

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): March 25, 2021

SYNOLOGIC, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-37566
(Commission
File Number)

26-1824804
(IRS Employer
Identification No.)

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

02142
(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 2.02 Results of Operations and Financial Condition

On March 25, 2021, Synlogic, Inc. (the "Company") announced its financial results for the quarter and full year ended December 31, 2020. The full text of the press release and subsequent presentations issued in connection with the announcement are furnished as Exhibit 99.1, 99.2 and 99.3, respectively, to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K (including Exhibit 99.1 and 99.2) 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 9.01 Financial Statements and Exhibits.

- (d) Exhibits
The following exhibits relating to Item 2.02 shall be deemed to be furnished, and not filed:

Exhibit No.	Description
99.1	Press Release dated March 25 2021
99.2	Presentation dated March 25 2021
99.3	Presentation dated March 25 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: March 25, 2021

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

Synlogic Reports Fourth Quarter and Full Year 2020 Financial Results and Provides Business Update

-- SYN8802 advances to Phase 1B Proof of Concept After Proof of Mechanism Demonstrated in Dietary Hyperoxaluria Study --

-- Synlogic ended 2020 with \$100.4 million in cash, cash equivalents, and short-term investments, extending projected runway into 2023 --

-- Management to host conference call and webcast at 8:30 a.m. ET today --

CAMBRIDGE, Mass., March 25, 2021 /PRNewswire/ -- Synlogic, Inc. (Nasdaq: SYBX), a clinical stage company bringing the transformative potential of synthetic biology to medicine, today reported financial results for the fourth quarter and full year ended December 31, 2020, and provided an update on programs and progress.

"2021 is an incredibly exciting year for the company. We now have demonstrated proof of mechanism in humans from both of our lead metabolic programs, Phenylketonuria (PKU) and Enteric Hyperoxaluria, and expect to have important clinical readouts in patients from both programs later this year," said Aoife Brennan, M.B. Ch.B., Synlogic's President and Chief Executive Officer. "We believe there is significant unmet need in PKU and Enteric Hyperoxaluria and that our Synthetic Biotic medicines can address these and other metabolic diseases in ways not possible with other modalities."

"Enteric Hyperoxaluria is a historically underserved area in which dangerously high levels of urinary oxalate cause progressive kidney damage," said Richard Riese, M.D., Synlogic's Chief Medical Officer. "Part A of the Phase 1 study of SYN8802 in healthy volunteers demonstrates compelling levels of Urinary Oxalate lowering at a well-tolerated dose in Dietary Hyperoxaluria cohorts, and we are thrilled to be advancing this program."

Dr. Riese further stated, "We are also excited to continue to advance the SynPheny-1 Phase 2 study of SYN1618 for the treatment of PKU, as well as the Phase 1 clinical study of SYN1891 in solid tumors and lymphomas. Patient interest continues to be robust. We are looking forward to top line results from both trials later in 2021."

2020 Highlights & 2021 Priorities

The Metabolic Portfolio:

Progression of a proof-of-concept Phase 2 clinical trial of SYN1618 for the treatment of Phenylketonuria (PKU), with data expected in the second half of 2021. SYN1618 is an orally administered Synthetic Biotic medicine being developed as a potential treatment for PKU.

- Synthetic Biotic medicines offer potential for a safe, tolerable, reversible and oral therapy, which reduces plasma Phe levels by consuming Phe in the GI tract.
- SynPheny-1 is designed to evaluate plasma Phe lowering of a solid oral formulation of SYN1618 in adult PKU patients who do not benefit from, or do not tolerate, existing therapies such as Kuvan or Palyzliq.
- SYN1934, an evolved Synthetic Biotic medicine in the PKU portfolio, has progressed to IND enabling studies.
 - SYN1934 consumes Phe in the GI tract and contains a high activity PAL enzyme developed using directed evolution from the SYN1618 PAL enzyme.
 - SYN1934 may offer additional Phe lowering capacity, or the ability to dose at lower levels, relative to SYN1618.
- Synlogic will provide full results of the SYN1618 Phase 1 study of a solid oral formulation in healthy volunteers at the American College of Medical Genetics (ACMG) meeting in April 2021.

Completion of Part A of the Phase 1 study of SYN8802 in Healthy Volunteers. Part B in patients with Enteric Hyperoxaluria following Roux-en-Y gastric bypass surgery has been initiated. SYN8802 is an orally administered Synthetic Biotic medicine being developed as a potential treatment for Enteric Hyperoxaluria. Synlogic has completed dosing of five cohorts in part A, 45 total subjects. Findings include:

- SYN8802 was generally well tolerated in healthy volunteers. There were no serious or systemic adverse events. The most frequent adverse events were mild or moderate, transient, and GI-related.
- Dietary Hyperoxaluria was successfully induced in Healthy Volunteers.
 - Subjects placed on 600 mg of daily dietary oxalate had urinary oxalate levels of 44.8 mg/24h at baseline.
- Dose responsive changes in urinary oxalate levels were observed with a significant reduction in urinary oxalate relative to placebo across three dose levels.
- A dose of 3e11 live cells administered three times daily with meals was selected as the dose for part B of the study.
- This dose was well-tolerated and resulted in a change from baseline urinary oxalate reduction of 28.6% (90% CI: -42.4 to -11.6), compared to placebo.
- At the end of dosing, the mean 24-hour urinary oxalate level was 40.1 mg for subjects treated with SYN8802 3e11 live cells, compared to 58.1 mg for placebo subjects. Upper limit of normal urinary oxalate levels are 45 mg per 24 hours.

Full results of the study will be presented at a future medical meeting. Data from Part B in patients with Enteric Hyperoxaluria following Roux-en-Y gastric bypass surgery is expected in the second half of 2021.

The Immunomodulation Portfolio:

Advancement of SYN1891 into combination arm dosing with PDL1 checkpoint inhibitor in an ongoing Phase 1 clinical study in patients with advanced solid tumors or lymphoma. SYN1891 is an intratumorally administered Synthetic Biotic medicine engineered to act as a dual innate and adaptive immune activator.

- SYN1891 is currently being evaluated in a Phase 1 study that has two parts:
 - Part A is a monotherapy arm that has enrolled five dose cohorts to date. The maximum tolerated dose has not been reached and dose escalation continues.
 - Part A of the study has demonstrated target engagement and activation of the STING pathway.
 - Part B of the study was initiated in December 2020 and combines escalating dose levels of SYN1891 with a fixed dose of the PD-L1 checkpoint inhibitor atezolizumab to establish a recommended Phase 2 dose for the combination regimen.
 - An update on the study will be shared at the American Association of Cancer Research (AACR) meeting in April 2021.
 - Data from both arms will continue to be reported as appropriate over the course of 2021, with mature combination therapy data expected by the end of the year.

Corporate Update:

- **Synlogic expands Board of Directors.** Synlogic recently appointed Michael Heffernan and Lisa Kelly-Croswell to its Board of Directors.
 - Mr. Heffernan is a seasoned entrepreneur and biopharmaceutical leader with over 25 years of experience building and leading development stage and commercial companies.
 - Ms. Kelly-Croswell is a global Human Resources executive with over 30 years of experience in assignments commonly involving rapid business growth, performance turnarounds and innovation.
- **Synlogic strengthens Leadership Team.**
 - Dr. Caroline Kurtz was promoted to Chief Development Officer. Dr. Kurtz joined Synlogic in October 2016 and is responsible for program leadership and portfolio planning and progression. With over 25 years of experience in the pharmaceutical industry, Dr. Kurtz has led multiple programs through mid and late-stage clinical development.
 - Daniel Rosan was promoted to Senior Vice President and Head of Finance. Mr. Rosan joined Synlogic in March 2020 and has over 20 years of industry experience.
 - Synlogic appointed Dr. Jamie Austin to the role of Incoming Head of Regulatory Affairs. Dr. Austin has over 15 years of industry experience.
- **Synlogic advances strategic partnerships.**
 - Synlogic and the MIT Voigt Lab are collaborating with the Air Force Research Laboratory (AFRL) and the Department of Defense (DoD) to engineer novel investigational medicines to address battle fatigue.
 - Synlogic and Ginkgo Bioworks continue to advance their long-term strategic platform collaboration that provides expanded synthetic biology capabilities to Synlogic.

Fourth Quarter 2020 Financial Results

As of December 31, 2020, Synlogic had cash, cash equivalents and short-term investments of \$100.4 million.

For the three months ended December 31, 2020, Synlogic reported a consolidated net loss of \$14.6 million, or \$0.39 per share, compared to a consolidated net loss of \$12.8 million, or \$0.37 per share, for the corresponding period in 2019.

Research and development expenses were \$11.4 million for the three months ended December 31, 2020 compared to \$11.3 million for the corresponding period in 2019.

General and administrative expenses for the three months ended December 31, 2020 were \$3.3 million compared to \$3.5 million for the corresponding period in 2019.

There was no revenue for the three months ending December 31, 2020 compared to \$1.2 million for the three months ended December 31, 2019. Revenue for the prior period was associated with Synlogic's collaboration with AbbVie to develop Synthetic Biotic medicines for the treatment of Inflammatory Bowel Disease, which was terminated in May 2020.

Full Year 2020 Financial Results

For the year ended December 31, 2020, consolidated net loss was \$59.2 million, or \$1.65 per share, compared to a consolidated net loss of \$51.4 million, or \$1.70 per share, for the year ended December 31, 2019. Revenues were \$0.5 million for the year ended December 31, 2020, compared to \$2.2 million for the same period in 2019. Total operating expenses were \$61.0 million for the year ended December 31, 2020, compared to \$56.6 million for the same period in 2019.

Financial Outlook

Based upon its current operating plan, Synlogic expects to have sufficient cash to be able to fund the base operating plan into 2023.

Conference Call & Webcast Information

Synlogic will host a conference call and live webcast at 8:30 a.m. ET today, Thursday, March 25, 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 4897219. A replay will be available for 30 days on the Investors and Media section of the Synlogic website.

About PKU

Phenylketonuria (PKU) is an inherited metabolic disease that manifests at birth and is marked by an inability to break down Phe, an amino acid that is 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 Enteric Hyperoxaluria

Enteric Hyperoxaluria is an acquired metabolic disorder caused by increased absorption of dietary oxalate, which is present in many healthy foods, making it almost impossible to control with diet alone. Enteric Hyperoxaluria often occurs as a result of a primary insult to the bowel, such as inflammatory bowel disease, short bowel syndrome, or as a result of surgical procedures such as Roux-en-Y bariatric weight-loss surgery.

Enteric Hyperoxaluria results in dangerously high levels of urinary oxalate, which causes progressive kidney damage, kidney stone formation, and nephrocalcinosis. Enteric Hyperoxaluria has no approved treatment options.

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; our expectations about sufficiency of our existing cash balance; 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 SEC. 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 will 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.

Synlogic, Inc.
Condensed Consolidated Statements of Operations
(unaudited)

(in thousands, except share and per share data)

	For the three months ended		For the year ended	
	December 31, 2020	December 31, 2019	December 31, 2020	December 31, 2019
Revenue	\$ —	\$ 1,231	\$ 545	\$ 2,224
Operating expenses				
Research and development	11,407	11,254	47,474	41,905
General and administrative	3,286	3,456	13,537	14,728
Total operating expenses	14,693	14,710	61,011	56,633
Loss from operations	(14,693)	(13,479)	(60,466)	(54,409)
Other income, net	105	681	1,293	3,036
Net loss	\$ (14,588)	\$ (12,798)	\$ (59,173)	\$ (51,373)
Net loss per share - basic and diluted	\$ (0.39)	\$ (0.37)	\$ (1.65)	\$ (1.70)
Weighted-average common shares used in computing net loss per share - basic and diluted	37,792,966	34,224,070	35,835,744	30,284,068

Synlogic, Inc.
Condensed Consolidated Balance Sheets
(unaudited)

(in thousands, except share data)

	December 31, 2020	December 31, 2019
Assets		
Cash, cash equivalents, short and long-term investments	\$ 100,444	\$ 127,073
Fixed assets	10,776	13,021
Other assets	32,620	48,480
Total assets	\$ 143,840	\$ 188,574
Liabilities and stockholders' equity		
Current liabilities	\$ 8,301	\$ 8,863
Long-term liabilities	20,404	22,806
Total liabilities	28,705	31,669
Total stockholders' equity	115,135	156,905
Total liabilities and stockholders' equity	\$ 143,840	\$ 188,574
Common stock and common stock equivalents		
Common stock	38,183,273	32,266,814
Common stock warrants (pre-funded)	2,548,117	2,548,117
Total common stock	40,731,390	34,814,931

CONTACT: Media: Lauren Arnold, MacDougall, Phone: 781-235-3060, Email: larnold@macbiocom.com, Investor: Daniel Rosan, Synlogic, Inc., Phone: 617-401-9152, Email: dan.rosan@synlogictx.com

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

Q4 Financial Results & Business Update
25 March 2021

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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.

