

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): January 7, 2019

**SYNLOGIC, INC.**

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction  
of incorporation)

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

001-37566  
(Commission File Number)

26-1824804  
(IRS Employer  
Identification No.)

02142  
(Zip Code)

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

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

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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))

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.

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**Item 7.01. Regulation FD Disclosure.**

On January 7, 2019, Synlogic, Inc. (the “Company”) 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 Company’s updated Investor Presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K. The Investor Presentation is current as of January 7, 2019, and the Company disclaims any obligation to update the Investor Presentation after such date.

In accordance with General Instruction B.2 on Form 8-K, the information set forth in this Item 7.01 and the Investor Presentation attached to this report as Exhibit 99.1 is “furnished” and shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section, nor shall such information be deemed incorporated by reference in any filing under the Securities Exchange Act of 1934, as amended, or the Securities Act of 1933, as amended.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

[99.1](#) [Investor Presentation of Synlogic, Inc., dated January 7, 2019](#)

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**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: January 7, 2019

By: /s/ Todd Shegog  
Name: Todd Shegog  
Title: Chief Financial Officer

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# Synlogic

DESIGNED FOR LIFE

Corporate Overview  
January 2019

synlogic



# Forward Looking Statements

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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: inborn errors of metabolism, liver disease, inflammatory and immune disorders, and cancer; the future clinical development of Synthetic Biotic medicines; the potential of our technology to treat hyperammonemia and phenylketonuria; the expected timing of our anticipated clinical trial initiations; 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 13, 2018. The forward-looking statements contained in this presentation reflect our current views with respect to future events. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our view as of any date subsequent to the date hereof.

# Synthetic Biotic™ Medicines Designing for LIFE

## ***Patient Need***

There remain many indications for which conventional medicines do not provide effective solutions for all patients

## ***Conventional Approaches Limited***

Single mechanism agents do not address complex biology, often lead to systemic exposure without control

## ***An Engineered Living Medicine Solution***

Synlogic is harnessing nature and technology to create LIVING medicines designed to significantly improve patients' LIVES

# Synthetic Biotic™ Medicines

## A Novel Class of Engineered Living Medicines

### SYNTHETIC

- Designed genetic circuits to execute biological functions
- Degradation of disease-causing metabolites
- Production of therapeutic molecules

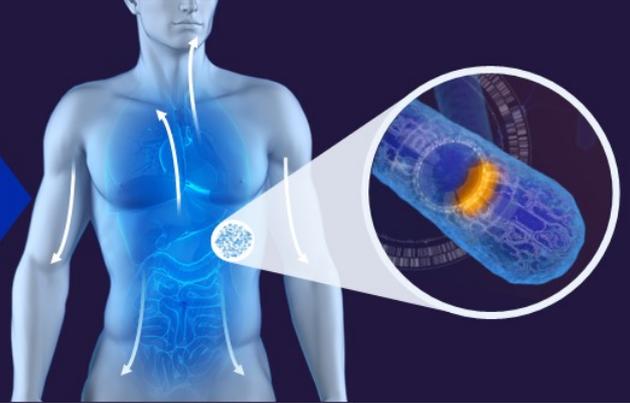
### BIOTIC

- Bacterial chassis
- Non-pathogenic
- Amenable to genetic manipulation

PATHWAYS, COMBINATIONS, BIOMARKERS

PROGRAMMABLE POTENCY AND CONTROL

LOCAL ACTIVITY, REDUCED SYSTEMIC TOXICITY



# Synthetic Biotic Portfolio: Breadth and Potential

Initial Applications Designed to Target Different Sites of Action in Metabolic and Immunomodulatory Diseases

## METABOLIC DISEASES

Rare  
Metabolic  
Disease

Broad  
Metabolic  
Disease

*Small or  
Large  
Intestine*

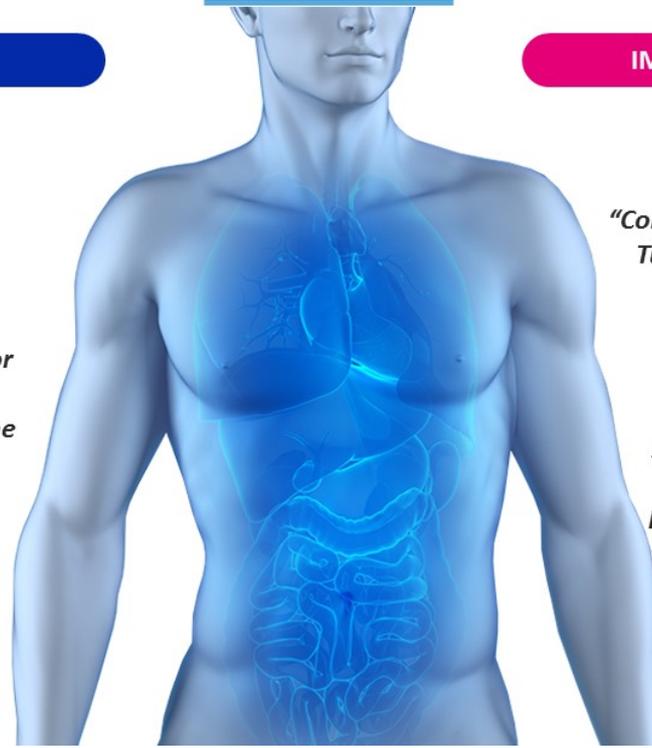
## IMMUNOMODULATION

*"Cold" Solid  
Tumors*

Immuno-  
Oncology

*Small or  
Large  
Intestine*

Inflammatory  
and  
Autoimmune



# Synthetic Biotic Portfolio

	Research	IND-Enabling Studies	Phase 1	Phase 2
Hyperammonemia – Urea Cycle Disorder	SYNB1020			
Phenylketonuria	SYNB1618			
Additional Rare Metabolic Diseases				
Hyperammonemia – Hepatic Encephalopathy (HE)	SYNB1020			
Inflammatory Bowel Disease	abbvie			
Immuno-Oncology Solid Tumors	SYNB1891			
Additional Oncology Applications				

**Rare Metabolic Diseases**  
 Broad Metabolic Disease  
 Immunomodulation

# SYNB1020 for Hyperammonemia Indications

Characterized by Systemic Ammonia Accumulation

## HEPATIC ENCEPHALOPATHY (HE)

**Neuropsychiatric complication in patients with end-stage liver disease (cirrhosis)**

- Liver dysfunction leads to ammonia accumulation
- Toxic to brain, leading to HE crisis & hospitalization

**Patients:**

- 165,000 diagnosed overt patients in US
- Up to 70% of patients with cirrhosis characterized as covert (subclinical)

**Treatment:**

- Lactulose: laxative with significant side effects
- Rifaximin: reduction in overt HE recurrence

**Target Profile to Address Unmet Need:**

- Reduce episodes of hospitalization
- Improve cognitive outcomes, Quality of Life

## UREA CYCLE DISORDERS (UCD)

**Genetic defects in Urea Cycle**

- Deficiency in one of the six enzymes
- Nitrogen accumulates as toxic ammonia leading to metabolic crisis

