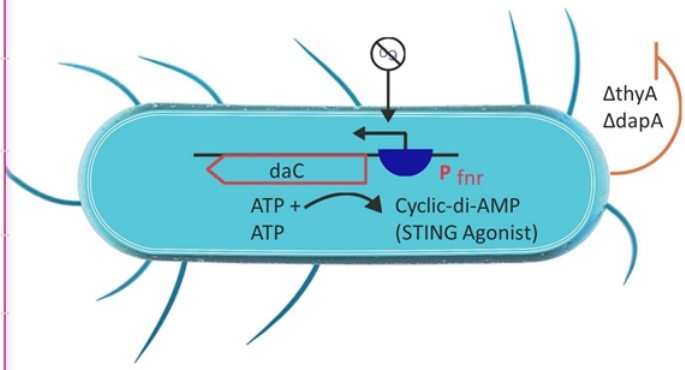
SYNB1891 potential for improved efficacy relative to other STING approaches

SYNB1891 monotherapy demonstrated meaningful pharmacodynamic effects

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

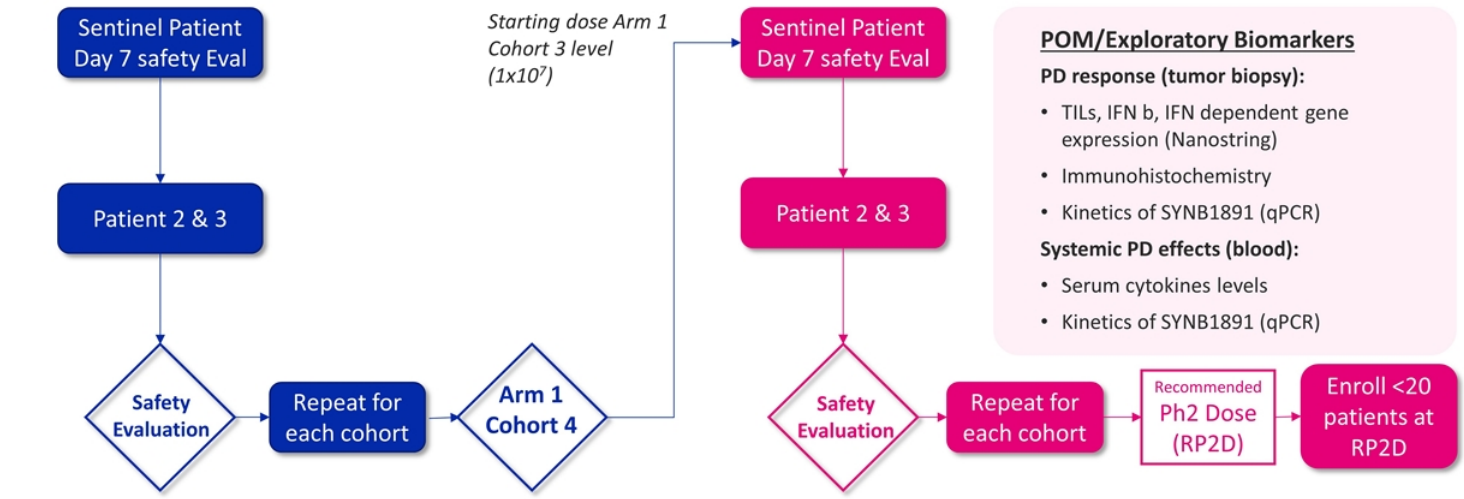
SYNB1891 Design

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



Phase 1 design: multidose tolerability, IT mono and combo

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



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

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**

Synlogic Announces Positive Phase 2 Data Demonstrating Reduction in Plasma Phenylalanine Levels in Patients with Phenylketonuria

– SYNB1618 demonstrated proof of concept with meaningful reduction of plasma phenylalanine (Phe) levels in an interim analysis of the Phase 2 SynPheny-1 Study –

– SYNB1934, an optimized strain of SYNB1618, demonstrated two-fold increase in biomarkers of Phe metabolism compared to SYNB1618 –

– Phase 2 SynPheny-1 study will incorporate SYNB1934. Company to prepare to start Phase 3 program with the most promising strain in Phenylketonuria (PKU) in 2022 –

– Conference call and webcast to discuss results at 8:30 AM –

Cambridge, Mass., September 20, 2021 – Synlogic, Inc. (Nasdaq: SYBX), a clinical stage company bringing the transformative potential of synthetic biology to medicine, today announced positive data from clinical studies evaluating both SYNB1618 and SYNB1934, investigational Synthetic Biotic™ medicines for the treatment of phenylketonuria (PKU).