Opening Remarks

Dr. Aoife Brennan
MB CHB

President & CEO

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Recent highlights: Execution across the portfolio

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 mid-year

SYNB8802 in Enteric Hyperoxaluria

Proof of mechanism demonstrated in Phase 1A with Dietary Hyperoxaluria induced in healthy volunteers

Phase 1B patient data expected mid-year

Immunomodulation

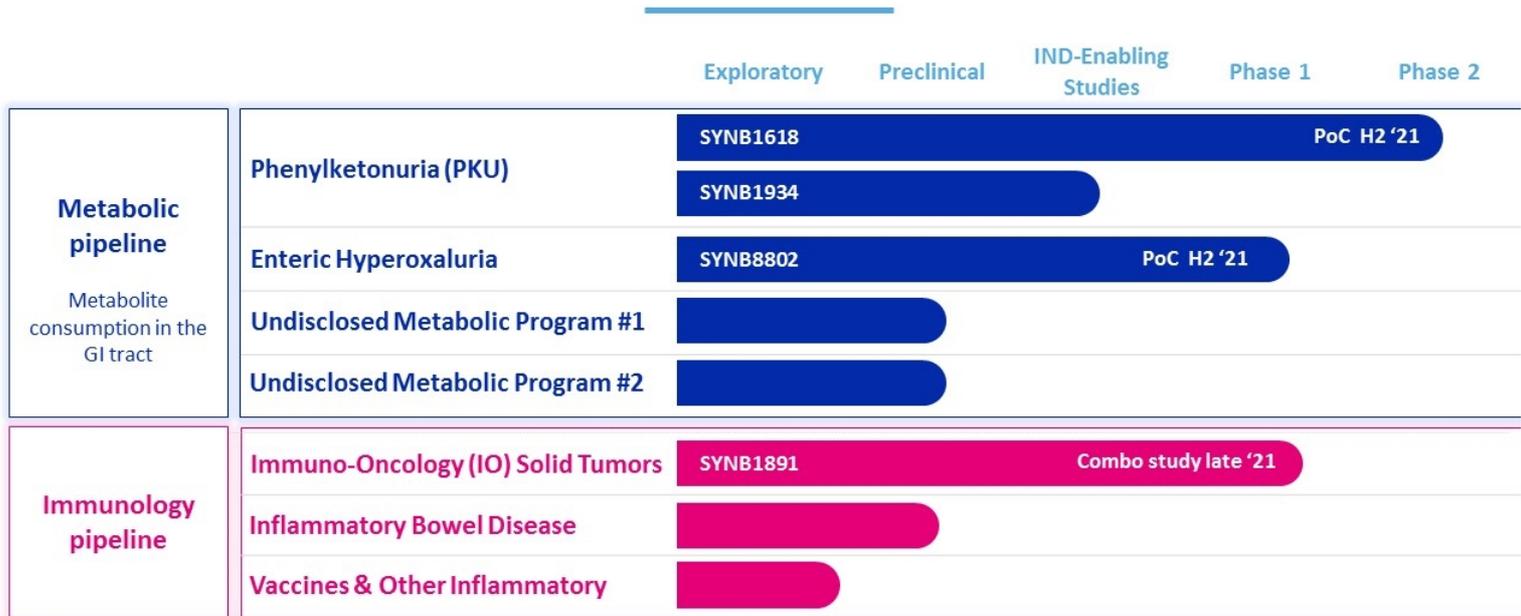
SYNB1891 in Solid Tumors

Monotherapy demonstrated target engagement, meaningful pharmacodynamic effects, good safety

Combination with anti-PD1 and continued dose escalation ongoing

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

Robust pipelines with meaningful catalysts





Progress in Metabolic Programs

Dr. Richard Riese, MD, PhD
Chief Medical Officer



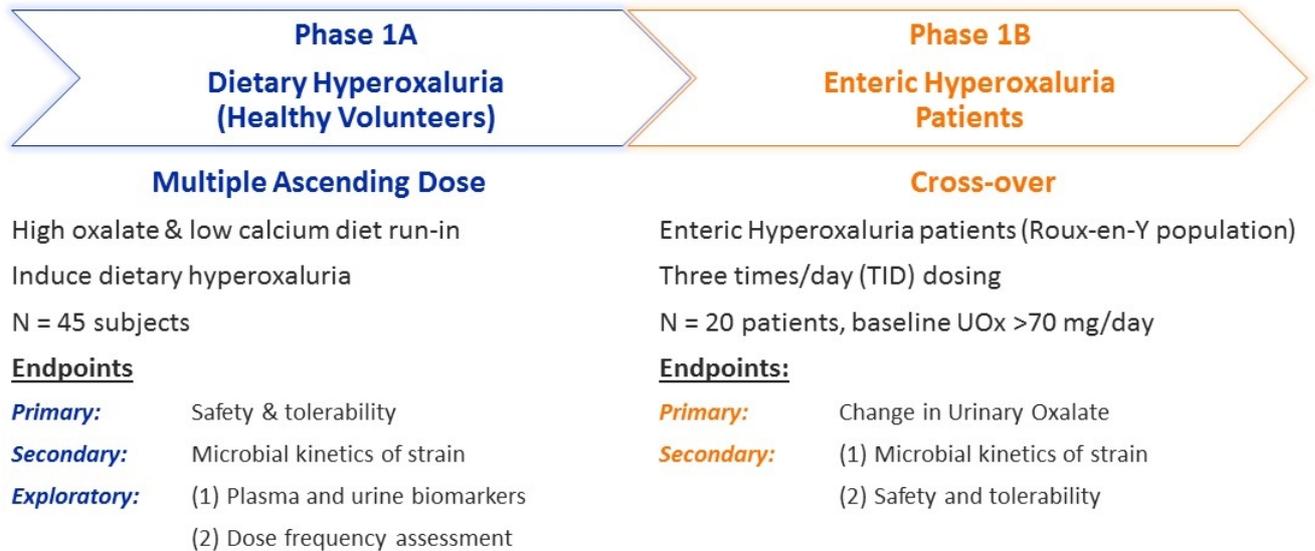
Enteric Hyperoxaluria (HOX)

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

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

SYNB8802 proof of concept study on track for 2021 data read out

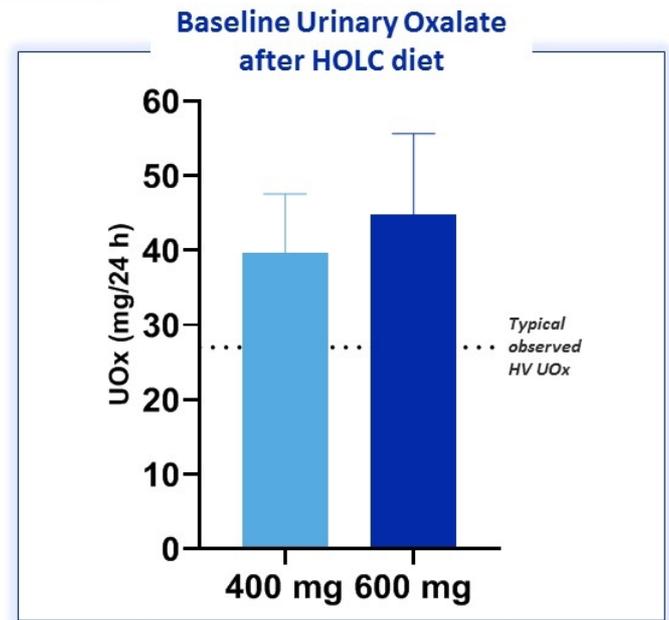
Ph1 design provides POC opportunity in 2021



Dietary hyperoxaluria model is translationally relevant to patient population

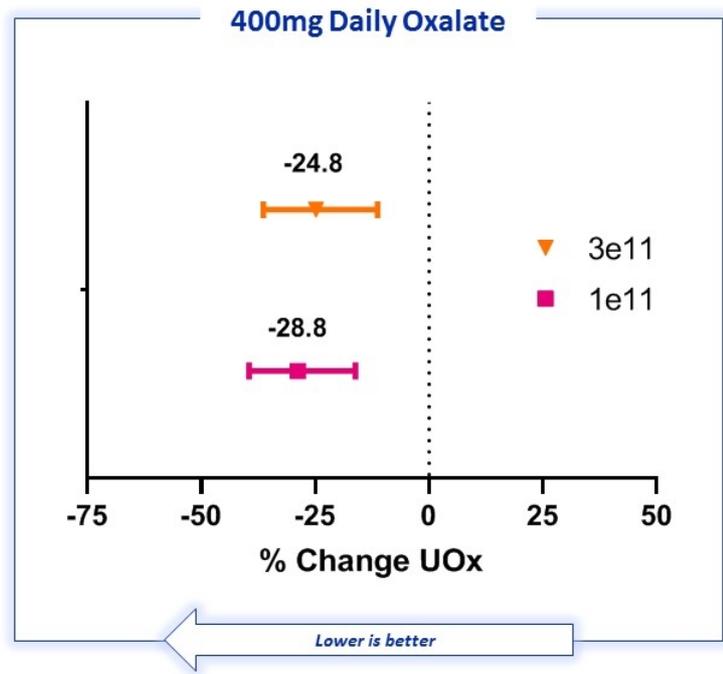
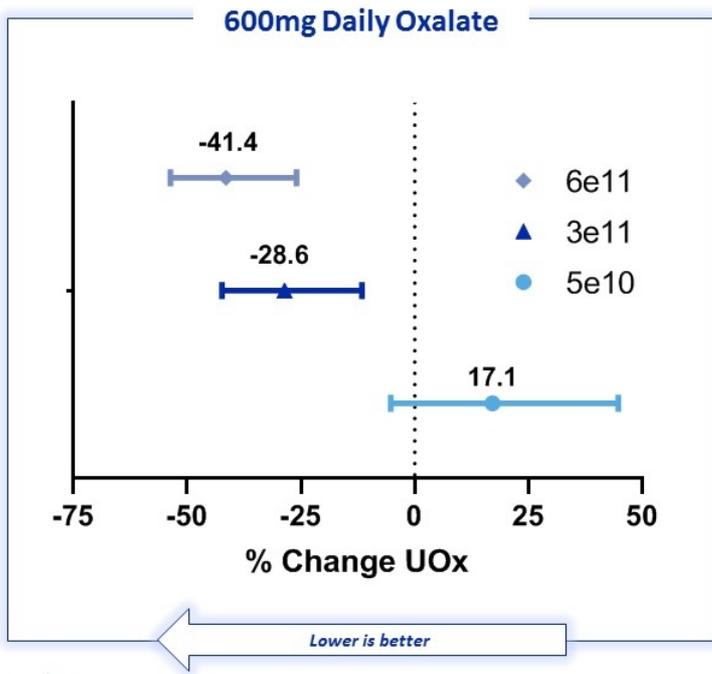
High oxalate diet successfully elevated UOx levels in HV