**Patients:**

- ~2,000 diagnosed in US; similar in EU

**Treatment:**

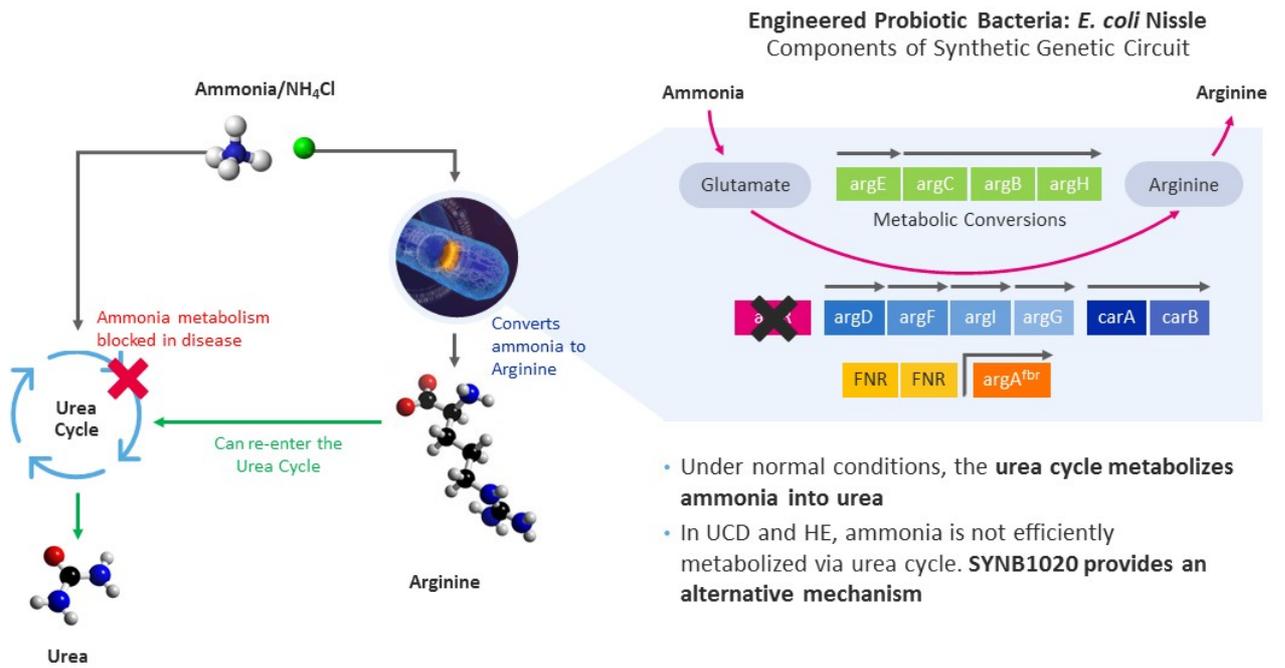
- Ammonia scavengers: Buphenyl® (sodium phenylbutyrate), Ravicti® (glycerol phenylbuterate)
- Low protein diet with amino acid supplements

**Target Profile to Address Unmet Need:**

- Maintain blood ammonia in normal range, avoid crisis
- Protein liberalization: 50-100% more per day
- Oral administration

# SYNB1020 Mechanism of Action:

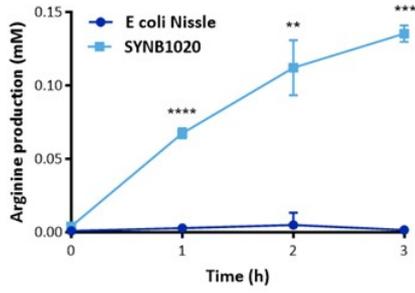
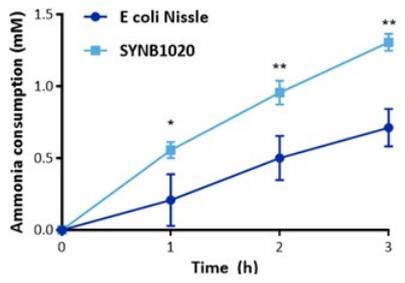
Conversion of Toxic Ammonia into Beneficial Arginine for the Treatment of UCD and HE



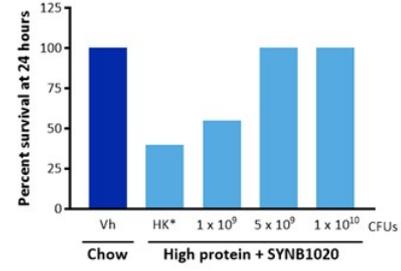
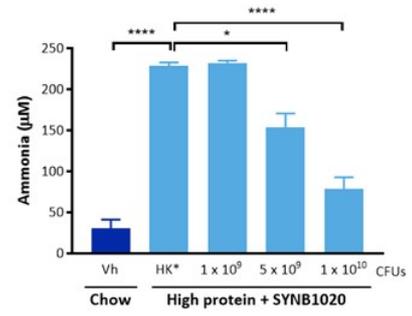
# SYNB1020 Preclinical Characterization

Potent and Efficacious Ammonia Reduction and Improved Survival

## IN VITRO



## UCD MOUSE MODEL



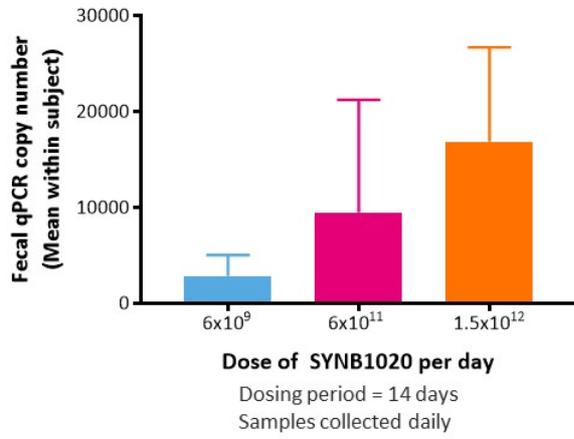
\* HK: heat killed

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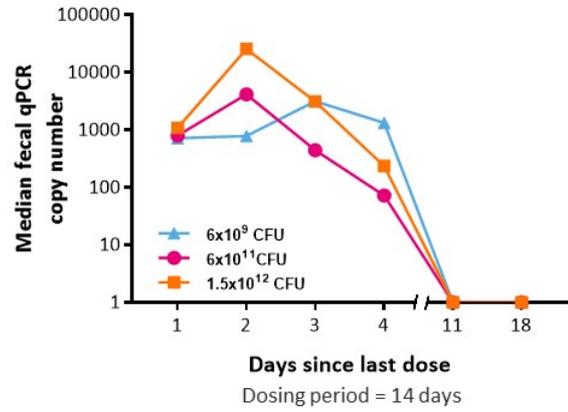
# SYNB1020 Clinical Data in Healthy Volunteers