SYNB1618 demonstrated clinically meaningful reductions of phenylalanine (Phe) at several dose levels, across multiple time points, in an interim analysis of the Phase 2 SynPheny-1 study. SYNB1934, an optimized strain evolved from SYNB1618, demonstrated two-fold higher activity than SYNB1618 in a head-to-head Phase 1 study in healthy volunteers, as measured by biomarkers of Phe metabolism.

Synlogic intends to incorporate SYNB1934 into an arm of the Phase 2 SynPheny-1 trial with final results expected in the first half of 2022. Based on the favorable clinical data from the SYNB1618 and SYNB1934 programs available to date, the Company intends to initiate planning for a pivotal Phase 3 study for the most promising strain.

“The PKU program demonstrated clear proof of concept in this analysis, with SYNB1618 achieving a clinically meaningful reduction of phenylalanine in patients across multiple endpoints and time points,” said Aoife Brennan, M.B. Ch.B., Synlogic’s President and Chief Executive Officer. “Additionally, our second PKU candidate SYNB1934 provides greater potency, which will allow us to optimize the clinical profile to address the profound needs of patients with PKU.”

“Together, these data provide strong support for the ability of Synthetic Biotic medicines to make a meaningful difference to patients. These events mark a major milestone for Synlogic’s Synthetic Biotic platform. We look forward to completing our Phase 2 SynPheny-1 study and advancing the PKU program into a pivotal study,” continued Dr. Brennan.

“In addition to our strong clinical results, we’re highly encouraged by the predictive validity of our prospective biomarker driven modeling of therapeutic effect,” said David Hava, Ph.D., Chief Scientific Officer. “Patient clinical data observed to date was consistent with our preclinical predictions of Phe metabolism by the strains. The ability to translationally model clinical activity enables rapid and effective strain optimization, which we have applied both to PKU and other inherited and acquired metabolic disorders.”

Interim SYNB1618 Synpheny-1 Phase 2 Results

Synpheny-1 (NCT04534842) is an open-label, single arm Phase 2 study in patients with PKU. The study evaluated a dose-ramp regimen consisting of four dose levels of SYNB1618 over 15 days of treatment. The primary endpoint was reduction of the area under the curve (AUC) for plasma D5-phenylalanine (D5-Phe) after a meal challenge. Secondary endpoints include changes from baseline in fasting levels of plasma Phe at multiple timepoints, and incidence of treatment-emergent adverse events (TEAEs). Dietary intake of Phe was carefully managed during the study through individualized diet management plans.

The interim analysis included 8 patients. Clinical results demonstrated meaningful reductions of Phe, consistent with prospective biomarker-driven modeling. These results included:

- 20% reduction in fasting plasma Phe after 14 days of dosing, at a dose of 1e12 live cells;
    - Fasting plasma Phe level began to trend down after seven days of dose titration, at a dose up to 3e11 live cells, and was statistically significant at the 1e12 dose at day 14
- 40% reduction in labeled plasma D5-Phe after meal challenge at day 15, at a dose of 2e12 live cells; and
- Rebound of plasma Phe levels following cessation of dosing, confirming therapeutic effect

Safety and tolerability were consistent with prior studies, with no serious adverse events or systemic events of any kind. AEs were primarily GI related and mild to moderate in nature. There were no treatment drug related discontinuations.

SYNB1934 Phase 1 Results

SYNB1934 was evolved from SYNB1618 to potentially provide increased Phe lowering activity for patients living with PKU. Clinical studies of SYNB1934 were initiated following preclinical *in vivo* and *in vitro* studies demonstrating an approximately two-fold improvement in the ability of SYNB1934 to break down Phe compared to SYNB1618.