- 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



Dose-responsive and reproducible Uox lowering demonstrated

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

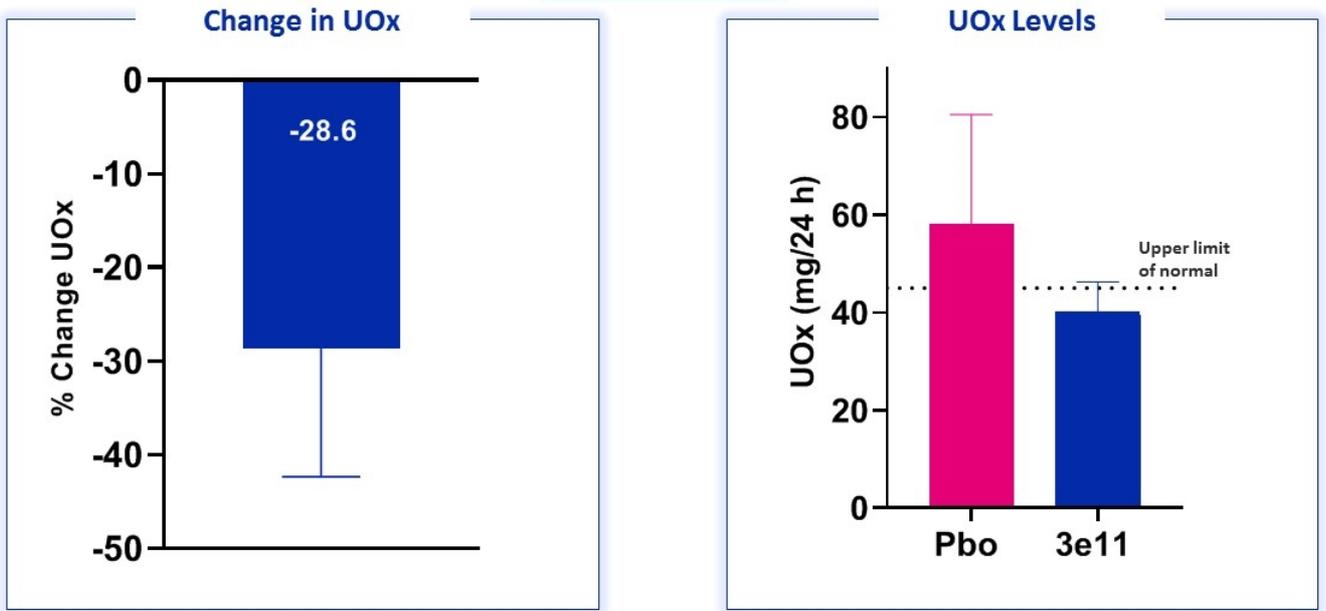


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LS mean change over Placebo, +/- 90% CI, all days baseline and treated

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SYNB8802 3e11 live cells dose advancing to Ph1B in patients



Urinary oxalate lowering demonstrated at a well tolerated dose

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



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

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



SynPheny POC Study in 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



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

4th Quarter and Year End 2020

Summary Results

<u>Balance Sheet (unaudited)</u>			<u>31 Dec 2020</u>	<u>31 Dec 2019</u>
Cash, Cash Equivalents, and Marketable Securities			\$100.4 M	\$127.1M
	<u>Three Months Ended</u>		<u>For the Year Ended</u>	
<u>Statement of Operations (unaudited)</u>	<u>31 Dec 2020</u>	<u>31 Dec 2019</u>	<u>31 Dec 2020</u>	<u>31 Dec 2019</u>
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)
<i>Weighted Average Shares Outstanding*</i>	<i>37.8 M</i>	<i>34.2 M</i>	<i>35.8 M</i>	<i>30.3 M</i>

Concluding Remarks

Dr. Aoife Brennan
MD CHB

President & CEO

synlogic



Available For Questions



Aoife Brennan, MB ChB
President & CEO



Antoine Awad
Chief Operating Officer



Richard Riese, MD PhD
Chief Medical Officer



Dave Hava, PhD
Chief Scientific Officer



Gregg Beloff, JD MBA
Interim CFO



Caroline Kurtz, PhD
Chief Development Officer



Daniel Rosan
Head of Finance & Investor Relations

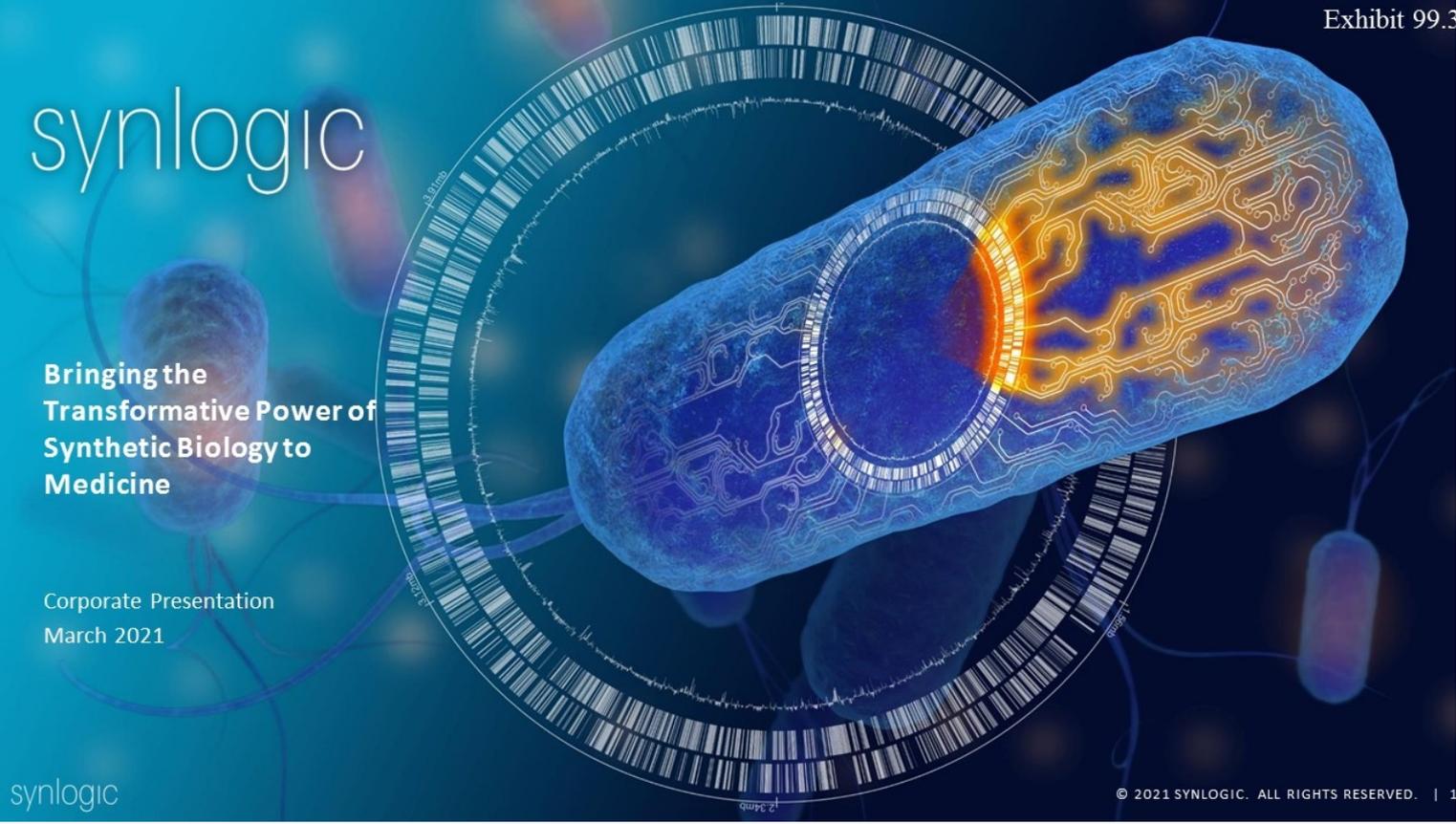
synlogic

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

Corporate Presentation
March 2021

synlogic

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Forward Looking Statements

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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

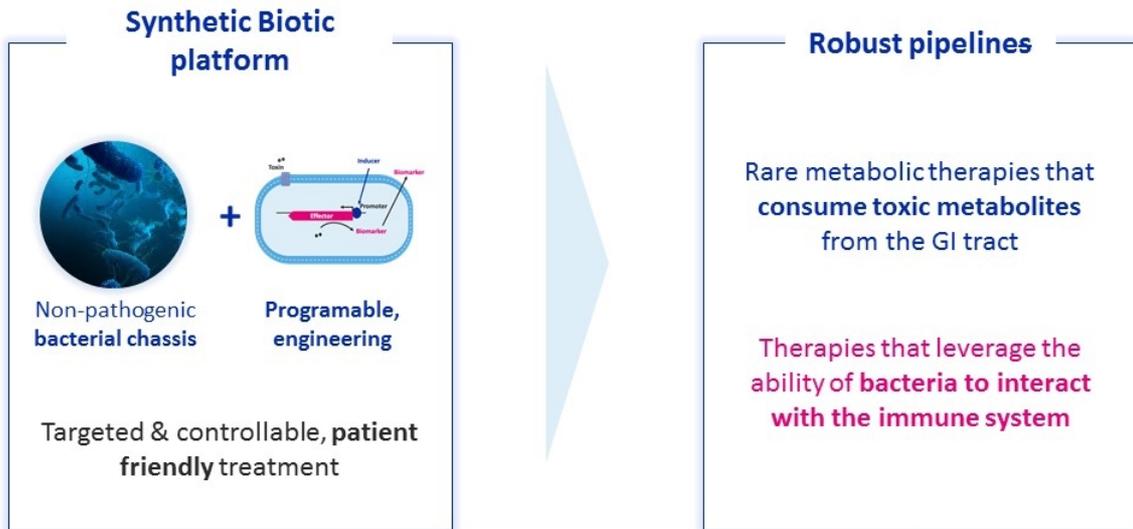
SYNB1891 in Solid Tumors

Monotherapy target engagement, meaningful pharmacodynamic effects, good safety

Combination with anti-PD1 and dose escalation ongoing

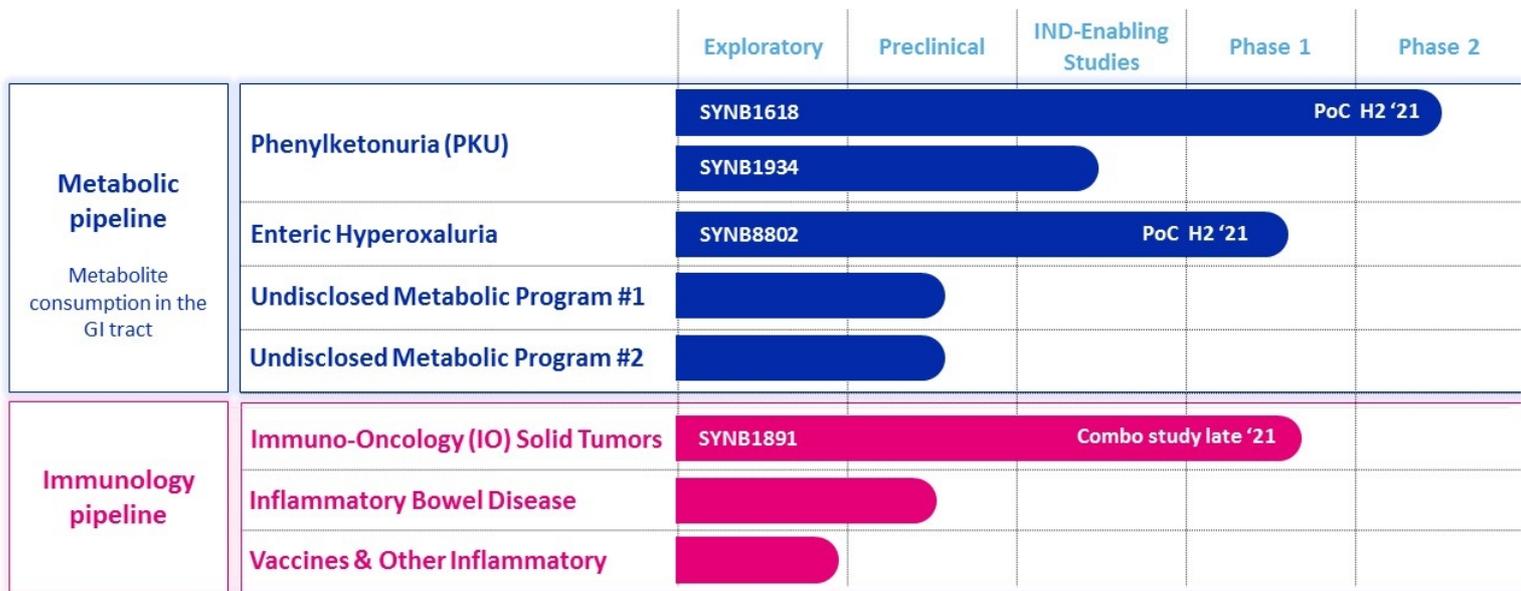
2021 data with potential to demonstrate clinical benefit of the Synthetic Biotic platform