Dose-dependent Increase in SYNB1020 in Feces, Clearance on Cessation of Dosing

## DOSE-DEPENDENT INCREASE IN FECES



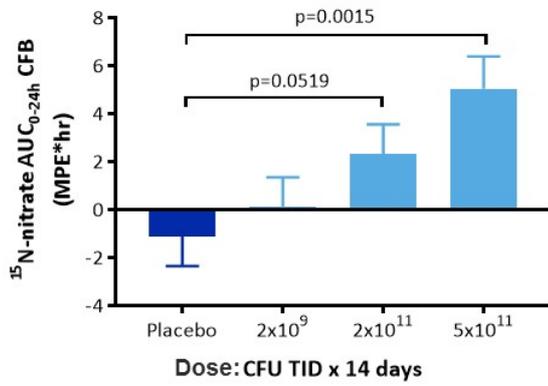
## CLEARANCE



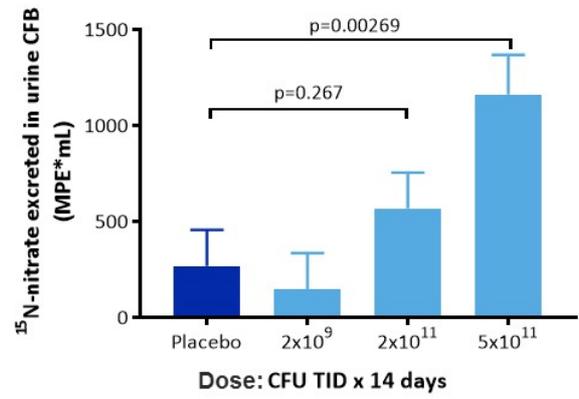
# Nitrate as a Biomarker for SYNBI020 Activity

Dose-dependent Production of Plasma and Urinary Nitrate

## PLASMA NITRATE



## URINARY NITRATE



# SYNB1020 Clinical Development

## Hepatic Encephalopathy Phase 1b/2a in Patients with Cirrhosis and Elevated Ammonia

PROGRAM	2018				2019			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Hepatic Encephalopathy	Phase 1b / 2a							
Urea Cycle Disorder (planned)	Phase 1b / 2a							

### Hepatic Encephalopathy Clinical Trial

- Randomized, double-blind placebo-controlled study ongoing at multiple sites in the US
- Primary outcome: establish safety/tolerability in patients with cirrhosis and elevated ammonia
- Secondary outcome: reduction of ammonia



# SYNB1618 for Phenylketonuria (PKU)

## Goal: Managing Plasma Phe Levels

### PKU is a rare inherited amino acid metabolism disorder

- Causes build up of amino acid phenylalanine (Phe) in the body
- Today, less than half of adults are at or below target Phe levels of 120-360  $\mu\text{mol} / \text{L}$
- If left untreated, symptoms include cognitive impairment, convulsions, behavioral problems, skin rash

### Patients:

- 16,500 diagnosed in US, similar in EU5

### Treatment:

- Phenylalanine is found in all proteins therefore low protein diet is followed (no meat, dairy, nuts, eggs)
- KUVAN® (sapropterin dihydrochloride): PAH cofactor. 20-40% of patients are responders
- Palynziq™ (pegvaliase-pqpz): injectable, pegylated, bacterial enzyme (phenylalanine ammonia-lyase or PAL) for treatment of adult patients

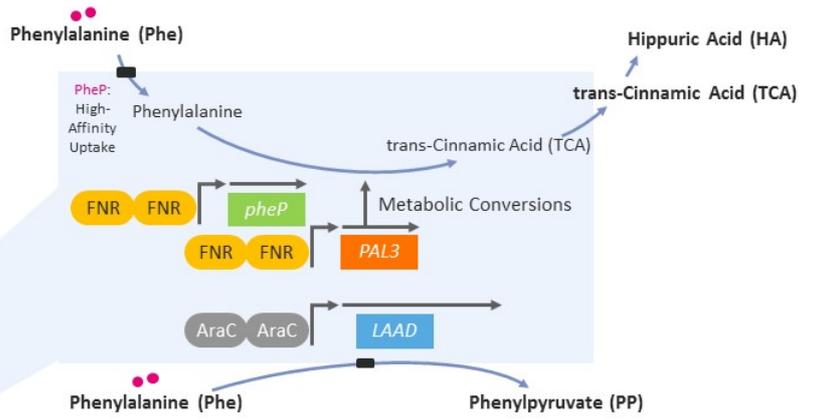
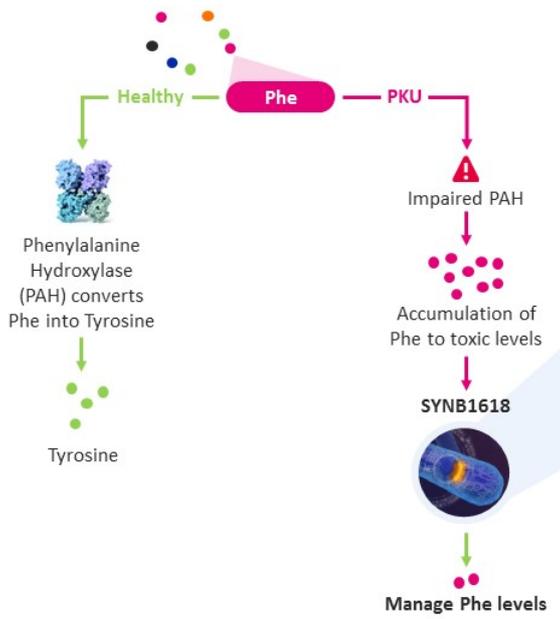
### Target Profile to Address Unmet Need:

- Manage Phe below target levels to prevent irreversible cognitive damage
- Increase natural protein intake: classic PKU patients' natural protein intake is typically less than 10g
- Oral dosing without systemic toxicity

# SYNB1618 Mechanism of Action

Amino acids from dietary proteins  
(absorption and recirculation)

Engineered Probiotic Bacteria: *E. coli* Nissle  
Components of Synthetic Genetic Circuit



When Phe is not efficiently metabolized (PKU)  
SYNB1618 provides an alternative mechanism

- PAL3: produces TCA which is converted to HA in the liver and is excreted in urine
- LAAD: produces phenylpyruvate (PP)

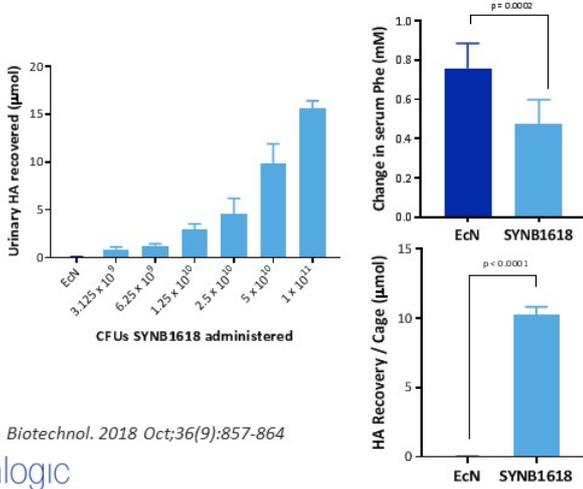
# SYNB1618 Preclinical Characterization

Biomarkers Demonstrate Activity of SYNB1618 in Mouse Model of PKU and Healthy NHPs

**nature  
biotechnology**

Development of synthetic live bacterial therapeutic for the human metabolic disease phenylketonuria  
*Vincent M Isabella et al, Synlogic, Inc.*