The Phase 1 multiple ascending dose study of SYNB1934 (NCT04984525) evaluated the safety, tolerability and Phe consumption activity of SYNB1934, including a head-to-head comparison with SYNB1618 in healthy volunteers using biomarkers of Phe consumption such as trans-cinnamic acid (TCA). Results included:

- Dose dependent increase in plasma TCA area under the curve;
- Two-fold higher activity level than SYNB1618 in a head-to-head comparison based on biomarkers of Phe consumption
- Safety and tolerability in cohorts 1 – 3 were similar to other Synthetic Biotic medicines, including SYNB1618, at equivalent doses. The most common adverse events were GI-related, mild to moderate in severity, and some events led to discontinuation of dosing
- Dosing continues in the dose escalation portion of the study and the maximum tolerated dose has not been reached

SYNB1934 clinical results were consistent with preclinical data and previously presented prospective biomarker driven modeling. The Company believes that the increased activity of SYNB1934, relative to SYNB1618, could provide the opportunity to optimize the clinical profile based on individual patient needs.

Next Steps

Synlogic intends to complete the SynPheny-1 study with a cohort of patients receiving SYNB1934 and anticipates final SynPheny-1 results in the first half of 2022.

Based on the clinical data from the SYNB1618 and SYNB1934 programs available to date, the Company intends to initiate planning for a pivotal Phase 3 study of the most promising strain.

Synlogic continues to evaluate Synthetic Biotic medicines for other metabolic diseases such as Enteric Hyperoxaluria, including development of predictive efficacy models. Preclinical and Phase 1A data suggest SYNB8802 has the potential to consume clinically meaningful levels of dietary oxalate in patients with disease. The Company is continuing to enroll Part B of the Phase 1 study of SYNB8802 and due to ongoing challenges presented by the COVID-19 pandemic, anticipates study data will be available in the first half of 2022.

Synlogic continues to advance preclinical programs targeting additional inherited and acquired metabolic indications. The company expects to file an IND for an additional metabolic indication in 2022.

Patients can learn more about the SynPheny-1 study (NCT04534842) by visiting https://pkuresearchstudy.com. More information about Synlogic's programs and pipeline can be found at https://www.synlogictx.com.

Conference Call & Webcast Information

Synlogic will host a conference call and live webcast at 8:30 a.m. ET today, Monday, September 20, 2021. To access the live webcast, please visit the "Event Calendar" page within the Investors and Media section of the Synlogic website. Investors may listen to the call by dialing +1 (844) 815-2882 from locations in the United States or +1 (213) 660-0926 from outside the United States. The conference ID number is 1154745. A replay will be available for 30 days on the Investors and Media section of the Synlogic website.

About Phenylketonuria

Phenylketonuria (PKU) is an inherited metabolic disease that manifests at birth and is marked by an inability to break down Phe, an amino acid commonly found in many foods. Left untreated, high levels of Phe become toxic and can lead to serious neurological and neuropsychological problems affecting the way a person thinks, feels, and acts. Due to the seriousness of these symptoms, infants are screened at birth in many countries to ensure early diagnosis and treatment to avoid intellectual disability and other complications.

About Synlogic

Synlogic™ is bringing the transformative potential of synthetic biology to medicine. With a premiere synthetic biology platform that leverages a reproducible, modular approach to microbial engineering, Synlogic designs Synthetic Biotic medicines that target validated underlying biology to treat disease in new ways. Synlogic's proprietary pipeline includes Synthetic Biotics for the treatment of metabolic disorders including Phenylketonuria (PKU) and Enteric Hyperoxaluria. The company is also building a portfolio of partner-able assets in immunology and oncology.

Forward-Looking Statements

This press release 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

press release regarding strategy, future operations, clinical development plans, 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 press release, the words “may,” “could,” “should,” “anticipate,” “believe,” “estimate,” “expect,” “intend,” “plan,” “predict” and similar expressions and their variants, as they relate to Synlogic may identify forward-looking statements. Examples of forward-looking statements, include, but are not limited to, statements regarding the potential of Synlogic’s platform to develop therapeutics to address a wide range of diseases including: cancer, inborn errors of metabolism, metabolic diseases, and inflammatory and immune disorders; the future clinical development of Synthetic Biotic medicines; the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology; the expected timing of Synlogic’s clinical trials and availability of clinical trial data. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including: the uncertainties inherent in the clinical and preclinical development process; the ability of Synlogic to protect its intellectual property rights; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading “Risk Factors” in Synlogic’s filings with the Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Synlogic’s current views with respect to future events. Synlogic anticipates that subsequent events and developments could cause its views to change. However, while Synlogic may elect to update these forward-looking statements in the future, Synlogic specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Synlogic’s view as of any date subsequent to the date hereof.

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