A new class of medicines



**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 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



**Unmet
Medical
Need**



**Validated
Biology**



**Unique
Advantages**



**Platform
Proof of
Mechanism**

Phenylketonuria (PKU)

Many patients unable to control Phe
~30% BH4 oral therapy response rates

Lower dietary Phe intake = lower plasma Phe
levels = improved cognitive outcomes

Modality able to consume Phe in the GI tract
before it can cause damage

SYNB1618 consumes Phe and produces the
TCA biomarker in both HVs and patients

Enteric Hyperoxaluria (HOX)

High kidney disease risk
No effective interventions or treatments

Lower dietary oxalate intake = lower urinary
oxalate = improved kidney outcomes

Modality able to consume oxalate throughout
GI tract, including colon

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



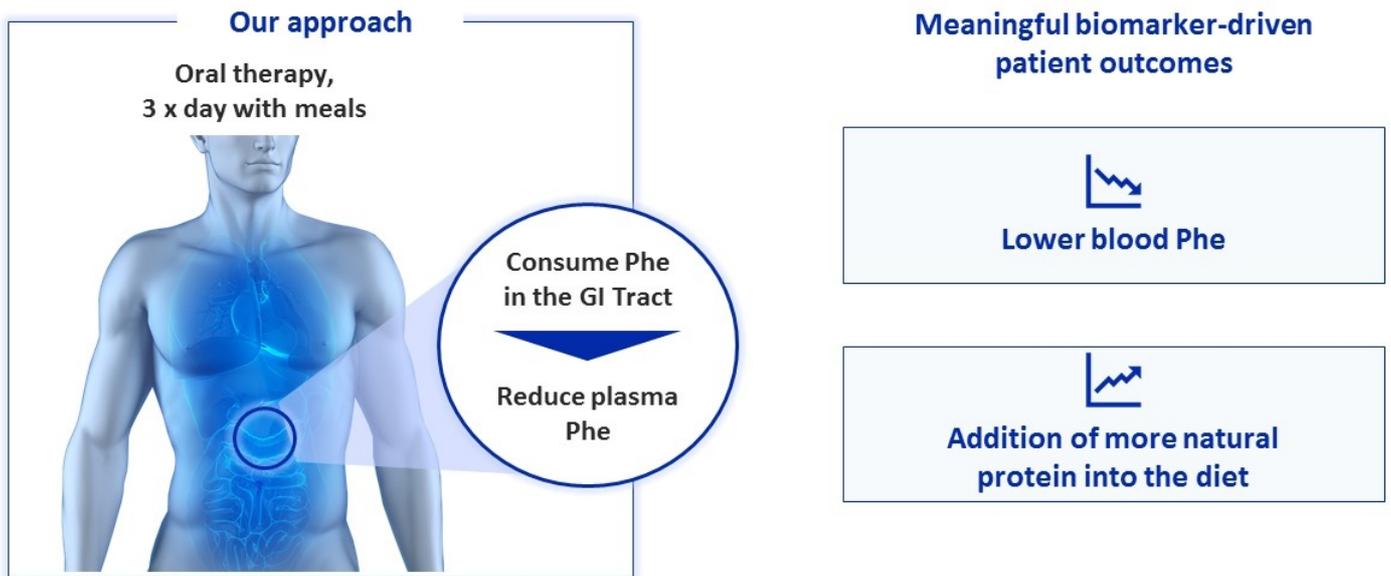
Julia,
living with PKU

Early diagnosis and strict diet control enables better Phe management.

Parents expect PKU child to achieve full potential.

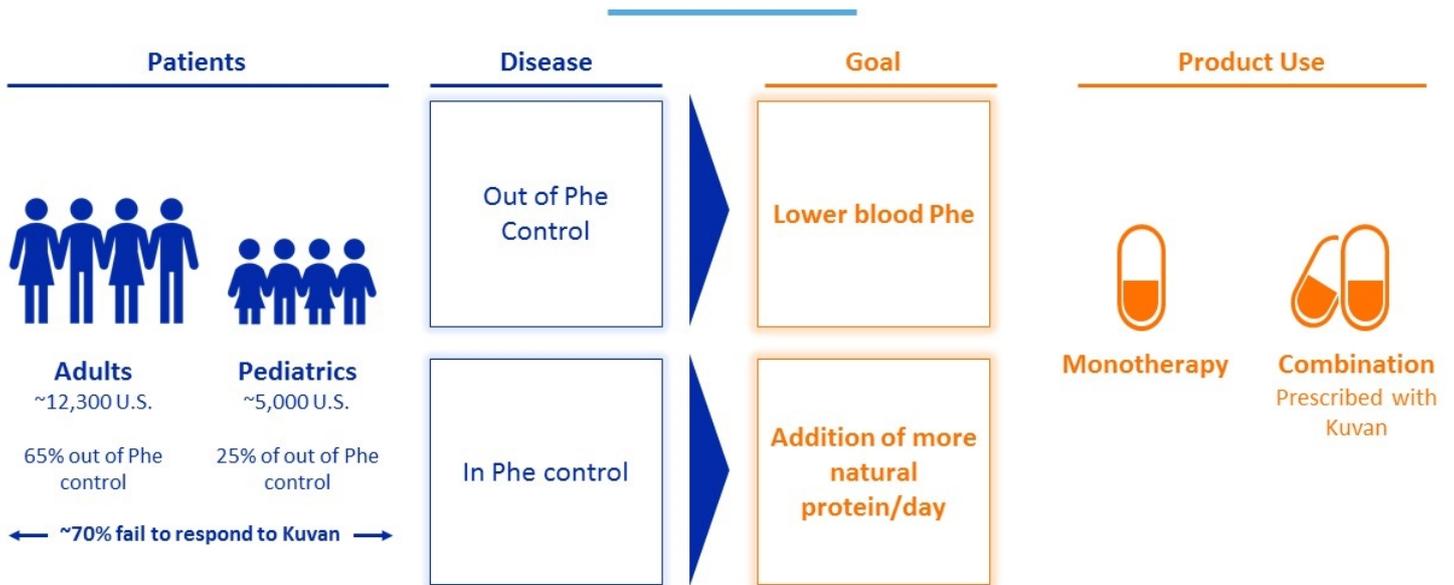
Reality: 25% – 65% of patients still struggle to maintain blood Phe within target range

An innovative approach in area of high unmet medical need



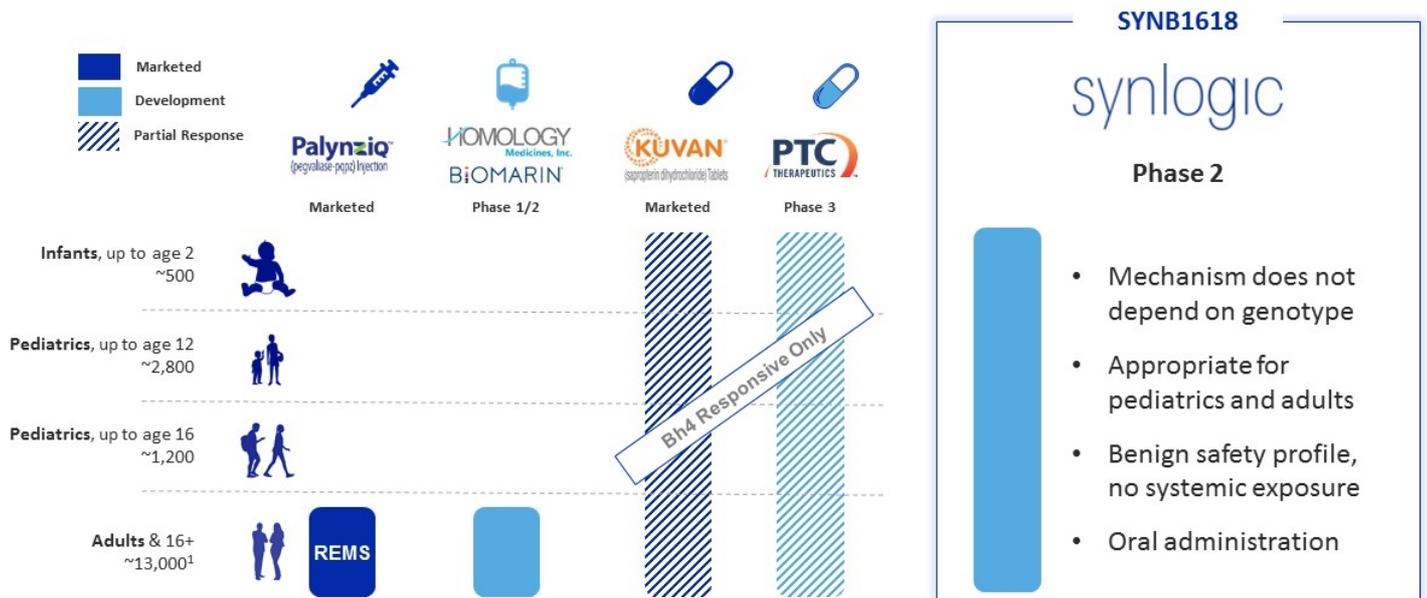
Synlogic has initiated a Ph2 Study in PKU patients (SynPheny)

Multiple areas of unmet need continue across PKU patient types

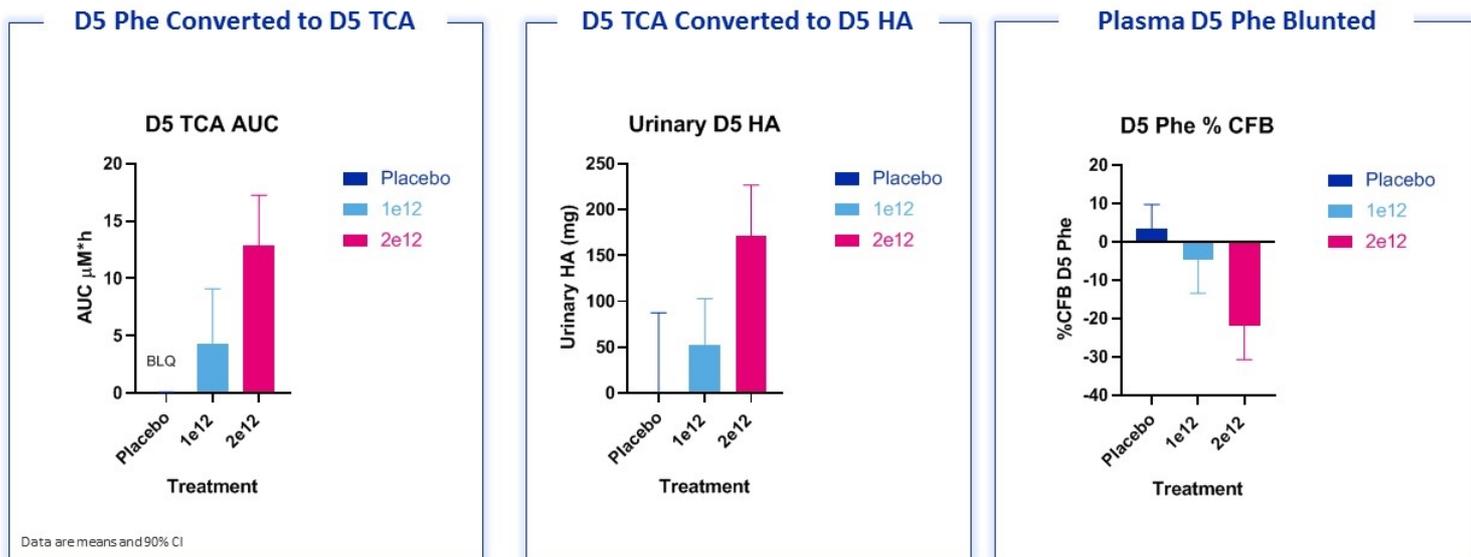


Significant market opportunity, large unmet need, with potential for new products to capture share