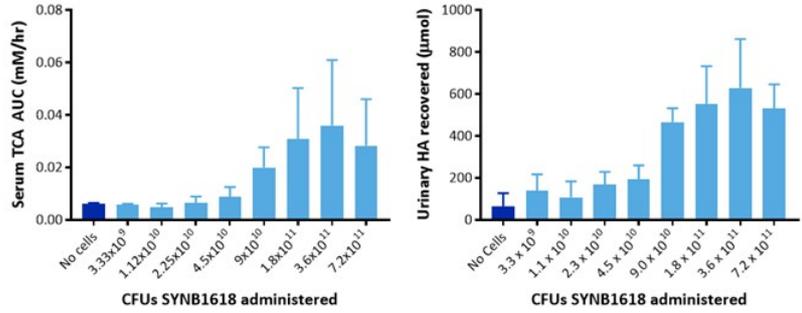
## IN VIVO EFFICACY IN (PKU) PAH<sup>enu2/enu2</sup> MOUSE



Nat. Biotechnol. 2018 Oct;36(9):857-864

synlogic

## DOSE RESPONSE IN HEALTHY NHP'S



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# SYNB1618 in the Clinic: Safety

Interim Analysis of Phase 1/2a SAD/MAD Study Demonstrates Safety and Clearance in Healthy Volunteers

56 healthy volunteers

Received at least one dose  
of SYNB1618 or placebo

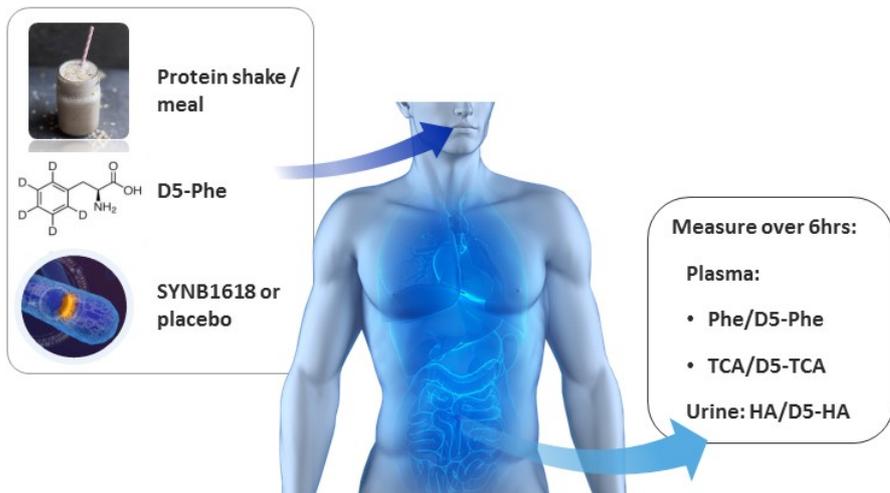
Adults  
Age range: 18-62 yrs old

- ✓ There were no treatment-related serious adverse events, no systemic toxicity or infections
- ✓ Treatment-emergent adverse events were either mild or moderate in severity, and reversible. Most adverse events were GI-related
- ✓ Single dose MTD was defined as  $2 \times 10^{11}$  CFU. Doses above this level were associated with dose-limiting GI adverse events
- ✓ All subjects cleared the bacteria. There was no evidence of colonization, and no subject required antibiotics

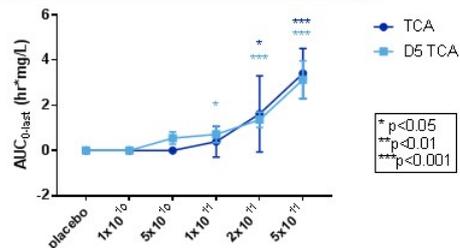
Based on pharmacodynamic data and tolerability profile, a dose of  $7 \times 10^{10}$  CFU was identified for the second part of the study in PKU patients

# SYNB1618 in the Clinic: Activity

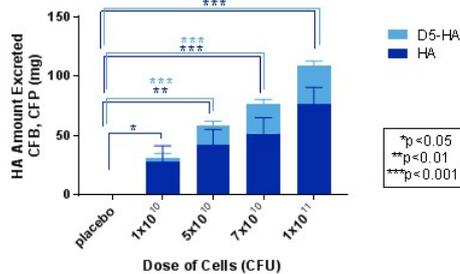
Statistically Significant Dose-dependent Activity of SYNB1618 in Healthy Volunteers



## TCA AUC SINGLE DOSE RESPONSE



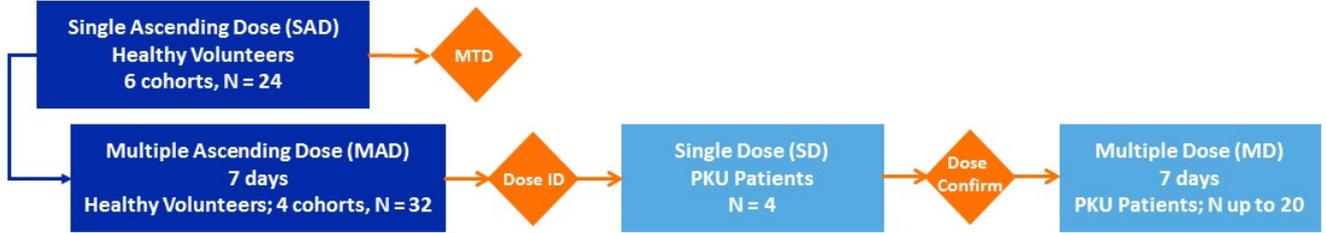
## MAD URINARY HA AND D5-HA



# SYNB1618 Clinical Development

Phase 1/2a in Healthy Volunteers with Patient Cohort

PROGRAM	2018				2019			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
SAD / MAD Healthy Volunteers		Phase 1 / 2a						
SD / MD PKU Patients				Phase 1 / 2a				

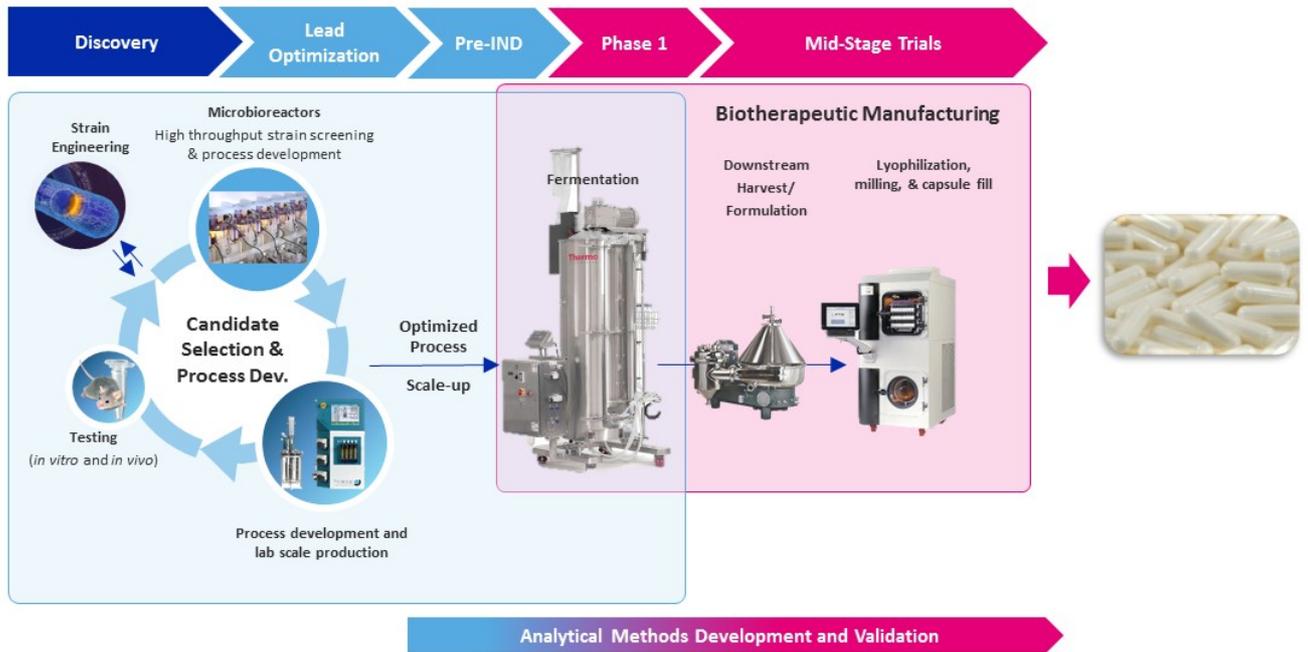


## PKU Clinical Trial Design

- Randomized, double-blind placebo-controlled study ongoing at multiple sites in the US
- Primary outcome: establish safety/tolerability following single and multiple doses in HV and PKU patients
- Secondary outcome: SYNB1618 kinetics in feces
- Exploratory: change from baseline in plasma and urinary biomarkers

# Synlogic Internal GMP Manufacturing Capabilities

In-house Process Development and Clinical Manufacturing for Early & Mid-Stage Trials



# Metabolic Programs: Progress and 2019 Milestones

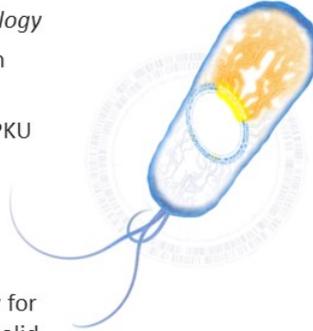
## 2018 Accomplishments

### SYNB1618

- ✓ Preclinical data published in *Nature Biotechnology*
- ✓ Safe, well-tolerated, proof of mechanism in healthy volunteers
- ✓ FDA Fast Track Designation for treatment of PKU

### SYNB1618 and SYNB1020

- ✓ Initiated studies in patients
- ✓ Established in-house manufacturing capability for mid-stage clinical studies. Developed path to solid oral formulation



## 2019 Milestones

### SYNB1618

- Complete ongoing study in PKU patients
- Data expected mid-2019 (safety, tolerability and biomarkers)

### SYNB1020

- Complete ongoing study in cirrhosis patients
- Data expected mid-2019 (safety, tolerability and ammonia-lowering)
- With ammonia-lowering data define development plan
- Advance **preclinical pipeline**

# Immuno-Oncology

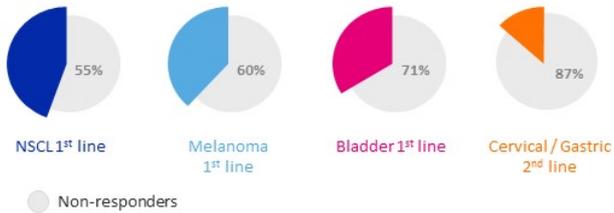
# Synlogic Vision for Immuno-Oncology

Expand the Benefits of Immunotherapy Broadly Across Tumor Types

## CHECKPOINT INHIBITORS HAVE TREATMENT FAILURES

For indications where immune checkpoint inhibitors are indicated, 55-87% of patients fail to respond

### Failure Rates for Select FDA Approved CPI Monotherapy



Other tumors, where CPIs are not indicated, show little-to-no response to checkpoint inhibitors

## Bacteria Recognized as Earliest Immunotherapy

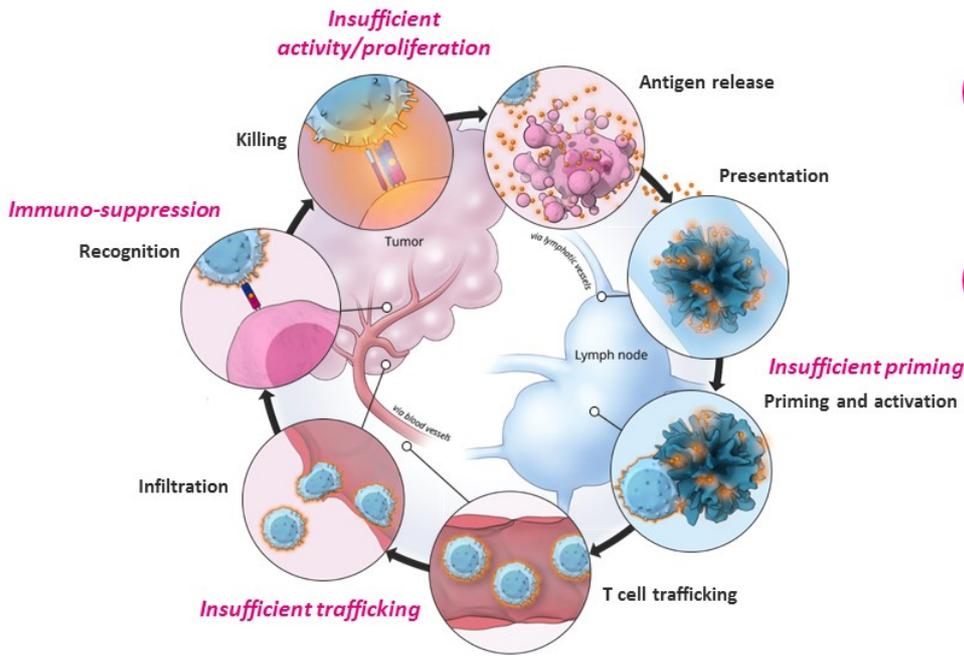
“Nature often gives us hints to her profoundest secrets, and it is possible that she has given us a hint in which, if we will but follow, may lead us on to the solution of this difficult problem.”



DR. WILLIAM B. COLEY  
IMMUNO-ONCOLOGY PIONEER

**Enable broad response and remission through engagement of multiple immunomodulatory pathways to enhance tumor inflammation and promote robust T cell responses**

# A Tumor Can Evade Multiple Critical Aspects of the Cancer-Immunity Cycle



**MONOTHERAPIES OFTEN FAIL TO OVERCOME TUMOR EVASION MECHANISMS**

Recognized Need to Combine Mechanisms to Broaden the Benefit of Immunotherapy

**ENGINEER LIVING SOLUTIONS: SYNTHETIC BIOTIC MEDICINES**

Rationally Designed for Combinatorial Effect

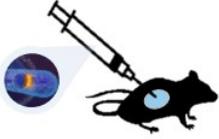
Locally Inflamm the tumor microenvironment (TME)