SYNB1618 is uniquely positioned to address those needs

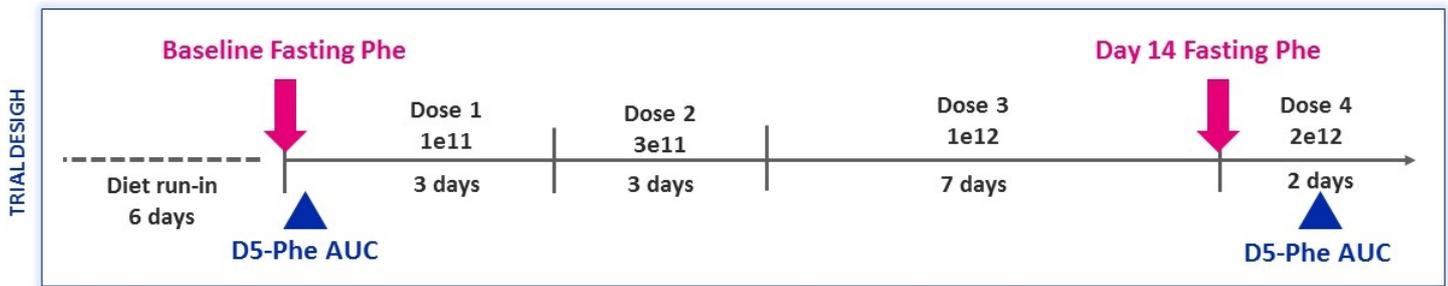


Solid oral SYN1618 reduced Phe and elevated biomarkers in Ph1



Achieved Proof of Mechanism: SYN1618 consumed D5 Phe in GI tract & lowered plasma D5 Phe

SynPheny-1 design enables Proof of Concept



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



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

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	 	 

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

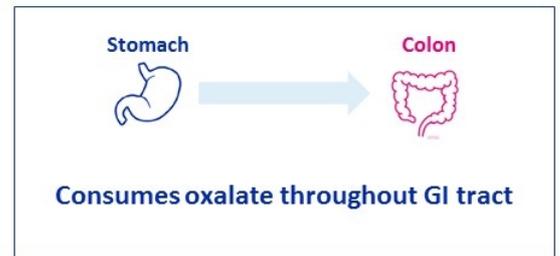
Urinary oxalate levels remain markedly elevated in all patients, despite aggressive medical regimen

An innovative approach in area of high unmet medical need

Our approach



Differentiation from other approaches



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 	✓	✓
Small intestine 	✓	✓
Colon 		✓

Healthy people absorb ~10% of dietary oxalate, mostly via stomach and small intestine

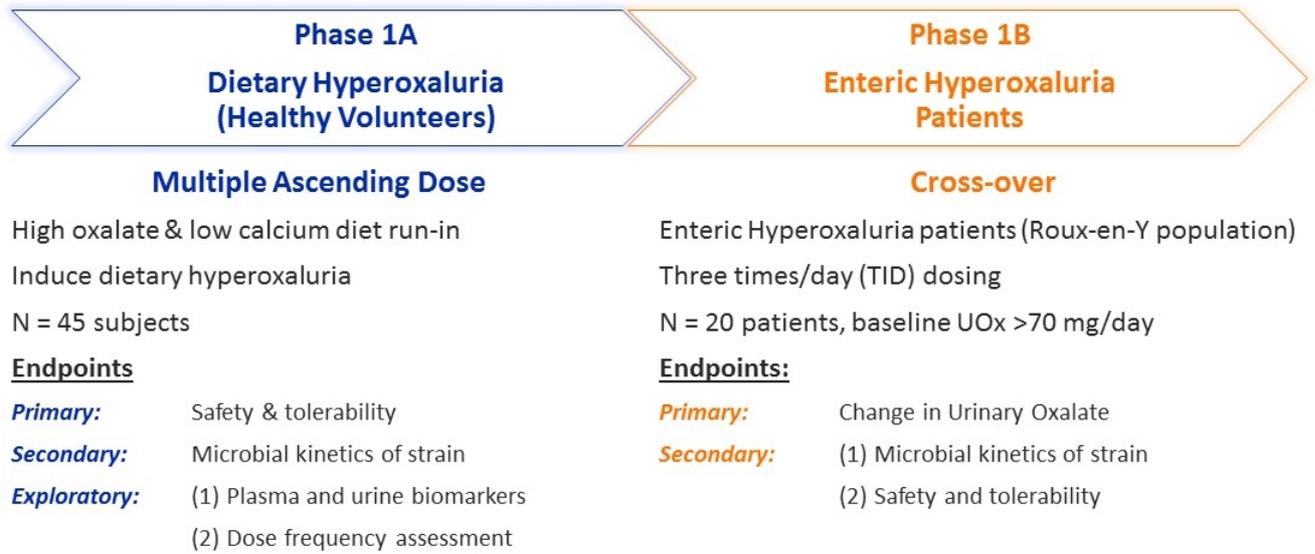
Patients absorb ~20-30% of dietary oxalate, through entire GI tract including colon

Optimal treatment

Absorbs oxalate throughout GI tract, esp. in colon

synlogic	Oral enzyme	Oxalobacter formigenes
✓	✓	
✓	✓	
✓		✓

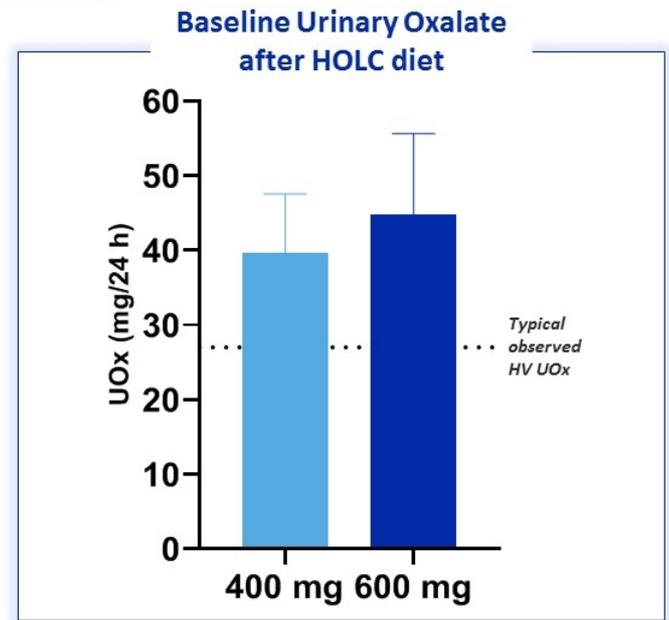
Ph1 design provides POC opportunity in 2021



Dietary hyperoxaluria model is translationally relevant to patient population

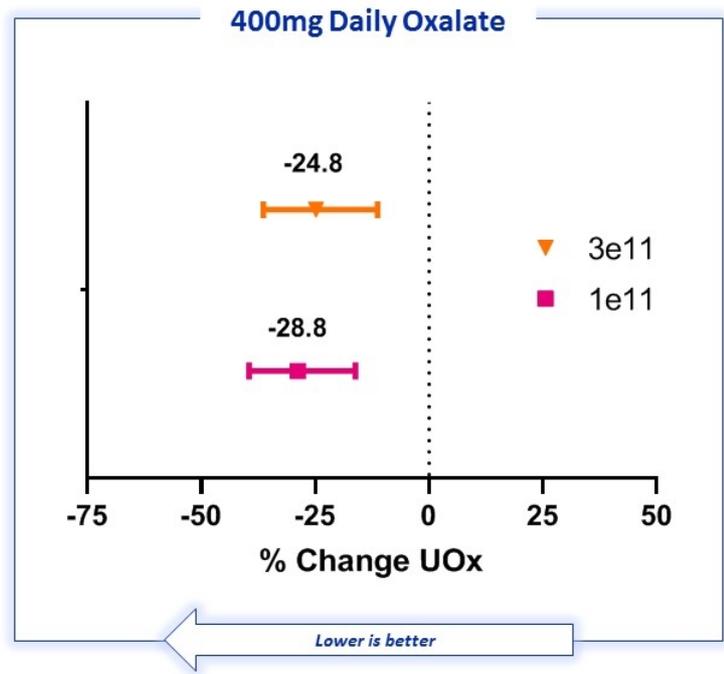
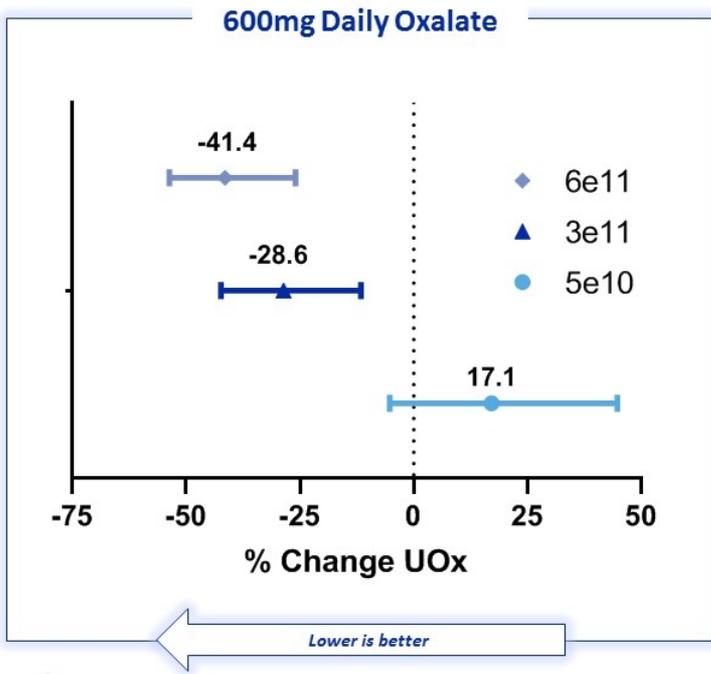
High oxalate diet successfully elevated UOx levels in HV