Systemically Drive Tumor-Antigen Specific Immunity

*In Situ* Vaccination: Neo-antigen Priming and Sustained Immune Response

# Intra-tumoral Injection of Synthetic Biotic Chassis: Tumor Colonization Without Leakage; Local Innate Immunity

## CHASSIS DISTRIBUTION

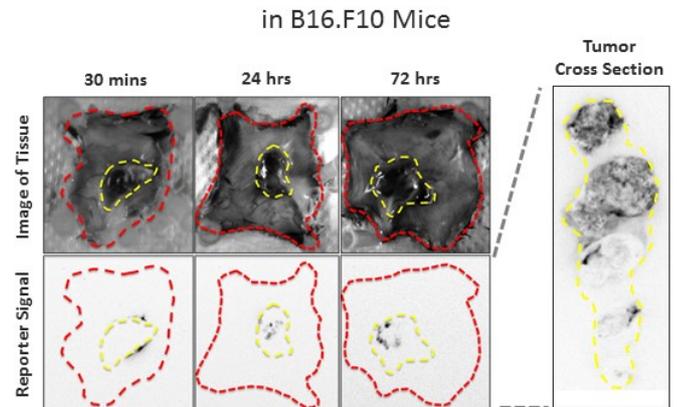


Robust proliferation in tumor.  
No significant leakage

Survival/proliferation in tumors 10-15 days  
post-single dose. Potential for limited injections

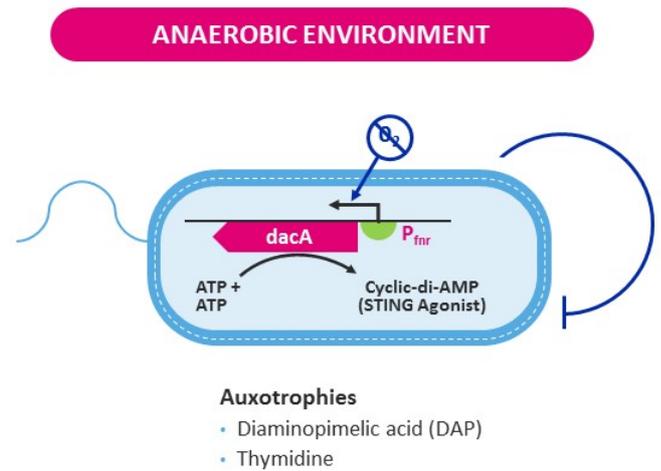
Elicits innate responses (IL-6 and TNF $\alpha$ )  
in the tumor. Not in circulation

## BEHAVIOR WITHIN TUMOR



# Dual Innate Immune Activator: Synthetic Biotic Medicine Producing STING Agonist (SYNB1891)

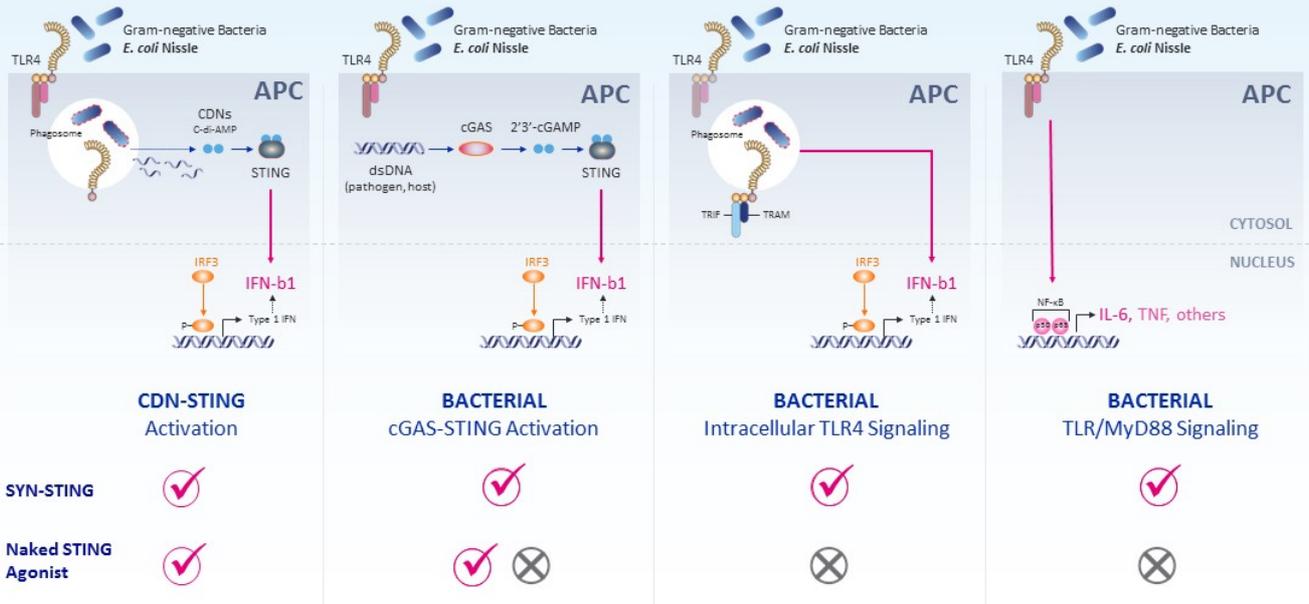
- Synthetic biology applied to confer activities for efficacy and control for safety
- Designed as a dual innate immune activator: combined benefit of bacterial chassis and STING agonist
- The *dacA* gene is integrated into genome under the control of inducible promoter ( $P_{fmr}$ ) to produce c-di-AMP (CDA)
- Dual biosafety feature via auxotrophies – no proliferation in tumor, systemic circulation or environment
- Learnings inform future combinations



# Innate Immune Activation through Multiple Pathways

Uniquely Signals Through CDN-STING and Bacterial Chassis in Target Cells to Drive Efficacy

TUMOR

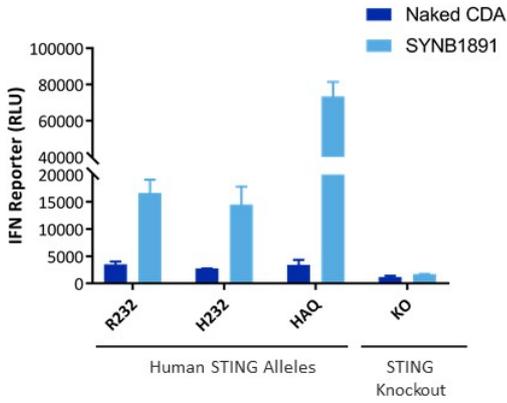


Promotes Trafficking, Immune Activation/Proliferation, Priming

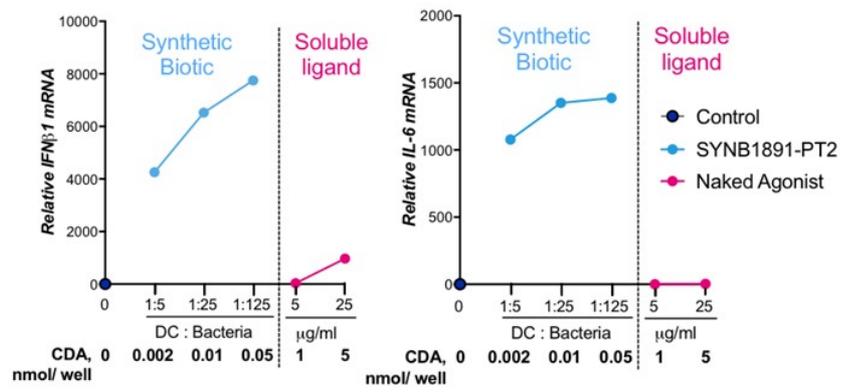
# SYNB1891 *In Vitro* Characterization

Interferon Production Across Multiple Human STING Alleles Greater than Naked STING Agonist  
Additional Proinflammatory Pathways Engaged

## REPORTER HUMAN MONOCYTIC LINE

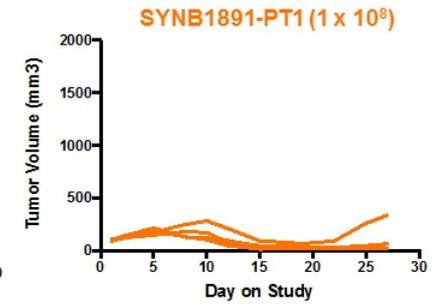
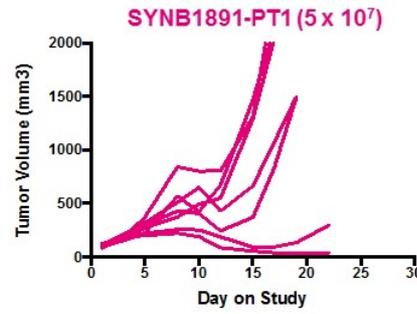
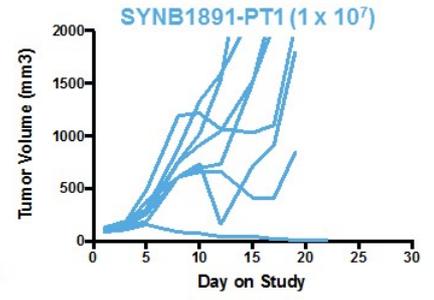
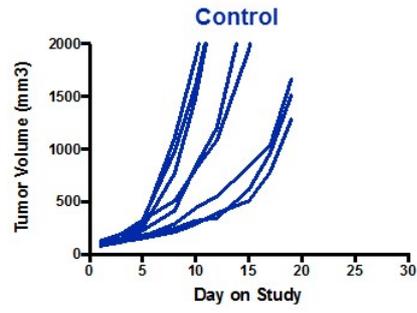
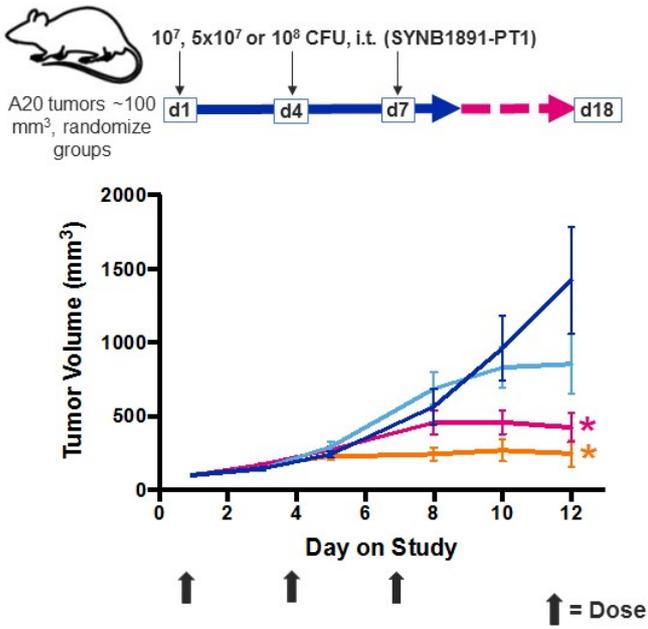


## HUMAN PRIMARY DENDRITIC CELLS



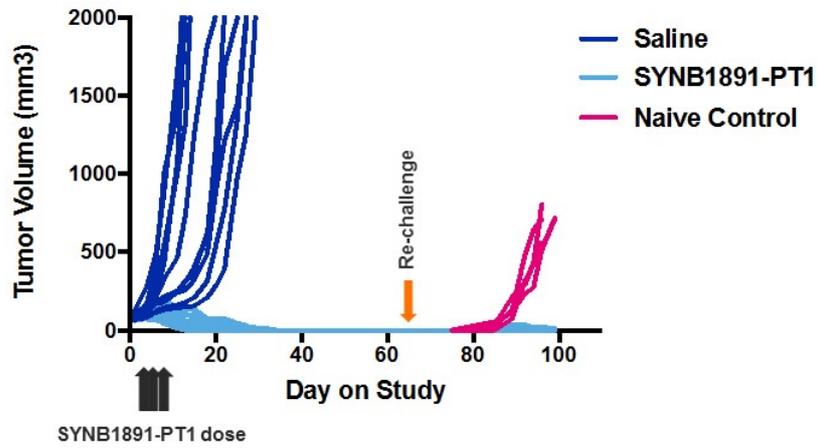
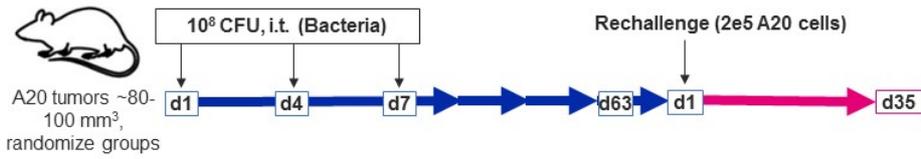
# SYNB1891 *In Vivo* Characterization

Dose-dependent Anti-tumor Activity of SYNB1891 Prototype Strain (PT1) as a Single Agent



# SYNB1891 *In Vivo* Characterization

SYNB1891 Prototype Strain (PT1) Leads to Systemic Anti-tumor Immunity



# Dual Innate Immune Activator SYN1891

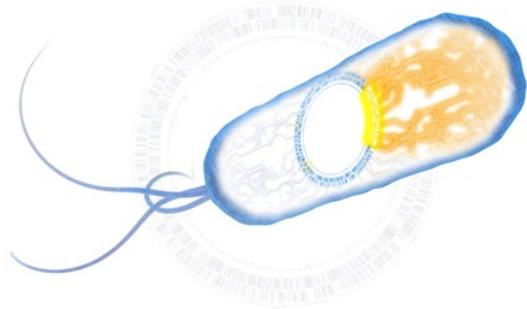
A STING Agonist-producing Synthetic Biotic Designed to Locally Inflamm the TME and Systemically Drive Tumor Antigen-Specific Immunity

## PROGRESS TOWARDS THE CLINIC

- Tumor Colonization without Leakage
- Enhanced Activity vs. Naked STING Agonist
- Intracellular Activation of STING and Bacterial-Induced Immune Pathways Within APCs
- Dose-dependent Anti-tumor Activity
- Immunological Memory
- IND Submission 2H19

## PROMISE OVER OTHER APPROACHES

- STING Agonism in Target Cells that Drive Efficacy
- Sparing Cells Where STING Agonism is Detrimental
- Activation of Multiple Innate Immune Pathways
- Low Systemic Risk