- 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



Dose-responsive and reproducible Uox lowering demonstrated

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

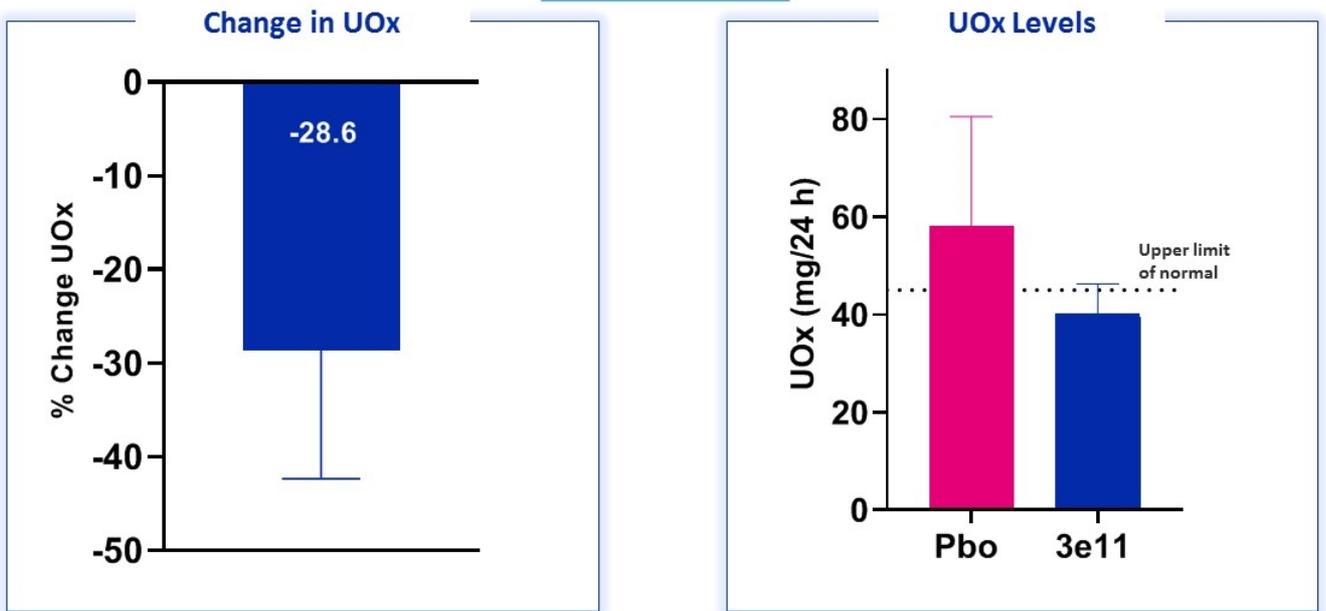


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LS mean change over Placebo, +/- 90% CI, all days baseline and treated

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SYNB8802 3e11 live cells dose advancing to Ph1B in patients



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

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



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
	Ph1A study in HV read-out	SYNB8802	
	Initiate Ph1B study in patients	SYNB8802	
	Ph1B proof of concept read-out		SYNB8802
Enteric Hyperoxaluria			
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

<u>Balance Sheet (unaudited)</u>			<u>31 Dec 2020</u>	<u>31 Dec 2019</u>
Cash, Cash Equivalents, and Marketable Securities			\$100.4 M	\$127.1M
	<u>Three Months Ended</u>		<u>For the Year Ended</u>	
<u>Statement of Operations (unaudited)</u>	<u>31 Dec 2020</u>	<u>31 Dec 2019</u>	<u>31 Dec 2020</u>	<u>31 Dec 2019</u>
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)
<i>Weighted Average Shares Outstanding*</i>	<i>37.8 M</i>	<i>34.2 M</i>	<i>35.8 M</i>	<i>30.3 M</i>

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



Richard Riese, MD PhD
Chief Medical Officer



Antoine Awad
Chief Operating Officer



Daniel Rosan
Head of Finance &
Investor Relations

Board of Directors

Peter Barrett, Chair
Atlas Venture

Chau Khuong
Orbimed Advisors

Mike Burgess
Turnstone Biologics

Nick Leschly
Bluebird Bio

Michael Heffernan
Collegium

Ed Mathers
NEA

Patricia Hurter
Lyndra Therapeutics

Richard Shea
Syndax

Lisa Kelly-Crowell
Boston Medical Center Health System

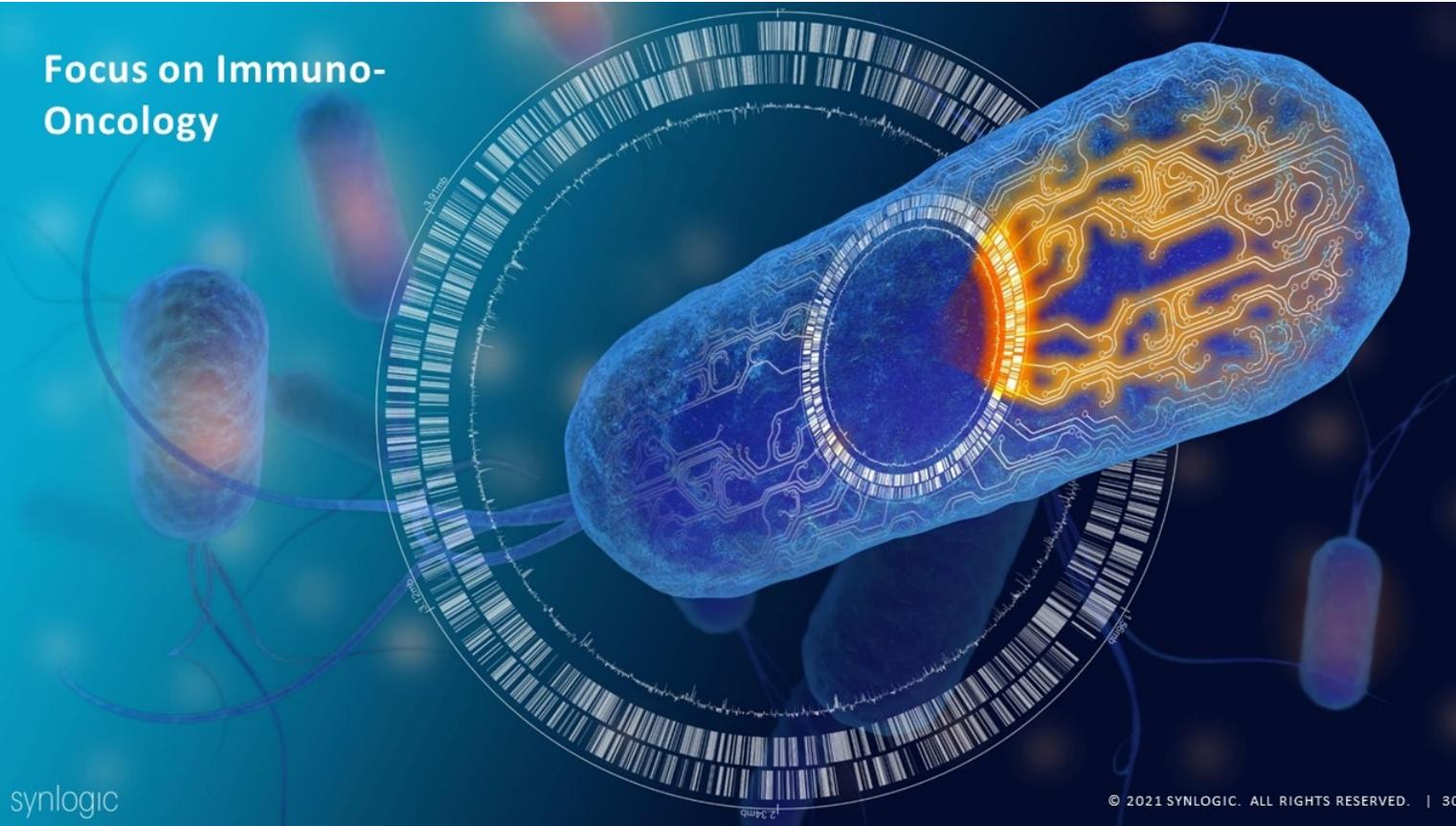
Collaborators



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

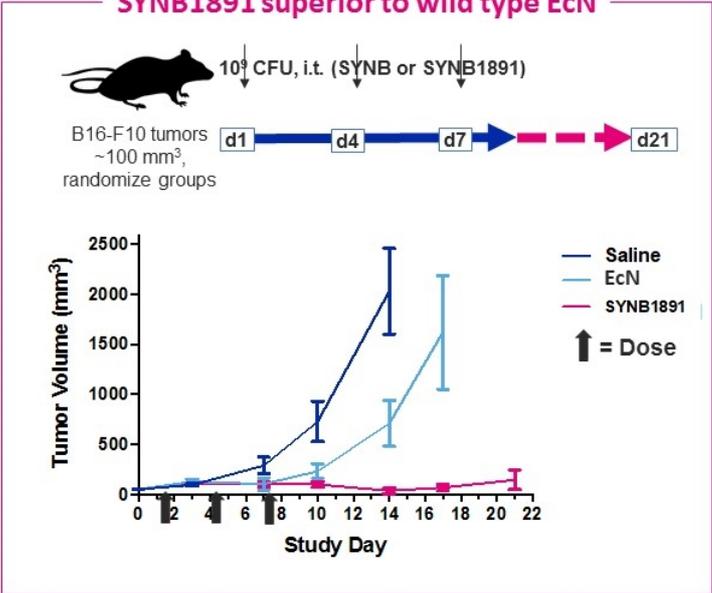
SYNB1891 potential for improved efficacy relative to other STING approaches

SYNB1891 monotherapy demonstrated meaningful pharmacodynamic effects

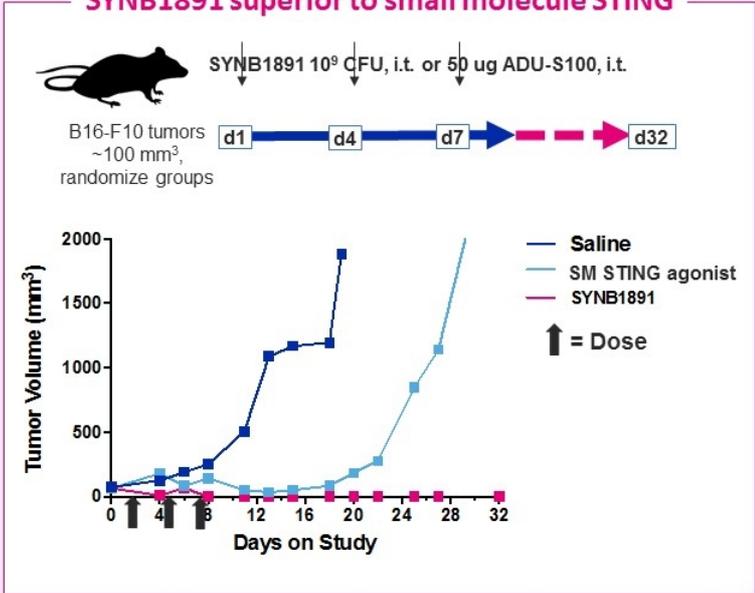
Phase 1 in combination with Tecentriq initiated: Data will be available in 2021

SYNB1891 induces potent anti-tumoral effects

SYNB1891 superior to wild type EcN



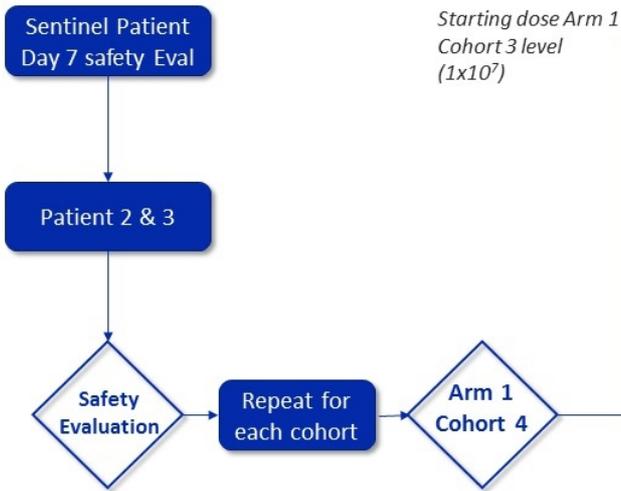
SYNB1891 superior to small molecule STING



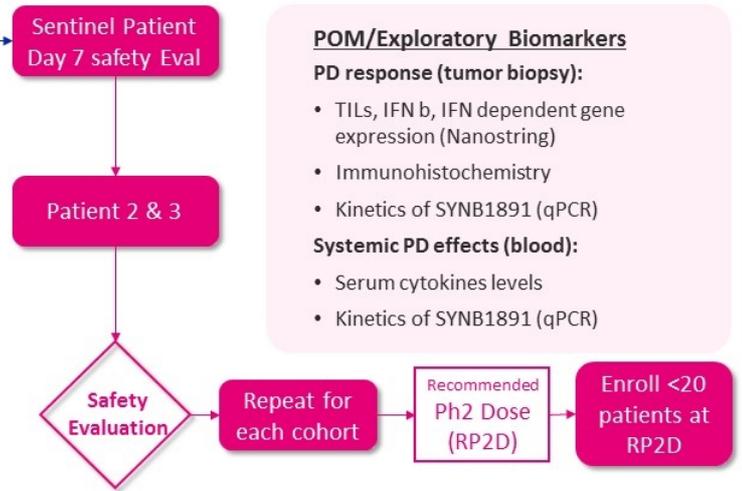
Phase 1 design: multidose tolerability, IT mono and combo

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

Arm 1: Monotherapy Cohorts

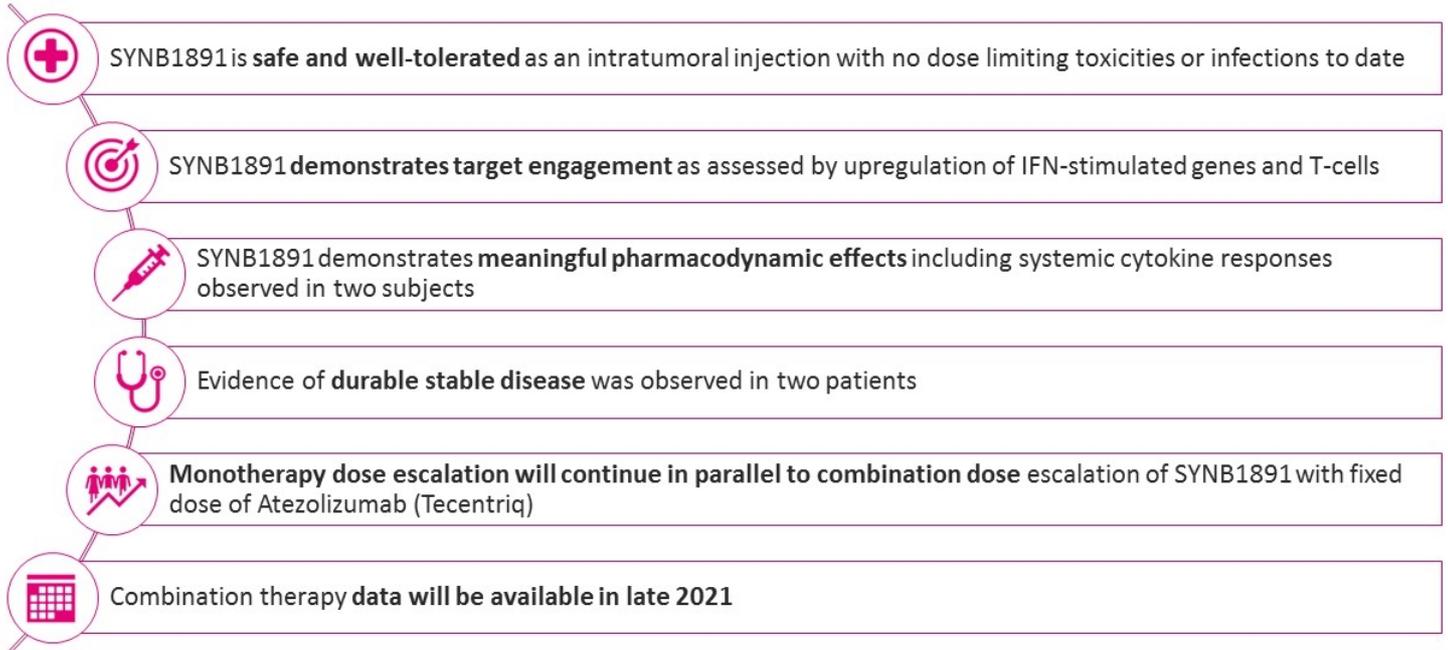


Arm 2: Combination Cohorts - Atezolizumab

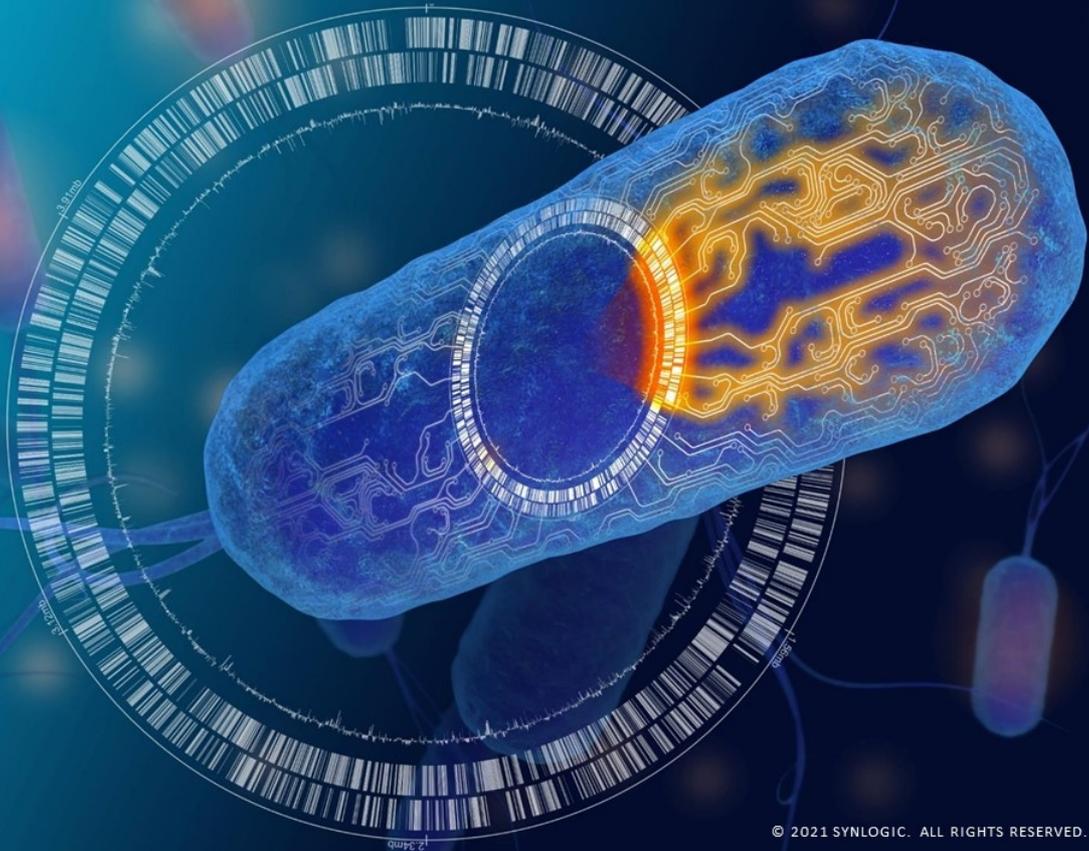


Combination with PD-1 will identify Phase 2 dose, provide evidence of target engagement, safety, and support for target tumor type

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



Engineering Synthetic Biotic Medicines



A new class of medicines

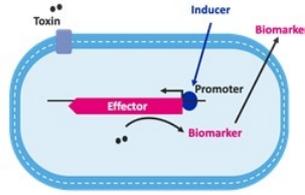
Non-pathogenic
bacterial chassis



E. coli Nissle



Programmable, controllable
engineering



Inducer-Promoter Switch

Effector Design

Safety Features



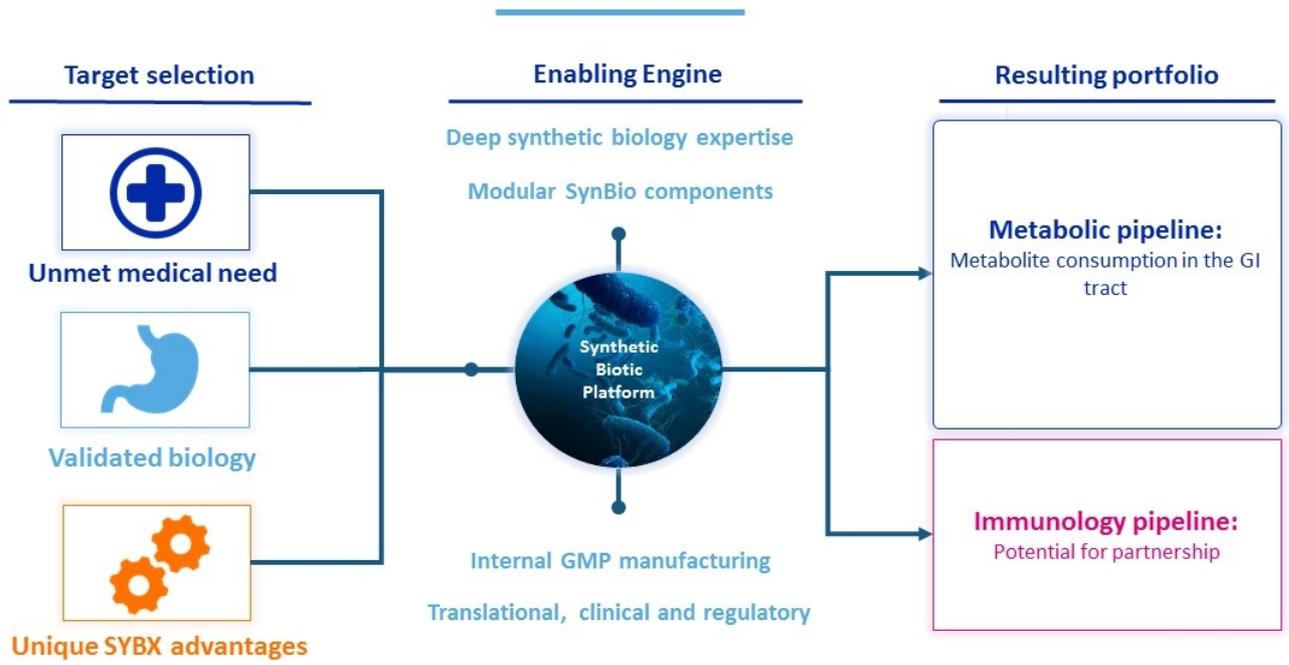
Synthetic Biotic Medicine

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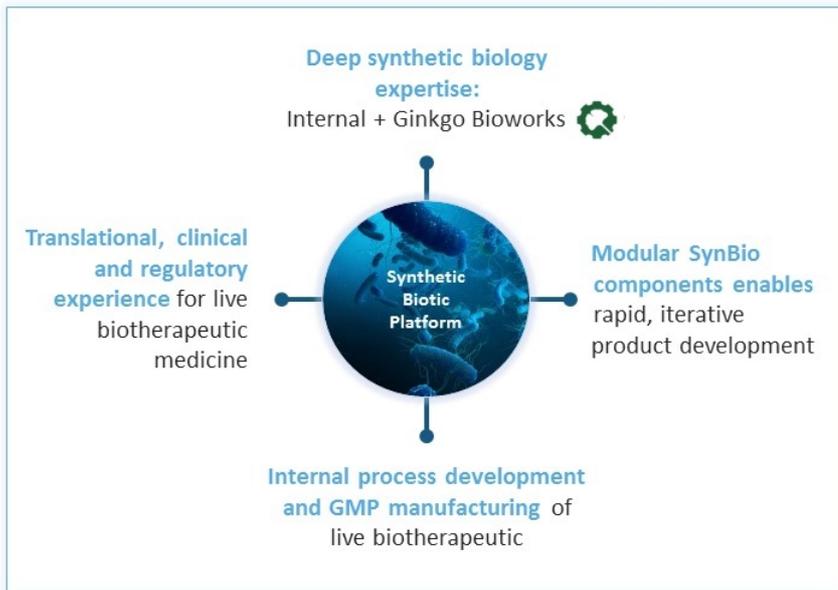
- Drug-like properties
- Does not colonize
- No *in vivo* reproduction or risk of genetic drift