# Additional Synthetic Biotic Effectors

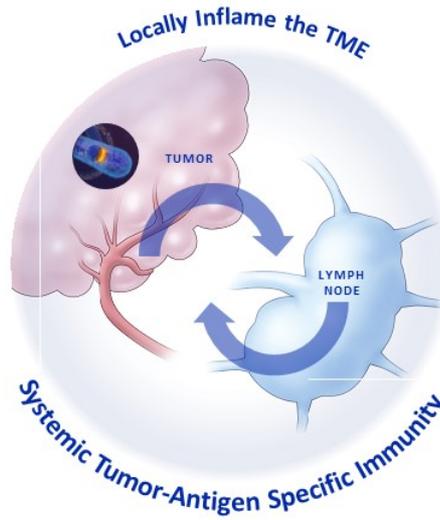
VISION: Rational Design to Locally Inflamm the TME  
AND Systemically Drive Tumor-Antigen Specific Immunity

## RELIEVE IMMUNOSUPPRESSION

- Kyn Consumption
- Ade Consumption
- $\alpha$ PD-1 scFv

## PROMOTE TRAFFICKING

- Chassis effect
- CXCL10
- Hyaluronidase



## PROMOTE AND SUSTAIN IMMUNE ACTIVATION

- IL-15; IL-12
- Arg Production
- 4-1BBL
- OX40L

## PRIME FOR TUMOR-ANTIGEN-SPECIFIC VACCINATION

- Chassis effect
- 5FC $\rightarrow$ 5FU
- STING
- $\alpha$ CD40 scFv/CD40L
- TNF $\alpha$
- IFN $\gamma$
- $\alpha$ CD47 ScFv / Sirp $\alpha$
- GM-CSF

# Broad Ambitions in Immuno-Oncology

Vision: Expand and Exceed the Effect of Cancer Immunotherapies

**SYNB1891**

**DISCOVERY PORTFOLIO**

**INTRATUMORAL**



**COMBINATIONS**

**HARNESS THE MICROBIOME**

**ORAL**



# Summary

# Synthetic Biotic™ Medicines Designing for LIFE

*Synlogic is designing microbes that are engineered to compensate for missing functions in a variety of diseases*

*The Company has demonstrated that Synthetic Biotic medicines function as designed in humans*

*Synlogic is building a path to a broad portfolio of products that could change patients' LIVES*

# Progress and 2019 Milestones

## 2018 Accomplishments

### SYNB1618 in PKU

- ✓ Preclinical data published in *Nature Biotechnology*.
- ✓ Safe, well-tolerated, proof of mechanism in HVs
  - ✓ FDA Fast Track Designation

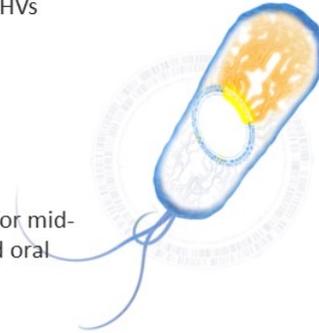
### SYNB1618 and SYNB1020

- ✓ Initiated studies in patients

- ✓ Established in-house manufacturing capability for mid-stage clinical studies. Developed path to solid oral formulation

### IO Lead Candidate, SYNB1891, selected

- ✓ Initiated IND enabling studies
- ✓ Advanced AbbVie collaboration



## 2019 Milestones

### SYNB1618 in PKU

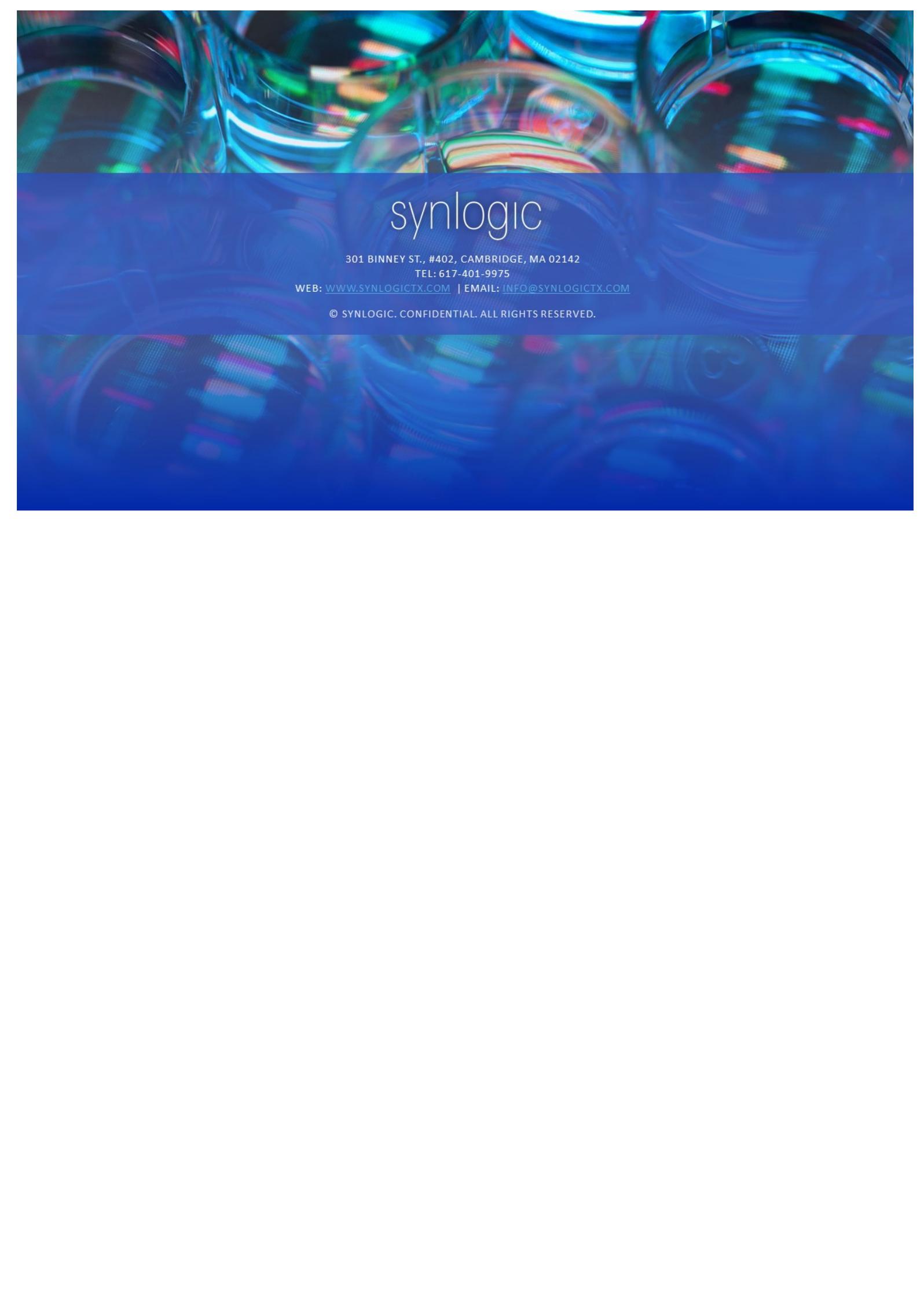
- Complete ongoing study in patients
- Data expected mid-2019 (safety, tolerability and biomarkers)

### SYNB1020 in Hyperammonemia

- Complete ongoing study in patients with cirrhosis
- Data expected mid-2019 (safety, tolerability and ammonia-lowering)
- With ammonia-lowering data define development plan

### SYNB1891 in Immuno-Oncology

- IND submission 2H2019
- Advance collaborations and preclinical pipeline



# synlogic

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