Reusable parts enable rapid iteration of rationally designed prototypes

Synthetic Biotic Platform accelerates pathway into the clinic



Synthetic Biotic Platform is enabling engine for drug development



>200 humans dosed with Synthetic Biotic medicines

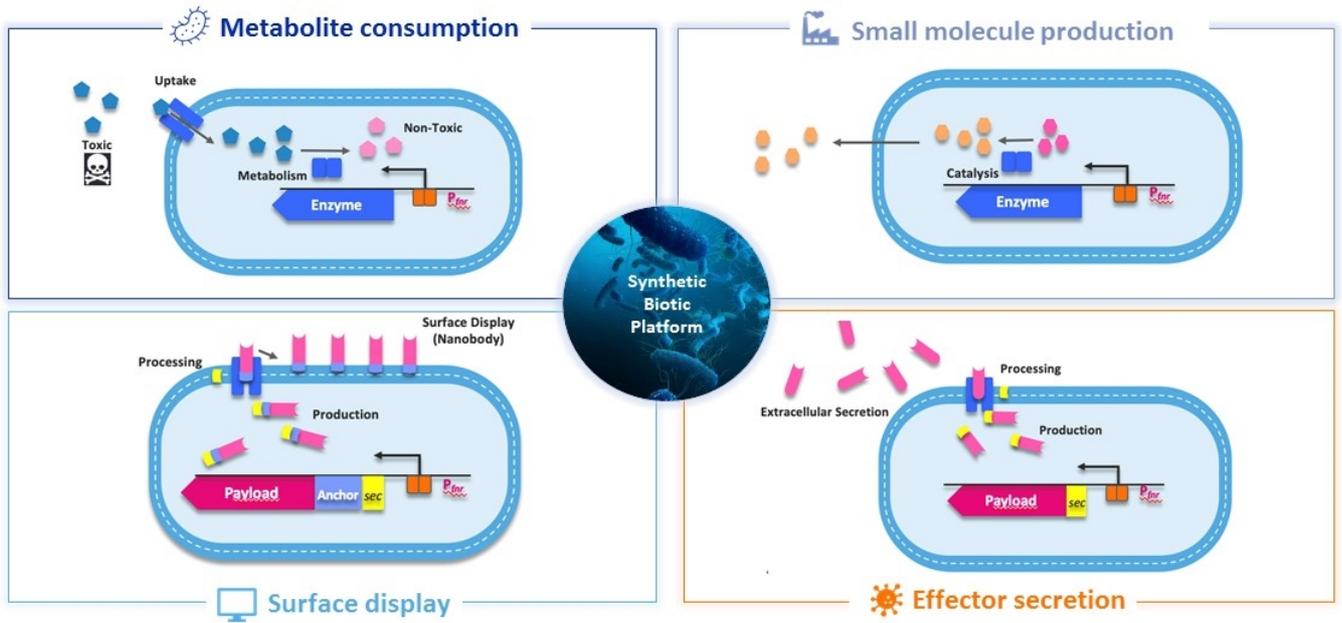
4 INDs opened with the U.S. FDA

Supportive regulatory feedback from global agencies

Safe chassis organism (>100 years of human experience)

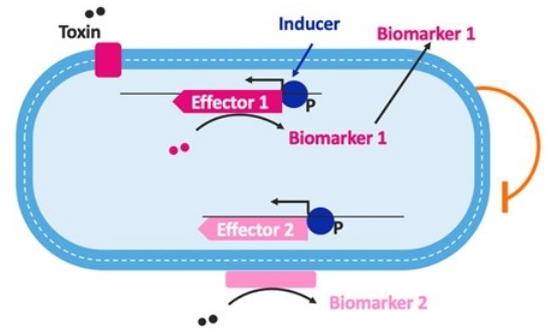
Rapid pipeline expansion possible with reusable engineering

Versatile platform enables diverse therapeutic strategies for range of diseases



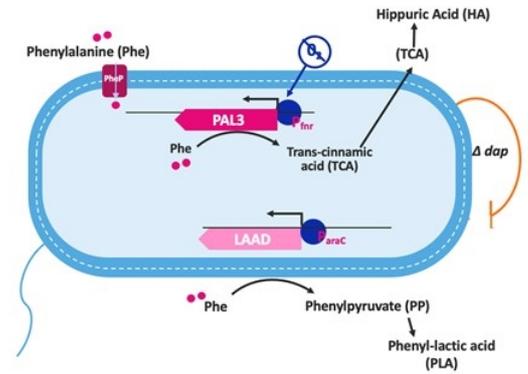
Reusable parts enable rapid iteration of rationally designed prototypes

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



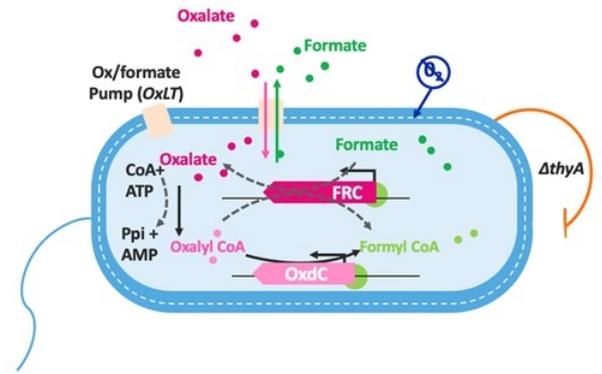
SYNB1618 Design

Component	SYNB1618 Design
Therapeutic strategy	Metabolite consumption: Built from Synthetic Library Specifically to Consume Phe
Bacterial Chassis	<i>E. coli</i> 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: Promoters control expression during manufacturing and at site of action
Safety Features	Δdap: Auxotrophy – requires diaminopimelic acid (DAP) to grow

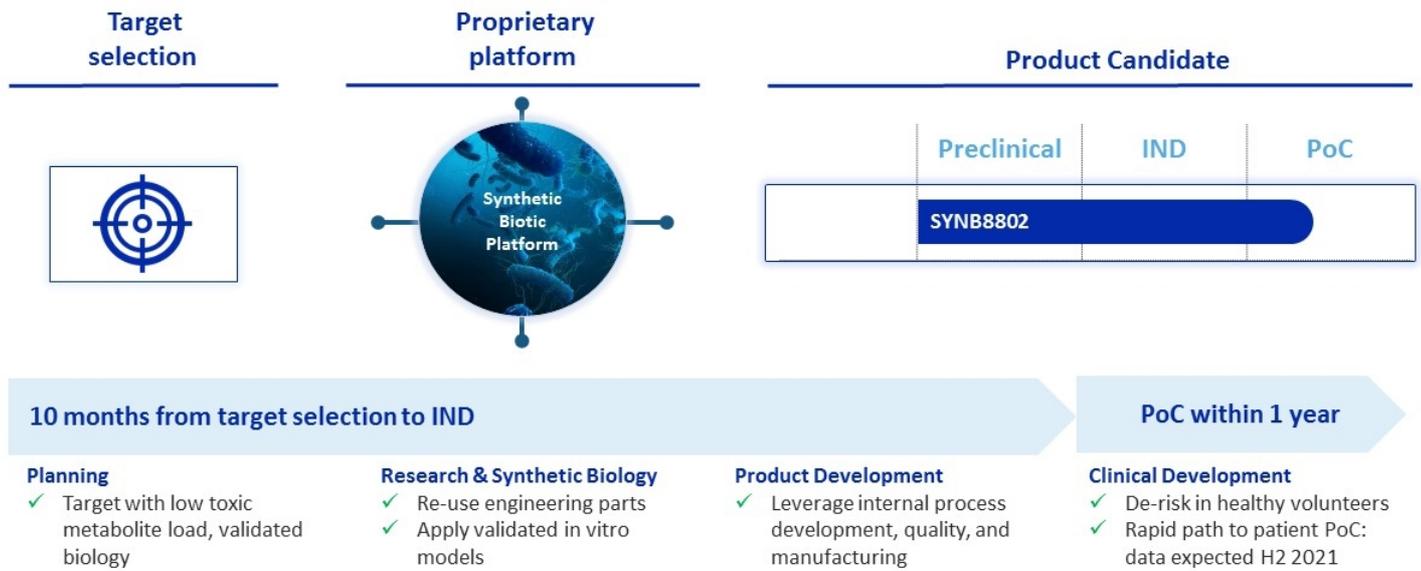


SYNB8802 Design

Component	SYNB8802 Design
Therapeutic strategy	Metabolite consumption: Engineered to Convert Oxalate to Formate for the Treatment of Enteric Hyperoxaluria
Bacterial Chassis	<i>E. coli</i> 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	$\Delta thyA$: Controls growth



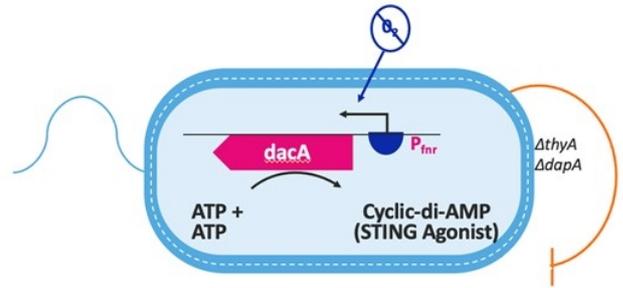
Reusable parts enables rapid progress to proof of concept: SYNB8802 case study

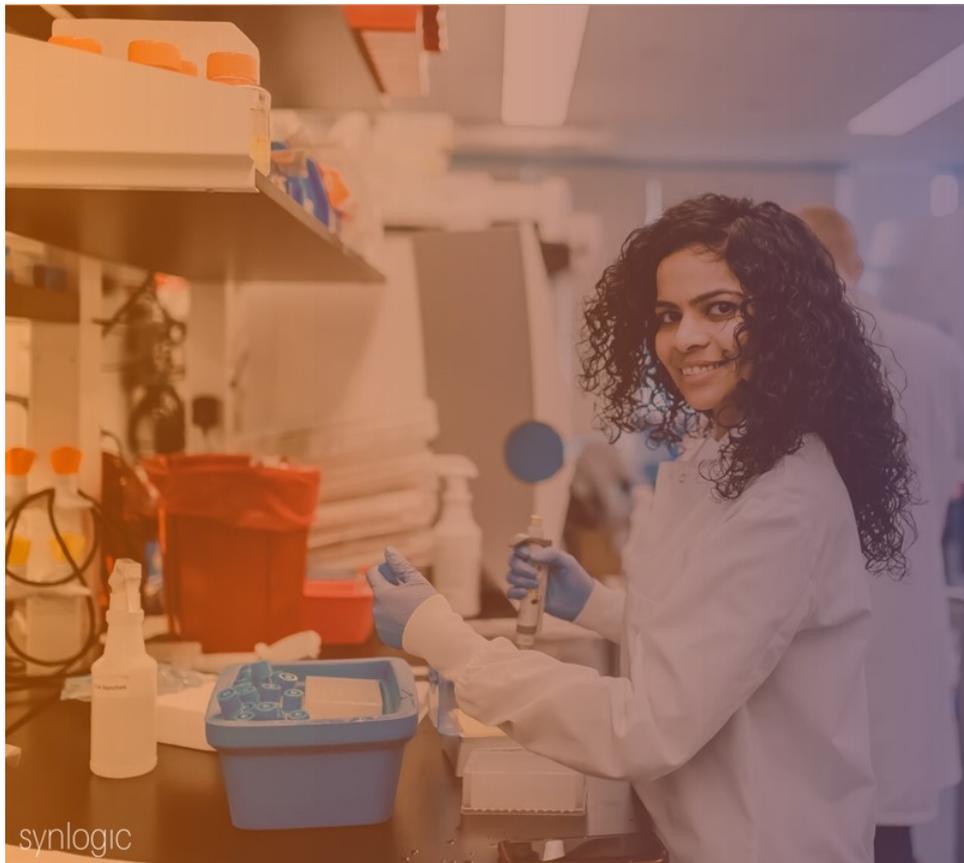


Portfolio of metabolic opportunities available with similar engineering

SYNB1891 Design

Component	SYNB1891 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	<i>E. coli</i> 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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